2024年
中国生物物理学会
微流控系统学分会
委员论文集

2024 Proceedings of the Microfluidic Systems Subgroup of
the Biophysical Society of China

中国生物物理学会微流控系统学分会

专家简介：

荣誉会长：林炳承 研究员



中国科学院大连化学物理研究所，研究员，博导。英国皇家化学会会士（2010-），德国洪堡基金 (AvH) 学者（1986-88, 1996, 2018），亚太微分离分析系列学术会议（APCE）学术指导委员会主席（2016-）， 第 1-9 届中国微流控芯片高端论坛主席（2013-）。曾为 Electrophoresis 杂志副主编（2004-2014），Lab on a Chip 杂志编委（2007-2010），国际微分离分析战略委员会委员（2014-）。1990 年代后期至今致力于微流控芯片及其应用研究。已发表学术论文约 350 篇；撰写，并由科学出版社出版《器官芯片》等微流控中文著作 4 部，主编，出版《Microfluidics: Technologies and Application》（Springer，2011）等微流控英文著作、年刊和专辑 6 部 (期)；持有微流控芯片等领域专利多项；1992-2007 年连续主持国家自然科学基金 11 项；直接培养博士、硕士研究生，博士后研究人员约 70 名，全国优秀博士学位论文指导教师；国务院特殊津贴专家；先后获国家科技进步二等奖等奖项。

微流控芯片二十五年

林炳承

在这样一本特殊的论文汇集上，我作些许回忆，纪念从事微流控芯片研究二十五年。

1978年，我参加了改革开放后的第一次全国研究生统考，10月，被中国科学院录取，成为大连化学物理研究所的研究生，并先后师从张乐沣教授和卢佩章教授取得硕士、博士学位。毕业后留所，随即入选为德国洪堡基金的学者，到德国，随后又在比利时从事色谱研究。1989年5月回国，带领课题组开启我国的毛细管电泳研究，历时十年，赶上了它作为主流技术主导人类基因组工程和大规模测序的历史进程。90年代后期，我将课题组引入全新的微流控芯片领域，至今整整25年，从芯片电泳到芯片实验室，从分子到细胞-器官，从简单分离到大规模筛选，现已完成了以微流控芯片为基础平台、以细胞为核心对象、覆盖从单细胞分析到全器官仿生的整体布局。

微流控芯片又称芯片实验室，是一种以在微米尺度空间对流体进行操控为主要特征的科学技术。现阶段，主流形式的微流控芯片指的是把化学和生物等领域中所涉及的样品制备、反应、分离、细胞培养、分选、裂解等基本操作单元集成或基本集成到一块几平方厘米甚至更小的芯片上，由微通道形成网络，以可控流体贯穿整个系统，用以实现常规化学、生物医学、材料学、光学等不同实验室的各种功能的一种技术。微流控芯片实验室的基本特征和最大优势是多种单元技术在流体可控的微小平台上灵活组合、规模集成。

微流控芯片已被认为是当代极为重要的新兴科学技术平台和国家层面产业转型的战略领域。2017 年，科技部把微流控芯片定位为一种“颠覆性技术”，而微流控芯片中的重要分支-器官芯片则被世界经济论坛（达沃斯论坛）评为 2016 年世界“十大新兴技术”之一，与无人驾驶汽车、石墨烯二维材料、区块链等并列。

20 世纪 90 年代后期起，我们在中国科学院大连化学物理研究所开始了已长达 25 年的微流控芯片研究历程。

1999 年，差不多在国际范围微流控芯片研究还被看成是科学研究前沿刚刚兴起的同一时间段，我们在十年毛细管电泳研究的基础上建立了微流控芯片研究团队，第一阶段的工作是从芯片电泳入手，集中于芯片设计研制，检测装置搭建和单元操作的芯片化。在此后的几年时间内，我们搭建了第一台微流控芯片激光诱导荧光仪，用注塑法制得第一批 PMMA 微流控芯片，并开始了第一轮应用研究，其中包括完成了对 226 例高血压病人、159 例肿瘤病人和 200 例乙肝病人的相关基因检测和筛查。特别是，在 2003 年 SARS 肆虐期间，课题组实现了基于微流控芯片的 18 例疑似 SARS 患者咽拭子样品冠状病毒的快速检测。2005 年，课题组第一批成果“全集成微流控芯片体液 DNA 分析系统”和“运动员体能指标微流控芯片检测系统”的研制先后通过了中国科学院和科技部组织的现场验收，这样一种当今已被人们熟知的“即时诊断(POCT)”技术的雏型，得到了与会专家的高度评价，认为成果符合未来疾病诊断家庭化、个体化的趋势，具有广阔的市场前景。

在这一阶段，课题组长年有20-30名学生在实验室工作，以博士生为主。他们来自化学、医学、药学、生物学、物理学和工程学等不同专业，其中有医学背景的占到了四分之一，满足了微流控芯片作为一种典型的多学科交叉科学技术的特殊需求。在这样一种环境中，同学们得以在学生时代就学会和不同领域的同学、同事密切接触，相互理解、相互渗透。2004年，我们搭建了大连化物所第一个细胞实验室，开始规模化微流控细胞芯片研究；经过3-4年的艰苦努力，课题组完成一系列的细胞培养，多种细胞共培养和多种细胞三维共培养的工作，2009-2010年，课题组先后完成兔软骨组织培养，以及带有肝微粒体的药物代谢等器官芯片的前期工作；其中，关于细胞水平高通量和高内涵药物筛选的研究，细胞水平药物代谢研究，以及模式生物水平高通量药物筛选研究的工作，在一年多时间内连续三次被本领域最重要刊物*Lab on Chip*作为封面/封底文章刊登，引起国际微流控芯片和药物筛选领域的广泛关注。模式生物线虫的工作发表后，下载量和引用率居高不下，并很快被英国皇家学会的*Chemical Biology*作为亮点报道。2010年10月，在北京香山会议上，我向与会代表正式宣布启动微流控仿生器官芯片的研究。2009-2010年，课题组在国际上率先提出用蜡作为疏水性材料和硝酸纤维素膜取代普通滤纸，用喷蜡打印的方法，大规模制备一次性使用的纸质芯片。2014年，大连微流控芯片研究团队大化所刘显明博士主持的数字液滴项目和南方科技大学程鑫教授的半导体有源矩阵技术结合，合作开始微流控数字液滴中央处理器的设计与实施研究，探讨两种截然不同的芯片深度对接的可能性，5年后，项目获国家自然科学基金重大仪器专项 （3192780013）支持，研究工作被推向全新的阶段，一旦成功，精准操控在平面上移动的成千上万计的用作反应器的数字液滴，有望被用于大规模测序和蛋白质研究中的文库制备。我们和国际微流控学术界长期保持频繁接触，我曾在德国，美国，加拿大，意大利和香港等处的大学担任客座教授或访问教授，组织或参与多种重要的国际会议，在思想上紧紧的和学科前沿同步。我们的论文多年入选为Web of Science数据库高引用论文（highly cited paper），并被*Analytical Chemistry*杂志重点介绍。团队的影响和重要论文的高引用率被长期保持，以至于到2016年，我仍被推举为亚太微分离分析系列学术会议（APCE）学术指导委员会主席，2018年，2019年还入选了Elsevier中国高被引用学者（Chinese Most Cited Researcher）的名录。

从2006年到2019年，我们先后撰写，并由科学出版社出版了《微流控芯片实验室》，《图解微流控芯片实验室》，《微纳流控芯片实验室》和《器官芯片》四部微流控领域专著。成书过程中，团队从思想、内容到逻辑、文字，对全书的方方面面作了反复的讨论、充实、推敲和斟酌，力求引证梳理兼有，分析综合并重，迹浅意深，言近旨远，特别是，以作者实验室的工作贯穿始终，字里行间渗透着来自第一线劳作的艰辛。与此同时，在我入选英国皇家化学会会士、担任国际*Electrophoresis*(电泳)杂志副主编和*Lab on a Chip*(芯片实验室)杂志编委期间，还先后主编了Lab on a Chip：Focus on China（RSC出版社），Miniaturization in Asia Pacific， Micro-Nanofluidics in Asia Pacific，（Wiley出版社）等5本专辑和1本英文专著Microfluidics: Technologies and Application（Springer出版社）。这4部中文著作，1部英文著作和5本英文专辑，连同团队关于微流控芯片的近300篇学术论文、70余份专利等，作为微流控芯片领域极为宝贵的财富积累，对我国及国际微流控芯片事业的发展起到了非常重要的推动作用。基于以上这些研究成果，我们团队先后获得2002年辽宁省自然科学奖一等奖，2007年辽宁省科技进步奖一等奖，以及2010年国家科学技术进步奖二等奖。2009年，中国科学院大连化学物理研究所建所60周年大庆，评选全所自1999年到2009年十年间的十大科研成果，课题组的“生物医学中的微流控芯片”作为生物技术部的唯一项目入选。

2011年6月，受所领导委托，我曾为所里的青年研究人员作了一个题为“思想先行”的报告。在报告中我提到，科学家要有扎实基础，敏锐直觉和宽阔视野，科学家应该具备的基本能力是“看得准，抓得住，做得好” 。也就是说，在科学发展的关键时刻，一定要能精准把握科学研究的前沿方向，看准是引导的基础；看准之后，要摆脱种种干扰，努力抓住，允许小的偏离，确保大势不变；真正抓住之后，更要“大胆假设，小心求证”，宁拙毋巧，宁朴勿华，倾其所有，一丝不苟地把它做好。在报告最后，我提到了这么一段话：“学术界总是要有点思想的，好的学术思想一般是独立的，独立的学术思想是一个科学家有别于其他科学家的本质属性，形成独立的学术思想应当被看成是科学家一生最重要的追求” 。在这种行为准则的影响下，我们不断强化前瞻性学术思想，精准操控自身的学科方向，带领团队，跨过一个个艰难险阻，超越自我。“思想先行”的典型例子是，从1992年到2007年的15年中，我们课题组以92%的极高成功率申请到包括3项重点基金在内的11项国家自然科学基金，这些数据，无论是密度还是强度，至今依然在大连化物所名列前茅。

此后，按所里政策，大连化物所微流控芯片团队的工作交由团队培养的博士秦建华管理。2011年五月，我受聘于大连理工大学，帮助原大连化物所微流控芯片团队博士、大连理工大学罗勇建立大工微流控芯片药学研究组，恢复器官芯片研究，次年，大工细胞室建成；2012年，原大连化物所微流控芯片团队博士后，大连医科大学刘婷姣研究组继续她们的微流控肿瘤芯片研究；年末，在刘中民教授支持下，微流控芯片材料研究小组在大连化物所低碳催化与工程研究部成立，开始基于微流控芯片的高性价比材料研制工作；2013年，科技部新药重大专项课题″基于微流控芯片的新药研究开发关键技术(2013ZX09507005) ″启动，大连团队的器官芯片研究纳入国家重大计划；2015年，原大连化物所微流控芯片团队博士陆瑶在耶鲁大学从事5年研究工作后回所，中国科学院大连化学物理研究所单细胞分析研究组成立，承担基于微流控芯片的单细胞分析和器官芯片微环境精准测量工作，我重新回组；2016年，化物所陆瑶组、大工罗勇组和大医刘婷姣组等三个由中国科学院大连化学物理研究所微流控芯片研究团队衍生的研

究组正式联合，成立理-工-医学科交叉，国立研究所和高等学校融为一体的大连微流控芯片研究团队，把大连的微流控芯片研究推向一个全新的阶段。大连微流控芯片研究团队一批成果也先后在*PNAS*，*Biomaterials*和*Advanced Science*等重要刊物发表。

微流控芯片的重要性在于：它是当代极为重要的新兴科学技术平台和国家层面产业转型的潜在战略领域，是一种注定要被深度产业化的科学技术，微流控技术需要向产业转化，微流控事业需要薪火相传。我曾在2001年被评为全国优秀博士论文指导教师，也曾在美国、加拿大和欧洲一些国家的很多所大学或研究机构担任客座教授，现已直接培养了70余名学生，以博士研究生和博士后为主。现在，这批学生中已有三十多位教授、副教授和公司的老总或高管，他们仍然从事微流控芯片领域的工作，正领导着各自的微流控芯片研究团队或微流控芯片公司，活跃在全国各地，有些团队的研究工作已卓有成效，有些公司的队伍和产品已初具规模。我自己也依然在一些单位协助培养研究生和博士后，推进微流控技术的深度发展。这些大连化物所的微流控芯片校友在中国微流控芯片事业的发展中占有举足轻重的地位，他们是中国第一代微流控芯片研究和开发队伍的中坚力量，他们的工作和国内其他团队的工作一起，构筑了中国微流控芯片研究和开发的核心基础。我们已经建立了一个微流控芯片的年会制度，年会定位为小型、高端，并以需求导向、产业引领、学科交叉和深入讨论为主要特色，现已持续11届，正逐渐发展成全国性的微流控芯片重要论坛。2023年，在叶嘉明博士等的努力下，我们在中国生物物理学会名下成立了微流控系统学分会，全面推动微流控芯片的学术活动。

滴水成渠，星火燎原。25年的不舍，终于成就了一件对国民经济的产业转型和可持续发展具有战略意义的利国利民大事，欣慰之心，油然而生，纵然有难以忘却的风风雨雨，终究无悔无怨。

林炳承，1944年11月生，祖籍宁波，长于上海，中国科学院大连化学物理研究所研究员。长期活跃在学术研究一线，从上世纪90年代初至今三十五年间，先后带领课题组开启我国的毛细管电泳研究和微流控芯片研究，成绩卓著，在国内外学术界产生重大影响。

专家简介：

会长：林金明 教授



博士，清华大学化学系教授。2001 年入选中国科学院“百人计划”并获得国家杰出青年科学基金的资助，同年受聘中国科学院生态环境研究中心研究员，博士生导师。2004 年受聘清华大学化学系教授，博士生导师，2008 年受聘教育部长江学者特聘教授。2023 年入选中国化学会会士、2016 年入选英国皇家化学会会士。目前主要从事：1）微流控细胞分析；2）食源性致病菌的快速检测技术研究；3）化学发光免疫分析。发表研究论文 600 多篇，被引 2 万余次，申请和授权发明专利 50 多项并有 10 多项专利获得实施，先后获得国内外学术奖励 20 多项。目兼任中国生物物理学会微流控系统学分会会长，中国微米纳米技术学会理事及微纳流控技术分会副理事长，中国化学会理事及分析化学学科副主任，中国分析测试协会常务理事，Trends in Analytical Chemistry 责任编辑，J. Pharm. Anal.副主编，Chinese Chemical Letters 副主编。

Food Control **(IF 5.6)** Published: January 2024

Development of nucleic acid extraction and real-time recombinase polymerase amplification (RPA) assay integrated microfluidic biosensor for multiplex detection of foodborne bacteria.

Yuting Shang , Gaowa Xing , Haifeng Lin , Yucheng Sun , Shulang Chen , Jin-Ming Lin

Rapid and accurate screening of foodborne bacteria is of great significance for food safety, particularly in the areas where health resources for grass-root service are inadequate. In this study, we fabricated a fully integrated micro-platform (named FID-MP) performing nucleic acid extraction, recombinase polymerase amplification (RPA), and signal detection for point-of-care testing (POCT) of multiplex pathogens. After the on-chip nucleic acid extraction, which adopted a filtration membrane, to obtain the DNA template of bacteria, the purified DNA was driven to the detection chip to conduct nucleic acid amplification. The fluorescent images can be read by using a smartphone under the portable signal detector. Using FID-MP, eight foodborne bacteria were detected with 100% specificity and similar sensitivities as compared to standard real-time RPA reactions. The entire process was accomplished within 60 min. Overall, FID-MP eliminates the need for bulk equipment and skilled personnel, holding promise to become a versatile sample-to-answer platform for foodborne bacteria monitoring.

Analytical Chemistry **(IF 6.7)** Published:16 January 2024

One-Shot Dual-Detection-Based Single-Molecule Super-Resolution Imaging Method for Real-Time Observation of Spatiotemporal Catalytic Activity Variations on the Plasmonic Gold Nanoparticle Surface.

Yingying Cao, Dongkyun Lee, Seungah Lee, Jin-Ming Lin, Seong Ho Kang

Understanding the relationship between the surface properties of a single plasmonic nanoparticle and its catalytic performance is critical for developing highly efficient nanocatalysts. In this study, a one-shot dual-detection-based single-molecule super-resolution imaging method in the evanescent field was developed to observe real-time spatiotemporal catalytic activity on a single plasmonic gold nanoparticle (AuNP) surface. The scattering intensity of AuNPs and the fluorescence of resorufin molecules produced on the AuNP surface were obtained simultaneously to investigate the

relationship between nanoparticles and catalytic reactions at a single-molecule level. Chemisorbed adsorbates (i.e., catalytic product and resorufin) changed the electron density of individual AuNPs throughout the catalytic cycle, resulting in the fluctuation of the scattering intensity of individual AuNPs, which was attributed to the electron transfer between reactant resazurin molecules and AuNPs. The increase in the electron density of individual AuNPs affected the catalytic reaction rate. Furthermore, sequential mapping of individual catalytic events at the subdiffraction limit resolution was completed for real-time surface dynamics and spatiotemporal activity variations on the single AuNP surface. The developed method can aid in understanding surface-property-dependent catalytic kinetics and facilitate the development of nanoparticle-based heterogeneous catalysts at subdiffraction limit resolution.

Small **(IF 12.96)** Published: 29 January 2024

Gravity-Oriented Microfluidic Device for Biocompatible End-to-End Fabrication of Cell-Laden Microgels.

Chen Shulang, Wu Zengnan, Zhang Qiang, Li Yuxuan, Yao Hongren, Chen Shiyu, Xie Tianze, Lin Jin-Ming

Droplet microfluidics are extensively utilized to generate monodisperse cell-laden microgels in biomedical applications. However, maintaining cell viability is still challenging due to overexposure to harsh conditions in subsequent procedures that recover the microgels from the oil phase. Here, a gravity-oriented microfluidic device for end-to-end fabrication of cell-laden microgels is reported, which integrates dispersion, gelation, and extraction into a continuous workflow. This innovative on-chip extraction, driven by native buoyancy and kinetically facilitated by pseudosurfactant, exhibits 100% retrieval efficiency for microgels with a wide range of sizes and stiffnesses. The viability of encapsulated cells is perfectly maintained at ≈98% with minimal variations within and between batches. The end-to-end fabrication remarkably enhances the biocompatibility and practicality of microfluidics-based cell encapsulation and is promising to be compatible with various applications ranging from single-cell analysis to clinical therapy.

Chemical Engineering Journal **(IF 15.1)** Published: 1 February 2024

On-microparticle construction of endothelialized liver microtissues for drug testing.

Zengnan Wu, Yajing Zheng, Jin-Ming Lin, Yuxuan Li, Yongning Lin, Xiaorui Wang, Ling Lin

With the advantage of uniformity and customizability, hydrogel microparticles are widely used to establish in vitro organoid modeling for drug testing. However, the practical values of current strategies are limited by the lack of near-physiological structures and functions. In this work, microparticle-based liver models with biomimetic endothelial barriers are engineered using a simple, biocompatible, and high-throughput method for the application of drug testing. The hepatocyte-laden hydrogel microparticles with a rough surface are prepared using a microfluidic spraying technique, and their surfaces allow for customized protein modifications. Under the action of topological texture and matrigel modifications, the microparticle surface can induce endothelial cell adhesion, extension, and junction, thus generating a continuous, tight monolayer endothelial barrier. Semi-permeability of endothelial barrier and enhanced liver function was demonstrated in the constructed microparticle tissue models. Finally, these models were utilized to reproduce a sensitive inhibitory action of the endothelial barrier on the biotransformation of prodrugs (i.e., tegafur). Overall, microparticle-based endothelialized liver models achieved not only heterotypic cell co-culture but also tissue morphogenesis, which is anticipated to accelerate comprehensive evaluations of the drug biotransformation and improve the translatability of drug testing results from in vitro to in vivo.

Journal of Pharmaceutical Analysis **(IF 6.1)** Published: 20 March 2024

Establishment of microneurovascular units in alginate hydrogel microspheres to reveal the anti-hypoxic effect of salidroside.

Chen Shiyu, Li Yuxuan, Zhang Yingrui, Yao Hongren, Xu Tong, Zhang Yi, Lin Jin-Ming, Meng Xian-Li.

Microneurovascular units (mNVUs), comprising neurons, microglia, and blood-brain barrier (BBB) endothelial cells, are pivotal to the central nervous system and are associated with cerebral hypoxia and brain injuries. Cerebral hypoxia triggers microglial overactivity, causing inflammation, neuronal injury, and disruption of the BBB [1]. Salidroside (Sal), a key compound in Tibetan medicine Rhodiola crenulata, mitigates hypoxia-induced metabolic disorders and neuronal damage by preserving mitochondrial function [2]. A method combining a three-dimensional (3D) simulated microenvironment with precise detection is needed to accurately understand the anti-hypoxic effects of drugs such as Sal using in vitro models, due to the simplicity of traditional monolayer cell cultures and the complexity of animal experiments [3]. We propose using an alginate hydrogel microsphere (AHMs)-based microfluidic approach for constructing mNVUs with BV2 microglia and HT22 neurons. The 3D microenvironment minimized shear stress, aiding precise control. Our method exposed mNVUs to a hypoxic microenvironment using deferoxamine (DFO), simulating overactivated microglia and injured neurons. Quantitative analysis of changes in metabolite content in the tricarboxylic acid (TCA) cycle was performed using mass spectrometry (MS) and metabolism of the Sal to evaluate the anti-hypoxic efficacy of Sal and the mechanism underlying anti-hypoxic inflammation through the nuclear factor-kappa B (NF-κB) pathway. This biofriendly, compatible platform is a potent tool for assessing cellular metabolism and brain protection drug screening, uncovering evident mNVU interactions through comparative HT22 and BV2/HT22 co-culture.

Small Methods **(IF 10.7)** Published: 16 April 2024

Understanding Macrophage-Tumor Interactions: Insights from Single-Cell Behavior Monitoring in a Sessile Microdroplet System.

Jiaxu Lin, Qiang Zhang, Tianze Xie, Zengnan Wu, Ying Hou, Yang Song, Yongning Lin, Jin-Ming Lin

Interaction between tumor-associated macrophages and tumor cells is crucial for tumor development, metastasis, and the related immune process. However, the macrophages are highly heterogeneous spanning from anti-tumorigenic to pro-tumorigenic, which needs to be understood at the single-cell level. Herein, a sessile microdroplet system designed for monitoring cellular behavior and analyzing intercellular interaction, demonstrated with macrophage-tumor cell pairs is presented. An automatic procedure based on the inkjet printing method is utilized for the precise pairing and co-encapsulation of heterotypic cells within picoliter droplets. The sessile nature of microdroplets ensures controlled fusion and provides stable environments conducive to adherent cell culture. The nitric oxide generation and morphological changes over incubation are explored to reveal the complicated interactions from a single-cell perspective. The immune response of macrophages under distinct cellular microenvironments is recorded. The results demonstrate that the tumor microenvironment displays a modulating role in polarizing macrophages from anti-tumorigenic into pro-tumorigenic phenotype. The approach provides a versatile and compatible platform to investigate intercellular interaction at the single-cell level, showing promising potential for advancing single-cell behavior studies.

Small **(IF 12.96)** Published: 20 April 2024

Fabrication and performance of bubble-containing multicompartmental particles: Novel self-orienting carriers.

Zengnan Wu, Yajing Zheng, Ling Lin,* Yongning Lin, Tianze Xie, Jiaxu Lin, Gaowa Xing, and Jin-Ming Lin

In this work, a class of bubble-containing multicompartmental particles with self-orienting capability is developed, where a single bubble is enclosed at the top of the super-segmented architecture. Such bubbles, driven by potential energy minimization, cause the particles to have a bubble-upward preferred orientation in liquid, enabling efficient decoding of their high-density signals in an interference-resistant manner. The particle preparation involves bubble encapsulation via the impact of a multicompartmental droplet on the liquid surface and overall stabilization via rational crosslinking. The conditions for obtaining these particles are systematically investigated. Methodological compatibility with materials is

demonstrated by different hydrogel particles. Finally, by encapsulating cargoes of interest, these particles have found broad applications in actuators, multiplexed detection, barcodes, and multicellular systems.

ACS Applied Materials & Interfaces (IF 8.3) Published: 26 April 2024

Chemical Plasma Membrane Perforation Generated by a Microfluidic Probe for Single-Cell Intracellular Protein Delivery.

Yang Song, Qiang Zhang, Jiaxu Lin, Yuxuan Li, Yucheng Sun, Jin-Ming Lin

Efficient and convenient delivery of exogenous molecules into cells is important for cell biology research. However, many intracellular delivery methods require carrier-mediated or physical field assistance, complicating the delivery process. Here, a general, simple, and effective method for in situ single-cell intracellular delivery is reported. A solution containing digitonin and cargo is precisely applied to single cells using a microfluidic probe. Digitonin binds to cholesterol in the plasma membrane to induce perforation, and the cargo enters the cell through the pore. By optimizing parameters, propidium iodide (0.67 kDa) and FITC-dextran (10, 40, and 150 kDa) can be successfully introduced into single cells within 3 min while maintaining cell viability. To prove the potential of this method for cell research, we delivered cytochrome C (13 kDa) and cyclophilin A (18 kDa) into cells by this method. The delivered cytochrome C successfully induces cell apoptosis by activating the caspase pathway, and cyclophilin A performs an antioxidant effect in the cells, which may enhance the drug resistance of glioma cells. It is believed that this method will be an attractive tool for single-cell intracellular delivery.

Chemical Communications (IF 4.3) Published: 2 May 2024

Evaluation of aconitine cardiotoxicity with a heart-on-a-particle prepared by a microfluidic device.

Tong Xu, Zengnan Wu, Hongren Yao, Yingrui Zhang, Shiyu Chen, Yuxuan Li, Xian-Li Meng, Yi Zhang, Jin-Ming Lin

A heart-on-a-particle model based on multicompartmental microgel is proposed to simulate the heart microenvironment and study the cardiotoxicity of drugs. The relevant microgel was fabricated by a biocompatible microfluidic-based approach, where heart function-related HL-1 and HUVEC cells were arranged in separate compartments. Finally, the mechanism of aconitine-induced heart toxicity was elucidated using mass spectrometry and molecular biotechnology.

Analytical Chemistry (IF 6.7) Published: 16 August 2024

Microfluidic Engineering of Addressable Multicompartmental Microspheres for Multicellular Systems.

Yongning Lin, Zengnan Wu, Yajing Zheng, Xiaorui Wang, Jin-Ming Lin, Ying Hou, Nan Li, Gaowa Xing, Ling Lin.

With the advantages of high-throughput manufacturing and customizability, on-microsphere construction of in vitro multicellular analytical systems has garnered significant attention. However, achieving a precise, biocompatible cell arrangement and spatial signal analysis in hydrogel microspheres remains challenging. In this work, a microfluidic method is reported for the biocompatible generation of addressable supersegmented multicompartmental microspheres. Additionally, these microspheres are developed as novel label-free multicellular systems. In the microfluidic approach, controllable microfluidics is used to finely tune the internal microstructure of the microspheres, and the gas ejector ensures the biocompatibility of the preparation process. As a proof of concept, six- and twenty-compartment microspheres were obtained without the addition of any biohazardous reagents. For microsphere decoding, the visualization of two basic compartments can provide clues for identifying label-free cells due to the structural regularity of the microspheres. Finally, by encapsulating cells of different types, these microspheres as multicellular systems were successfully used for cell coculture and drug testing. These biocompatible, scalable, and analyzable microspheres will open up new prospects for biomedical analysis.

Analytical Chemistry (IF 6.7) Published: 28 August 2024

Robust Long-Nanowire Fabrication by Clean-Phase-Assisted Micro Chemical Pen for Enhanced Bioassay Sensitivity.

Haifeng Lin, Ning Xu, Sifeng Mao, Hizuru Nakajima, Jin-Ming Lin, Katsumi Uchiyama, Nahoko Kasai, Ling Lin

Accurate assessment of phenotypic and genotypic characteristics of bacteria can facilitate comprehensive cataloguing of all the resistance factors for better understanding of antibiotic resistance. However, current methods primarily focus on individual phenotypic or genotypic profiles across different colonies. Here, a Digital microfluidic-based automated assay for whole-genome sequencing of single-antibiotic-resistant bacteria is reported, enabling Genotypic and Phenotypic Analysis of antibiotic-resistant strains (Digital-GPA). Digital-GPA can efficiently isolate and sequence antibiotic-resistant bacteria illuminated by fluorescent D-amino acid (FDAA)-labeling, producing high-quality single-cell amplified genomes (SAGs). This enables identifications of both minor and major mutations, pinpointing substrains with distinctive resistance mechanisms. Digital-GPA can directly process clinical samples to detect and sequence resistant pathogens without bacterial culture, subsequently provide genetic profiles of antibiotic susceptibility, promising to expedite the analysis of hard-to-culture or slow-growing bacteria. Overall, Digital-GPA opens a new avenue for antibiotic resistance analysis by providing accurate and comprehensive molecular profiles of antibiotic resistance at single-cell resolution.

Matter (IF 17.3) Published: 2 October 2024

Open aerosol microfluidics enable orthogonal compartmentalized functionalization of hydrogel particles.

Zengnan Wu, Yajing Zheng, Ling Lin, Yongning Lin, Tianze Xie, Wenjun Liao, Shiyu Chen, Yingrui Zhang, Jin-Ming Lin

Compartmentalized hydrogel microparticles are promising for applications in chemical, biological, and biomedical fields, owing to their customizability. However, simultaneous tailoring of the functionalities in both internal and surface compartments remains challenging. Here, an open aerosol microfluidic (OAMF) approach is reported to fabricate compartmentalized hydrogel particles, achieving orthogonal (independent and non-interfering) control over both internal and surface functionalization. The OAMF method utilizes microfluidic networks for shaping internal compartment layouts and employs reactive aerosols for precise surface engineering. As a proof of concept, particles featuring intricate internal and surface designs were created. In addition, the broad material versatility of particle customization is demonstrated by different hydrogels. Finally, potential applications of particles were explored as novel cell carriers. As exemplars, patterned cell cultures can be established both on the surface and inside of the particles. The proposed approach enables flexible design of engineered particles, advancing tissue engineering, drug screening, and cell therapeutic applications.

Biomicrofluidics (IF 2.6) Published: 4 November 2024

Microfluidics for foodborne bacteria analysis: Moving toward multiple technologies integration.

Gaowa Xing and Jin-MingLin

Food security related to bacterial pathogens has seriously threatened human life and caused public health problems. Most of the reported methods are targeted at known major pathogens commonly found in food samples, but to some extent, they have the disadvantage of lacking simplicity, speed, high throughput, and high sensitivity. Microfluidics has become a promising tool for foodborne bacteria analysis and addresses the above limitations. In this perspective, we briefly discussed the ongoing research and development in this field. We outline the major types of microfluidics, the strategies of target biorecognition, and signal amplification technologies in the microfluidic system for the foodborne bacteria analysis. We also proposed the future directions of microfluidics for foodborne bacterial analysis, which aims to inte grate multiple technologies toward intelligent analysis with high selectivity and sensitivity for unknown samples, multiple bacterial detection, and simultaneous detection of multiple food pollutants.

Chemical Engineering Journal (IF 15.1) Published: 15 December 2024

Thermo-responsive Microparticle Swimmer As a Remote Tool for Cell Delivery in Tissue Engineering.

Zengnan Wu, Yajing Zheng, Jin-Ming Lin, Gaowa Xing, Tianze Xie, Yongning Lin, Jiaxu Lin, Ling Lin

Developing biocompatible and flexible cell manipulation tools is crucial for effective cell delivery in tissue engineering. Herein, thermo-responsive microparticle swimmers, composed of an alginate core and a rough gelatin surface, are developed as a tool for remote cell manipulation and the construction of patterned cell models. The microparticles are fabricated using a novel bio-friendly surface assembly strategy, which leverages morphology-induced gelatin adsorption combined with temperature-cycling crosslinking to deposit multiple gelatin layers onto microfluidic-derived rough microparticles. Gelatin molecules can adsorb onto the rough surface at 25 °C and become cross-linked at 4 °C to form a stable coating layer while preserving the coarse morphology for additional assembly cycles. The gelatin layers remain intact at room temperature for cell loading and transport, but rapidly dissipate at 37 °C, enabling cell release. Moreover, complex manipulations of living cell populations, such as remote tweezing, can be achieved by the introduction of magneto-responsive moieties. These versatile microparticles provide an efficient tool for the in vitro construction of flexible and dynamic patterned cell models, with promising applications in tissue engineering, drug screening, and organoid development.

专家简介：

副会长：杨朝勇 教授



厦门大学特聘教授、上海交通大学分子医学研究院执行副院长、谱学分析与仪器教育部重点实验室副主任、美国化学会 Analytical Chemistry 副主编。长期致力于生物分析化学，在核酸化学生物学、微流控、单细胞空间组学测序等方向取得了创新性的成果。在 Nat. Biotechnol.、Nat. Commun.、Sci. Adv.、PNAS、JACS、Angew Chemie 等刊物发表论文 300 余篇，论文被引 19000 次，H 指数 75。获授权发明专利 70 余项。先后获得中美化学与化学生物学教授协会杰出教授奖、中国青年分析化学家奖、中国化学会-英国皇家化学会青年化学奖、美国化学会测量科学进展讲座奖等奖项与荣誉。

Nature Biotechnology **(IF 33.1)** Published: 16 January 2024

Decoder-seq enhances mRNA capture efficiency in spatial RNA sequencing.

Jiao Cao, Zhong Zheng, Di Sun, Xin Chen, Rui Cheng, Tianpeng Lv, Yu An, Junhua Zheng, Jia Song, Lingling Wu & Chaoyong Yang

Spatial transcriptomics technologies with high resolution often lack high sensitivity in mRNA detection. Here we report a dendrimeric DNA coordinate barcoding design for spatial RNA sequencing (Decoder-seq), which offers both high sensitivity and high resolution. Decoder-seq combines dendrimeric nanosubstrates with microfluidic coordinate barcoding to generate spatial arrays with a DNA density approximately ten times higher than previously reported methods while maintaining flexibility in resolution. We show that the high RNA capture efficiency of Decoder-seq improved the detection of lowly expressed olfactory receptor (Olfr) genes in mouse olfactory bulbs and contributed to the discovery of a unique layer enrichment pattern for two Olfr genes. The near-cellular resolution provided by Decoder-seq has enabled the construction of a spatial single-cell atlas of the mouse hippocampus, revealing dendrite-enriched mRNAs in neurons. When applying Decoder-seq to human renal cell carcinomas, we dissected the heterogeneous tumor microenvironment across different cancer subtypes and identified spatial gradient-expressed genes related to epithelial–mesenchymal transition with the potential to predict tumor prognosis and progression.

Analytical Chemistry **(IF 6.7)** Published: 23 April 2024

Well-Paired-Seq2: High-Throughput and High-Sensitivity Strategy for Characterizing Low RNA-Content Cell/Nucleus Transcriptomes.

Kun Yin, Meijuan Zhao, Yiling Xu, Zhong Zheng, Shanqing Huang, Dianyi Liang, He Dong, Ye Guo,Li Lin, Jia Song, Huimin Zhang, Junhua Zheng, Zhi Zhu, and Chaoyong Yang

Single-cell RNA sequencing (scRNA-seq) is a transformative technology that unravels the intricate cellular state heterogeneity. However, the Poisson-dependent cell capture and low sensitivity in scRNA-seq methods pose challenges for throughput and samples with a low RNA-content. Herein, to address these challenges, we present Well-Paired-Seq2 (WPS2), harnessing size-exclusion and quasi-static hydrodynamics for efficient cell capture. WPS2 exploits molecular crowding effect, tailing activity enhancement in reverse transcription, and homogeneous enzymatic reaction in the initial bead-based amplification to achieve 3116 genes and 8447 transcripts with an average of ~ 20000 reads per cell. WPS2 detected 1420 more genes and 4864 more transcripts than our previous Well-Paired-Seq. It sensitively characterizes transcriptomes of low RNA-content single cells and nuclei, overcoming the Poisson limit for cell and barcoded bead capture. WPS2 also profiles

transcriptomes from frozen clinical samples, revealing heterogeneous tumor copy number variations and intercellular crosstalk in clear cell renal cell carcinomas. Additionally, we provide the first single-cell-level characterization of rare metanephric adenoma (MA) and uncover potential specific markers. With the advantages of high sensitivity and high throughput, WPS2 holds promise for diverse basic and clinical research.

Lab on a Chip **(IF 7.5)** Published: 14 May 2024

Advanced sequencing-based high-throughput and long-read single-cell transcriptome analysis.

Shanqing Huang, Weixiong Shi, Shiyu Li, Qian Fan, Chaoyong Yang, Jiao Cao* and Lingling Wu

Cells are the fundamental building blocks of living systems, exhibiting significant heterogeneity. The transcriptome connects the cellular genotype and phenotype, and profiling single-cell transcriptomes is critical for uncovering distinct cell types, states, and the interplay between cells in development, health, and disease. Nevertheless, single-cell transcriptome analysis faces daunting challenges due to the low abundance and diverse nature of RNAs in individual cells, as well as their heterogeneous expression. The advent and continuous advancements of next-generation sequencing (NGS) and third-generation sequencing (TGS) technologies have solved these problems and facilitated the high-throughput, sensitive, full-length, and rapid profiling of single-cell RNAs. In this review, we provide a broad introduction to current methodologies for single-cell transcriptome sequencing. First, state-of-the-art advancements in high-throughput and full-length single-cell RNA sequencing (scRNA-seq) platforms using NGS are reviewed. Next, TGS-based long-read scRNA-seq methods are summarized. Finally, a brief conclusion and perspectives for comprehensive single-cell transcriptome analysis are discussed.

Science China Chemistry **(IF 10.4)** Published: 21 May 2024

DMF-scMT-seq Linking Methylome and Transcriptome within Single Cells with Digital Microfluidics.

Xing Xu, Xi Zeng, Xin Lin, Shiyan Lin, Shanshan Liang, Tian Tian, Rui Su, Jia Song, Chaoyong Yang

Single-cell joint analysis of methylome and transcriptome reveals how the methylation regulates the transcriptional activity. However, traditional bench-top protocols for single-cell DNA methylation and RNA transcription co-detection are labor-intensive, cost-ineffective and contaminant-prone. Herein, we establish the DMF-scMT-seq, a highly-efficient and cost-effective method to simultaneously analyze single-cell DNA methylation and transcriptional activity based on digital microfluidics. DMF-scMT-seq automates the workflow of single-cell isolation, cellular hypotonic lysis, nucleic acid separation and methylome/transcriptome library construction in a contactless and addressable way. The system ensures high accuracy (R>0.85), high gene detection ability (14,697 genes per cell at 4 million sequencing depth), and high CpG coverage (677,198 CpG sites per cell at 1 million sequencing depth). By using DMF-scMT-seq, the relationship of DNA methylation and RNA transcription under different genomic contexts is resolved. We further apply DMF-scMT-seq to study the dynamics of transcription regulation with methylation-inhibiting anti-tumor Decitabine, and identify the methylated promoter/gene body driven genes in response to Decitabine treatment. DMF-scMT-seq facilitates the construction of the correlation of DNA methylation and transcriptional activity at the single-cell level in a flexible, sensitive and accurate way, which is anticipated to be a powerful tool in studying single-cell biological systems.

Analytical Chemistry **(IF 6.7)** Published: 6 August 2024

DMF-DM-seq: Digital-Microfluidics Enabled Dual-Modality Sequencing of Single-Cell mRNA and microRNA with High Integration, Sensitivity, and Automation.

Yingwen Chen, Xuanqun Wang, Xing Na, Yingkun Zhang, Linfeng Cai, Jia Song, and Chaoyong Yang

Multimodal measurement of single cells provides deep insights into the intricate relationships between individual molecular

layers and the regulatory mechanisms underlying intercellular variations. Here, we reported DMF-DM-seq, a highly integrated, sensitive, and automated platform for single-cell mRNA and microRNA (miRNA) co-sequencing based on digital microfluidics. This platform first integrates the processes of single-cell isolation, lysis, component separation, and simultaneous sequencing library preparation of mRNA and miRNA within a single DMF device. Compared with the current half-cell measuring strategy, DMF-DM-seq enables complete separation of single-cell mRNA and miRNA via a magnetic field application, resulting in a higher miRNA detection ability. DMF-DM-seq revealed differential expression patterns of single cells of noncancerous breast cells and noninvasive and aggressive breast cancer cells at both mRNA and miRNA levels. The results demonstrated the anticorrelated relationship between miRNA and their mRNA targets. Further, we unravel the tumor growth and metastasis-associated biological processes enriched by miRNA-targeted genes, along with important miRNA-interaction networks involved in significant signaling pathways. We also deconstruct the miRNA regulatory mechanisms underlying different signaling pathways across different breast cell types. In summary, DMF-DM-seq offers a powerful tool for a comprehensive study of the expression heterogeneity of single-cell mRNA and miRNA, which will be widely applied in basic and clinical research.

Science Bulletin **(IF 20.5)** Published: 15 August 2024

Deciphering molecular response of cell-cell interactions at the single-cell level by precise on-demand cell assembly.

Weizhi Liu, Shanqing Huang, Ye Guo, Xingrui Li, He Dong, Juan Li, Chaoyong Yang, Zhi Zhu

Multicellular systems rely on the interactions between cells to coordinate cell signaling and regulate cell functions. Understanding the mechanism of cell–cell interactions (CCIs) is critical to many physiological and pathological processes, such as embryogenesis, differentiation, cancer metastasis, and immunological interactions. To better investigate the inherent interactions, recent studies on cell–cell coculture have been transformed from conventional bulk measurements to single-cell analysis. The improvement of measurement resolution at the single-cell level can help to capture the intermediates of less frequent cell subsets and elucidate the fundamental mechanisms of complex interactions among multiple cells. To investigate how cells interact and communicate with each other at the single-cell level, platforms capable of engineering cell assemblies with controlled cell composition are urgently needed.

PNAS **(IF 9.4)** Published: 20 August 2024

DNA-DISK: automated end-to-end data storage via enzymatic single-nucleotide DNA synthesis and sequencing on digital microfluidics.

Kunjie Li, Xiaoyun Lu, Jiaqi Liao, Heng Chen, Wei Lin, Yuhan Zhao, Dongbao Tang, Congyu Li, Zhenyang Tian, Zhi Zhu, Huifeng Jiang, Jun Sun*, Huimin Zhang* and Chaoyong Yang

In the age of information explosion, the exponential growth of digital data far exceeds the capacity of current mainstream storage media. DNA is emerging as a promising alternative due to its higher storage density, longer retention time, and lower power consumption. To date, commercially mature DNA synthesis and sequencing technologies allow for writing and reading of information on DNA with customization and convenience at the research level. However, under the disconnected and nonspecialized mode, DNA data storage encounters practical challenges, including susceptibility to errors, long storage latency, resource-intensive requirements, and elevated information security risks. Herein, we introduce a platform named DNA-DISK that seamlessly streamlined DNA synthesis, storage, and sequencing on digital microfluidics coupled with a tabletop device for automated end-to-end information storage. The single-nucleotide enzymatic DNA synthesis with biocapping strategy is utilized, offering an ecofriendly and cost-effective approach for data writing. A DNA encapsulation using thermo-responsive agarose is developed for on-chip solidification, not only eliminating data clutter but also preventing DNA degradation. Pyrosequencing is employed for in situ and accurate data reading. As a proof of concept, DNA-DISK successfully stored and retrieved a musical sheet file (228 bits) with lower write-to-read latency (4.4 min of

latency per bit) as well as superior automation compared to other platforms, demonstrating its potential to evolve into a DNA Hard Disk Drive in the future.

Analytical Chemistry (IF 6.7) Published: 20 September 2024

AMAR-seq: Automated Multimodal Sequencing of DNA Methylation, Chromatin Accessibility, and RNA Expression with Single-Cell Resolution.

Xi Zeng, Xiaoping Yang, Zhixing Zhong, Xin Lin, Qiuyue Chen, Shaowei Jiang, Mengwu Mo,Shichao Lin, Huimin Zhang, Zhi Zhu, Jin Li, Jia Song, and Chaoyong Yang

Parallel single-cell multimodal sequencing is the most intuitive and precise tool for cellular status research. In this study, we propose AMAR-seq to automate methylation, chromatin accessibility, and RNA expression coanalysis with single-cell precision. We validated the accuracy and robustness of AMAR-seq in comparison with standard single-omics methods. The high gene detection rate and genome coverage of AMAR-seq enabled us to establish a genome-wide gene expression regulatory atlas and triple-omics landscape with single base resolution and implement single-cell copy number variation analysis. Applying AMAR-seq to investigate the process of mouse embryonic stem cell differentiation, we revealed the dynamic coupling of the epigenome and transcriptome, which may contribute to unraveling the molecular mechanisms of early embryonic development. Collectively, we propose AMAR-seq for the in-depth and accurate establishment of single-cell multiomics regulatory patterns in a cost-effective, efficient, and automated manner, paving the way for insightful dissection of complex life processes.

ACS Appl Mater Interfaces (IF 10.38) Published: 2 October 2024

DMF-ChIP-seq for Highly Sensitive and Integrated Epigenomic Profiling of Low-Input Cells.

Mingyin Li, Xing Na, Fanghe Lin, Shanshan Liang, Yuehan Huang, Jia Song, Xing Xu, and Chaoyong Yang

Mapping genome-wide DNA-protein interactions (DPIs) provides insights into the epigenetic landscape of complex biological systems and elucidates the mechanisms of epigenetic regulation in biological progress. However, current technologies in DPI profiling still suffer from high cell demands, low detection sensitivity, and large reagent consumption. To address these problems, we developed DMF-ChIP-seq that builds on digital microfluidic (DMF) technology to profile genome-wide DPIs in a highly efficient, cost-effective, and user-friendly way. The entire workflow including cell pretreatment, antibody recognition, pA-Tn5 tagmentation, fragment enrichment, and PCR amplification is programmatically manipulated on a single chip. Leveraging closed submicroliter reaction volumes and a superhydrophobic interface, DMF-ChIP-seq presented higher sensitivity in peak enrichment than other current methods, with high accuracy (Pearson Correlation Coefficient (PCC) > 0.86) and high repeatability (PCC > 0.92). Furthermore, DMF-ChIP-seq was capable of processing the samples with as few as 8 cells while maintaining a high signal-to-noise ratio. By applying DMF-ChIP-seq, H3K27ac histone modification of early embryonic cells during differentiation was profiled for the investigation of epigenomic landscape dynamics. With the benefits of high efficiency and sensitivity in DPI analysis, the system provides great promise in studying epigenetic regulation during various biological processes.

Analytical Chemistry (IF 6.7) Published: 20 October 2024

DMF-Bimol: Counting mRNA and Protein Molecules in Single Cells with Digital Microfluidics.

Shanshan Liang,Chong Li,Yu Ning,Rui Su,Mingyin Li,Yihao Huang,Yuning Zou,Liu Yang, Xing Xu, and Chaoyong Yang

Analyzing single-cell protein and mRNA levels yields invaluable insights into cellular functions and the intricacies of biologically heterogeneous systems. Current joint mRNAs and protein analysis methodologies suffer from relative quantification, low sensitivity, possible background interference, and tedious manual manipulation. Therefore, we propose DMF-Bimol that leverages addressable digital microfluidics to automate digital counting of single-cell mRNA and protein

based on proximity ligation assay (PLA) and one-step RT-droplet digital PCR (RT-ddPCR). Through an engineered hydrophilic-hydrophobic interface, DMF-Bimol enables efficient single-cell isolation and lossless protein and nucleic acid processing. The closed droplet reaction system enhances the protein concentration and isolates exogenous contaminants, thereby dramatically improving the efficiency of the PLA reaction. The limit of detection of this approach achieves 3313 protein copies, marking a significant 17-fold enhancement in sensitivity over traditional benchtop PLA. This heightened sensitivity also uncovers a lower correlation between mRNA and protein levels in individual cells (Spearman r = 0.255) than bulk results, reflecting the complex relationship in heterogeneous cells. Using DMF-Bimol, we observed a significant upsurge of CD147 protein in CD138+ myeloma cells but consistent levels of CD147 mRNAs compared with normal leukocytes. This discovery indicates a possible consequence of CD147 oncogenic activation that tends to harness protein translation to bolster tumor cell survival and enhance invasiveness, highlighting the potential of DMF-Bimol in unveiling intricate dynamics in translation processes at the single-cell level.

***ACS Nano* (IF 15.8)** Published: 4 November 2024

Profiling Phenotypic Heterogeneity of Circulating Tumor Cells through Spatially Resolved Immunocapture on Nanoporous Micropillar Arrays.

Lianyu Lu, Yaohui Wang, Yue Ding, Yuqing Wang, Zhi Zhu, Jinsong Lu, Liu Yang, Peng Zhang, Chaoyong Yang

The phenotype of circulating tumor cells (CTCs) offers valuable insights into monitoring cancer metastasis and recurrence. While microfluidics presents a promising approach for capturing these rare cells in blood, the phenotypic profiling of CTCs remains technically challenging. Herein, we developed a nanoporous micropillar array chip enabling highly efficient capture and in situ phenotypic analysis of CTCs through enhanced and tunable on-chip immunoaffinity binding. The nanoporous micropillar array addresses the fundamental limits in fluidic mass transfer, surface stagnant flow boundary effect, and interface topographic and multivalent reactions simultaneously within a single device, resulting in a synergistic enhancement of CTC immunocapture efficiency. The CTC capture efficiency increased by approximately 40% for cancer cells with low surface marker expressing. By manipulating fluidic velocity (hydrodynamic drag force) on the chip, a cell adhesion gradient was generated in the capture chamber, enabling individual CTCs with varying expression levels of epithelial cellular adhesion molecules to be immunocaptured at the corresponding spatial locations where equilibrium drag force is provided. The clinical utility of the nanoporous micropillar array was demonstrated by accurately distinguishing early and advanced stages of breast cancer and further longitudinally monitoring treatment response. We envision that the nanoporous micropillar array chip will provide an in situ capture and molecular profiling approach for CTCs and enhance the clinical application of CTC liquid biopsy.

***Nature Communications* (IF 14.7)** Published: 14 November 2024

Dyna-vivo-seq unveils cellular RNA dynamics during acute kidney injury via in vivo metabolic RNA labeling-based scRNA-seq.

Kun Yin, Yiling Xu, Ye Guo, Zhong Zheng, Xinrui Lin, Meijuan Zhao, He Dong, Dianyi Liang, Zhi Zhu, Junhua Zheng, Shichao Lin, Jia Song, Chaoyong Yang

A fundamental objective of genomics is to track variations in gene expression program. While metabolic RNA labeling-based single-cell RNA sequencing offers insights into temporal biological processes, its limited applicability only to in vitro models challenges the study of in vivo gene expression dynamics. Herein, we introduce Dyna-vivo-seq, a strategy that enables time-resolved dynamic transcription profiling in vivo at the single-cell level by examining new and old RNAs. The new RNAs can offer an additional dimension to reveal cellular heterogeneity. Leveraging new RNAs, we discern two distinct high and low metabolic labeling populations among proximal tubular (PT) cells. Furthermore, we identify 90 rapidly responding transcription factors during the acute kidney injury in female mice, highlighting that high metabolic labeling PT cells exhibit heightened susceptibility to injury. Dyna-vivo-seq provides a powerful tool for the characterization

of dynamic transcriptome at the single-cell level in living organism and holds great promise for biomedical applications.

Small **(IF 12.96)** Published: 20 November 2024

Metabolic Labeling and Digital Microfluidic Single-Cell Sequencing for Single Bacterial Genotypic-Phenotypic Analysis.

Junnan Guo, Di Sun, Kunjie Li, Qi Dai, Shichen Geng, Yuanyuan Yang, Mengwu Mo, Zhi Zhu, Chen Shao, Wei Wang, Jia Song, Chaoyong Yang, and Huimin Zhang

Accurate assessment of phenotypic and genotypic characteristics of bacteria can facilitate comprehensive cataloguing of all the resistance factors for better understanding of antibiotic resistance. However, current methods primarily focus on individual phenotypic or genotypic profiles across different colonies. Here, a Digital microfluidic-based automated assay for whole-genome sequencing of single-antibiotic-resistant bacteria is reported, enabling Genotypic and Phenotypic Analysis of antibiotic-resistant strains (Digital-GPA). Digital-GPA can efficiently isolate and sequence antibiotic-resistant bacteria illuminated by fluorescent D-amino acid (FDAA)-labeling, producing high-quality single-cell amplified genomes (SAGs). This enables identifications of both minor and major mutations, pinpointing substrains with distinctive resistance mechanisms. Digital-GPA can directly process clinical samples to detect and sequence resistant pathogens without bacterial culture, subsequently provide genetic profiles of antibiotic susceptibility, promising to expedite the analysis of hard-to-culture or slow-growing bacteria. Overall, Digital-GPA opens a new avenue for antibiotic resistance analysis by providing accurate and comprehensive molecular profiles of antibiotic resistance at single-cell resolution.

Small Methods **(IF 10.7)** Published: 8 December 2024

Highly Multiplexing, Throughput and Efficient Single-Cell Protein Analysis with Digital Microfluidics.

Linfeng Cai, Li Lin, Shiyan Lin, Xuanqun Wang, Yingwen Chen, Huanghuang Zhu, Zhi Zhu, Liu Yang, Xing Xu, Chaoyong Yang

Proteins as crucial components of cells are responsible for the majority of cellular processes. Sensitive and efficient protein detection enables a more accurate and comprehensive investigation of cellular phenotypes and life activities. Here, a protein sequencing method with high multiplexing, high throughput, high cell utilization, and integration based on digital microfluidics (DMF-Protein-seq) is proposed, which transforms protein information into DNA sequencing readout via DNA-tagged antibodies and labels single cells with unique cell barcodes. In a 184-electrode DMF-Protein-seq system, ≈1800 cells are simultaneously detected per experimental run. The digital microfluidics device harnessing low-adsorbed hydrophobic surface and contaminants-isolated reaction space supports high cell utilization (>90%) and high mapping reads (>90%) with the input cells ranging from 140 to 2000. This system leverages split&pool strategy on the DMF chip for the first time to overcome DMF platform restriction in cell analysis throughput and replace the traditionally tedious bench-top combinatorial barcoding. With the benefits of high efficiency and sensitivity in protein analysis, the system offers great potential for cell classification and drug monitoring based on protein expression at the single-cell level.

专家简介：

副会长：马波 研究员



中国科学院青岛生物能源与过程所研究员，单细胞中心副主任，微流控系统团队负责人，青岛星赛生物联合创始人，董事长。2008 年获中科院大连化物所微流控芯片实验室分析化学专业博士学位。2008.5-2012.7 先后在美国加州大学洛杉矶分校 Crump 分子成像研究所和莱斯大学等研究机构从事博士后研究。2012 年 8 月加入中科院青岛生物能源与过程研究所单细胞研究中心。自 2003 年起致力于微流控芯片技术在生命科学中的基础和应用研究。已在 Science Advances, Nature Communications, Advanced Science, Small, Analytical Chemistry, Lab on a Chip 等学术期刊发表论文五十余篇，申请发明专利四十余项，授权三十余项（国际专利四项）。目前承担国家重点研发专项、国家基金委重大仪器，中科院重大科研仪器装备研制等重要科研项目。担任中国生物物理学会微流控系统学分会副会长，国家生物计量和质量控制标准化技术委员会委员，中国海洋工程咨询协会深海技术与工程分会理事。

Pharmaceutics **(IF 4.9)** Published: 19 March 2024

Intracellular Delivery of Therapeutic Protein via Ultrathin Layered Double Hydroxide Nanosheets.

He Zhang , Anle Ge, Yulin Wang , Boran Xia, Xichu Wang , Zhonghui Zheng, Changsheng Wei , Bo Ma, Lin Zhu , Rose Amal, Sung Lai Jimmy Yun, Zi Gu

The therapeutic application of biofunctional proteins relies on their intracellular delivery, which is hindered by poor cellular uptake and transport from endosomes to cytoplasm. Herein, we constructed a two-dimensional (2D) ultrathin layered double hydroxide (LDH) nanosheet for the intracellular delivery of a cell-impermeable protein, gelonin, towards efficient and specific cancer treatment. The LDH nanosheet was synthesized via a facile method without using exfoliation agents and showed a high loading capacity of proteins (up to 182%). Using 2D and 3D 4T1 breast cancer cell models, LDH–gelonin demonstrated significantly higher cellular uptake efficiency, favorable endosome escape ability, and deep tumor penetration performance, leading to a higher anticancer efficiency, in comparison to free gelonin. This work provides a promising strategy and a generalized nanoplatform to efficiently deliver biofunctional proteins to unlock their therapeutic potential for cancer treatment.

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 15 April 2024

An integrated microfluidic platform for on-demand single droplet dispenser with high accuracy by electrohydrodynamic (EHD) printing technique.

Anle Ge , Zhidian Diao , Yuandong Li , Chaojie Cui , Xixian Wang , Yang Liu , Jian Xu , Bo Ma

Droplet microfluidics has revolutionized single-cell analysis, allowing for ultra-high-throughput sorting of droplets to meet the demands of single-cell sorting. However, accurately and efficiently dispensing target droplets into specific containers for downstream analysis has remained a challenge. Here, we present an integrated microfluidic droplet dispenser based on the electrohydrodynamic (EHD) principle, capable of on-demand single droplet dispensing with high accuracy. Our system uses optical signal activation and EHD actuation to isolate and dispense droplets. The microfluidic droplet auto dispenser consists of four main modules: a pump-drive chip module, an optical automatic signal recognition module, a high voltage

control module, and an automated X-Y translation stage module. By optimizing the chip structure and voltage parameter, this platform successfully isolates single cells onto a Petri dish for downstream cultivation and heterogeneity analysis. In addition, the dispenser microfluidic system dispenses the sorted droplets in a "one droplet, one well" manner, providing an automated method for droplet interface from the micro- to macro- platform. This dispenser system provides a platform for phenotypic screening of single colony pick and single cell analysis.

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 1 May 2024

A microfluidics-free centrifugally-driven nano-liquid pipetting system (CNPS) for single-cell whole genome amplification.

Chunyu Li, Yanhai Gong, Fei Wu, Jian Xu, Bo Ma

We developed a microfluidics-free centrifugally-driven nano-liquid pipetting system (CNPS) for single-cell whole genome amplification. The capillary tube and the collection vessel (PCR tube or 96-well PCR plate), both of which are easily accessible, make up the basic components of the system. Unlike microfluidic chips that need a clean room and special skills to fabricate, the CNPS can be assembled in the typical biology laboratory without any special training. Centrifugation is used to directly pipette the nanoliter-volume liquid into the collection tube, which eliminates the requirement for extra equipment. The CNPS, which is compatible with the standard handheld pipette, allows for a smooth transition between the micro and macro worlds, thereby overcoming the problem of retrieving nanoliter-volume products. We further demonstrated the feasibility of the CNPS for nanoliter-volume single-cell multiple displacement amplification. Based on the sequencing results, the mapped reads cover on average 95.23%, 95.15%, and 80.94% for Saccharomyces cerevisiae, Escherichia coli, and Staphylococcus epidermidis, respectively. In sum, the CNPS has the potential to become an alternative powerful platform for single-cell genome sequencing with the ability to manipulate ultra-small volumes, as well as to enhance precision and sophistication by significantly minimizing sample losses and reducing amplification bias.

Bioresource Technology **(IF 9.6)** Published: 1 June 2024

Magnetic nanoparticle-mediated enrichment technology combined with microfluidic single cell separation technology: A technology for efficient separation and degradation of functional bacteria in single cell liquid phase.

Xuan, Yuanyan; Yin, Meng; Sun, Yujiao; Liu, Meijun; Bai, Guomin; Diao, Zhidian; Ma, Bo

Although there are many microorganisms in nature, the limitations of isolation and cultivation conditions have restricted the development of artificial enhanced remediation technology using functional microbial communities. In this study, an integrated technology of Magnetic Nanoparticle-mediated Enrichment (MME) and Microfluidic Single Cell separation (MSC) that breaks through the bottleneck of traditional separation and cultivation techniques and can efficiently obtain more in situ functional microorganisms from the environment was developed. MME technology was first used to enrich rapidly growing active bacteria in the environment. Subsequently, MSC technology was applied to isolate and incubate functional bacterial communities in situ and validate the degradation ability of individual bacteria. As a result, this study has changed the order of traditional pure culture methods, which are first selected and then cultured, and provided a new method for obtaining non-culturable functional microorganisms.

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 1 August 2024

Nature-inspired fungal fusarinine C-powered dual-mode fluorometric/colorimetric biosensing of fecal Helicobacter pylori with high-reliability.

Zhuangzhuang Wang , Mingxia Zhao , Yuan Wang , Bo Ma , Lili Wang , Yuetong Ji , Yuanyuan Ding , Zhe Chi

Conventional diagnostic approaches for Helicobacter pylori lack sufficient sensitivity, accuracy, and flexibility, especially

for low-density H. pylori infection. To overcome this limitation, we developed a highly reliable fluorometric/colorimetric dual-mode biosensing technique to detect minute quantities of H. pylori in human stool samples. Inspired by natural porphyrins, we discovered that the water-soluble fungal siderophore fusarinine C (FsC) emitted intense green fluorescence owing to intramolecular through-bond and intermolecular through-space conjugation, and turned reddish upon coordination with Fe3+. With FsC as an intrinsic fluorometric/colorimetric probe, a dual-mode biosensor was developed. It included an enrichment module of truncated H. pylori-specific-aptamer-modified superparamagnetic nanoparticles to capture H. pylori from samples, and a transduction module of alginate conjugated with FsC[Fe3+] and an optimized amount of FsC without Fe3+ to amplify the captured H. pylori to fluorescent and/or color signals. Remarkably, significantly increased sensitivity was achieved for this biosensor, with an actual limit of detection of 5 CFU/mL and single-cell-level detection resolution, as validated using laser-tweezer-sorted single H. pylori cells. Moreover, highly reliable dual-mode detection of low-density H. pylori (between 5 and 10 CFU/mL) was demonstrated. Using the colorimetric mode, a smartphone-biosensor platform for sensitive point-of-care testing of fecal H. pylori within 20 min was demonstrated, outperforming the clinical fecal antigen test strips; meanwhile, the fluorometric mode of the biosensor, owing to its greater sensitivity, can verify the colorimetric detection of minute H. pylori. This study first showcased a FsC-powered dual-mode biosensor for ultra-sensitive and accurate point-of-care detection of H. pylori with high reliability.

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 15 October 2024

A bacterial proliferation sensor based on naked-eye detection for rapid antimicrobial susceptibility testing from positive blood cultures.

Meijia Zhu , Teng Xu , Yongqiang Cheng , Bo Ma , Jian Xu , Anle Ge , Jing Dai , Hongwei Wang , Longyu Chen , Ziwei Zhang , Xiaoxiao Qi , Yifan Shao , Xi Zhang

The wide spread of antimicrobial resistance (AMR) is a crisis caused by the misuse of antibiotics. Despite the development of rapid antimicrobial susceptibility testing (AST) methods, there is an urgent need for an alternative rapid AST method that does not rely on testing equipment especially in resource-limited settings. In this work, a bacterial proliferation sensor based on naked-eye detection for rapid AST was developed. The sensor included the macroscopic bacterial culture chambers and bacterial growth detection microchannels for naked eye observation. After incubation at different antibiotic concentrations for 3–5 h, a one-step centrifugation effectively concentrated the suspended bacterial cells into visually observable microbars with length proportional to the number of cells, enabling to directly compare the bacterial accumulation under different drug concentrations. As a proof of concept, the sensor was able to determine the sensitivity of and () to drugs using the naked eye within 3–5 h. Furthermore, by combining with the thixotropic gel centrifugation method for bacteria separated from positive blood cultures (PBCs), we proposed a rapid and low-cost AST method for complex samples and evaluated the feasibility using clinical samples from cerebrospinal fluid-positive, blood-positive, ascites-positive and bile-positive culture bottles. The results were highly consistent with that from the clinical standard methods. The proposed sensor could achieve a rapid, low-cost, naked-eye detectable AST method for complex clinical samples, which would be applicable to the resource-limited areas.

Analytical Chemistry **(IF 6.7)** Published: 11 November 2024

Artificial Intelligence-Assisted Automatic Raman-Activated Cell Sorting (AI-RACS) System for Mining Specific Functional Microorganisms in the Microbiome.

Zhidian Diao, Xiaoyan Jing, Xibao Hou, Yu Meng, Jiaping Zhang, Yongshun Wang, Yuetong Ji, Anle Ge, Xixian Wang, Yuting Liang, Jian Xu, Bo Ma

The microbiome represents the natural presence of microorganisms, and exploring, understanding, and leveraging its functions will bring about significant breakthroughs in life sciences and applications. Raman-activated cell sorting (RACS) enables the correlation of phenotype and genotype at the single-cell level, offering a solution to the bottleneck in microbial

community functional analysis caused by challenges in cultivating diverse microorganisms. However, current labor-intensive manual procedures fall short in catering to the demands of single-cell functional analysis in microbial communities. To address this issue, we developed an artificial intelligence-assisted Raman-activated cell sorting system (AI-RACS) that integrates precise single-cell positioning, automated data collection, optical tweezers capture, and single-cell printing to elevate microbial single-cell RACS from manual to automated, validating the efficacy of the system by isolating aluminum-tolerant microbes from acidic soil microbiota. Leveraging the AI-RACS framework, we sorted 13 strains from red soil samples under near-in situ conditions, with all demonstrating strong aluminum tolerance. AI-RACS efficiently segregates microbial cells from intricate environmental samples, investigating their functional attributes and presenting a novel tool for microbial research and applications.

Analytical Chemistry **(IF 6.7)** Published: 12 November 2024

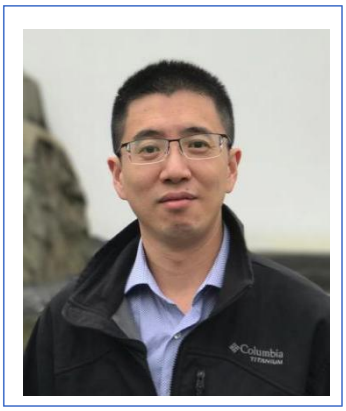
Ultrafast Evolution of Bacterial Antimicrobial Resistance by Picoliter-Scale Centrifugal Microfluidics.

Teng Xu, Yajie Dai, Anle Ge, Xueqian Chen, Yanhai Gong, Tze Hau Lam, Kelvin Lee, Xiao Han, Yuetong Ji, Wei Shen, Jiquan Liu, Luyang Sun, Jian Xu, Bo Ma

Experimental evolution is a powerful approach for scrutinizing and dissecting the development of antimicrobial resistance; nevertheless, it typically demands an extended duration to detect evolutionary changes. Here, a centrifugal microfluidics system is designed to accelerate the process. Through a simple step of on-chip centrifugation, a highly condensed bacterial matrix of ~ 1012 cells/mL at the enrichment tip of the chip channel is derived, enabling bacteria encapsulated to survive in antimicrobial concentrations several times higher than the minimum inhibitory concentration (MIC) and rapidly develop resistance in the first 10 h. After 48 h of on-chip evolution, the E. coli strain demonstrated a 64 to 128-fold reduction in sensitivity to disinfectants (triclosan) as well as antibiotics (ciprofloxacin and amikacin), a rate substantially swifter compared to conventional continuous inoculation-based experimental evolution. The speed and simplicity of this microfluidic system suggest its broad application for uncovering resistance mechanisms and identifying targets of biocides and antibiotics.

专家简介：

副会长：黄岩谊 教授



北京大学化学学院教授，北京大学生物医学前沿创新中心副主任，北大-清华生命科学联合中心研究员。1997 年本科毕业于北京大学化学专业，2002 年博士毕业于北京大学无机化学专业；先后在美国加州理工学院应用物理系、斯坦福大学生物工程系从事博士后研究工作；2006 年回到北京大学任教。主要从事微量核酸分析研究，集中工作在测序技术、单细胞分析和微流控技术的交汇点上，发表科学论文 180 余篇。曾担任国家科技部 863 计划“新一代测序仪及配套试剂”重大专项首席专家；是国家基金委优秀青年科学基金、国家杰出青年科学基金获得者，曾主持基金委重大研究计划集成项目、基金委国家重大科研仪器研制项目等；曾获得国家自然科学二等奖、教育部高等学校科学研究优秀成果奖自然科学一等奖、教育部全国优秀博士学位论文、教育部新世纪人才计划等；2014 年入选英国皇家化学会 Fellow。

Processes **(IF 2.8)** Published: 27 February 2024

An Injection-Mold Based Method with a Nested Device for Microdroplet Generation by Centrifugation.

Jichen Li, Wen Li, Bizhu Wu , Wenting Bu, Miaomiao Li, Jinyan Ou , Yuxiang Xiong, Shangtao Wu, Yanyi Huang, Yong Fan, Yongfan Men

Microdroplets have been widely used in different fields due to their unique properties, such as compartmentalization, single-molecule sensitivity, chemical and biological compatibility, and high throughput. Compared to intricate and labor-intensive microfluidic techniques, the centrifuge-based method is more convenient and cost-effective for generating droplets. In this study, we developed a handy injection molding based method to readily produce monodisperse droplets by centrifugation. Briefly, we used two three-dimensional (3D) printed master molds with internal cavities to forge two coupled sub-molds by injecting polydimethylsiloxane (PDMS) and casted these two PDMS sub-molds into a nested structure that clamps the micro-channel array (MiCA) by injecting polyurethane resin. This method enables the generation of various sizes of monodispersed microdroplets by centrifugation with proper parameters within 10 min. To assess the performance of this method, homogeneous fluorescent hydrogel microspheres were generated and droplet digital polymerase chain reaction (ddPCR) was carried out. Overall, this method offers high-throughput droplet generation, reduces costs compared to other methods, and is user-friendly.

专家简介：

委员：程鑫 研究员



美国密西根大学博士（2005），南方科技大学材料科学与工程系教授，实验室与设备管理部部长，精密光学工程中心主任，半导体学院（国家卓越工程师学院）执行院长。曾任教于德克萨斯农工大学，2013 年加入南方科技大学。从事半导体材料、器件和微纳加工方向的教学与科研工作。研究方向包括半导体图形化技术、纳米制造、微流控芯片、微机电传感器等。发表论文 110 余篇，获批中国和美国发明专利 30 余项。曾主持国家自然科学基金委重大科研仪器研制项目、广东省重点领域研发专项等政府科研项目 10 余项，与企业合作研发项目 10 余项，多个项目以技术成果转移方式孵化创新企业。

Optics and Lasers in Engineering **(IF 3.5)** Published: March 2024

Direct dielectrophoretic characterization of particles in the high-density microwell array using optical tweezers.

Xiao Luo , Chunhui Wu , Jie Zhang , Junyan Xu , Handong Tan , Beini Zhang , Jiesi Xie , Chaoran Tao , Kaicheng Huang , Xing Cheng , Weijia Wen

In this work, a quantitative and intuitive measurement of dielectrophoresis (DEP) behavior in a high-density dielectrophoretic microwell array chip was accomplished in assistance with the holographic optical tweezers. A one-dimensional force balance system with high reliability was achieved between the transverse optical trapping (TOT) force and the DEP force. The value of the DEP force was inferred by accurately calculating the TOT force, and the direction of the DEP force was observed with high-magnification microscopy. In order to estimate the availability and operability of the DEP force measurement system, we systematically investigated the influences of various external factors on the DEP behaviors of microspheres and live cells. All the quantitative measurement results, which agree well with the theory, showed that this system could serve as an accurate research tool for DEP behavior characterizations to optimize and improve the DEP-based manipulations of microparticles and live cells for a broad range of applications. The system also provides an approach to quantitatively obtain important parameters such as Clausius-Mossotti factors for cells in mediums, which could potentially be used to understand the dielectric properties of different types of cells for cell differentiation and diagnosis at the single-cell level.

Advanced Science **(IF 14.3)** Published: 3 April 2024

Fully Biodegradable Packaging Films for Fresh Food Storage Based on Oil-Infused Bacterial Cellulose.

Guoli Chen, Kaimin Wang, Pinghang Chen, Daohang Cai, Yan Shao, Rui Xia, Chun Li, Haochuan Wang, Fuzeng Ren, Xing Cheng and Yanhao Yu

Fully biodegradable packaging materials are demanded to resolve the issue of plastic pollution. However, the fresh food storage performance of biodegradable materials is generally much lower than that of plastics due to their high permeability, microbial friendliness, and limited stretchability and transparency. Here a biodegradable packaging material is reported with high fresh food storage performance based on an oil-infused bacterial cellulose (OBC) porous film. The oil infusion

significantly improved cellulose's food-keeping performance by reducing its gas permeability, increasing its stretchability and transparency, and enabling the active release of green vapor-phase preservative molecules, while maintaining its intrinsically high degradability. Strawberries stored in a container with the OBC lid at 23 °C after 5 days exhibited a moldy rate of 0%, in contrast to the 100% moldy rate of those stored by poly(ethylene). Enhanced storage performance is also obtained on tomatoes, pork, and shrimp. The OBC film is naturally degraded after being buried in wet soil at 30 °C for 9 days, identical to the degradation rate of bacterial cellulose. The liquid seal strategy broadly applies to different celluloses, providing a general option for developing cellulose-based biodegradable packaging materials.

Optics Express **(IF 3.2)** Published: 20 May 2024

Flexible wafer-scale bifunctional metasurface based on nanoimprinting.

Meiting Xie, Xuanming Zhang, Fei Lou, Xing Cheng and Lei Lei

Metasurfaces have demonstrated remarkable capabilities in manipulating light fields across diverse applications. However, current research tends to examine these functionalities in isolation, prompting a growing interest in integrating different functionalities within a singular metasurface device. In this paper, we propose and experimentally demonstrate a bifunctional metasurface capable of providing concealment and sensing functions simultaneously. Specifically, the proposed nanostructure effectively operates as a one-way mirror, exhibiting an average reflection rate of approximately 90% under external illumination, alongside an absorption rate of 87.9% from the opposite direction of incidence. This functionality renders it suitable for privacy-enhancing building windows. Meanwhile, this nanostructure also integrates liquid sensing capabilities boasting a sensitivity of 464 nm/RIU, which is particularly valuable for monitoring liquid-based corrosion. The experimental performance of the prepared 6-inch nanohole-patterned metasurface closely aligns with the simulations, and the utilization of flexible polyethylene terephthalate (PET) film, coupled with nanoimprint lithography technology, enables a direct and cost-effective manufacturing process that can be scaled up for widespread applications.

Nano Trends Published: 21 June 2024

Preventing unwanted atomic layer deposition by liquid sealing.

Haochuan Wang, Yanhao Yu, Shaohu Zhan, Yan Shao, Zhibin Yi, Chun Li, Rui Xia, Xing Cheng, Wenshuai Feng, Rui-Tao Wen, Guangfu Luo

Atomic layer deposition (ALD) is an essential thin film fabrication technique widely used in electronic and energy systems, but avoiding ALD in untargeted areas has been a long-standing challenge that excludes the possibility of creating patterns through bottom-up processes. We present a liquid sealing strategy to prevent unwanted ALD by combining shadow masks with viscous perfluoropolyether oil that conformally fulfills all gaps between the mask and substrate down to the molecular level. Due to the anti-adsorption and non-defective nature of the liquid sealant, ALD molecules are forced away from the masking areas, resulting in order-of-magnitude improvements in the patterning resolution compared with conventional shadow masks. The liquid sealant does not change the growth rate and film properties of ALD oxides and can be easily removed by solvents. This liquid sealing strategy applies to a variety of shadow masks (e.g., curved mask and anodic aluminum oxide), substrates (e.g., silicon, plastic, and elastomer), patterning materials (e.g., oxide and metal), and deposition methods (e.g., sputtering and thermal evaporation), providing new insights for bottom-up pattern fabrications.

Micromachines **(IF 3.0)** Published: 28 June 2024

A Lego-Like Reconfigurable Microfluidic Stabilizer System with Tunable Fluidic RC Constants and Stabilization Ratios.

Wuyang Zhuge, Weihao Li, Kaimin Wang, Zhuodan Chen, Chunhui Wu, Kyle Jiang, Jun Ding, Carl Anthony and Xing Cheng

In microfluidic systems, it is important to maintain flow stability to execute various functions, such as chemical reactions, cell transportation, and liquid injection. However, traditional flow sources, often bulky and prone to unpredictable fluctuations, limit the portability and broader application of these systems. Existing fluidic stabilizers, typically designed for specific flow sources, lack reconfigurability and adaptability in terms of the stabilization ratios. To address these limitations, a modular and standardized stabilizer system with tunable stabilization ratios is required. In this work, we present a Lego-like modular microfluidic stabilizer system, which is fabricated using 3D printing and offers multi-level stabilization combinations and customizable stabilization ratios through the control of fluidic RC constants, making it adaptable to various microfluidic systems. A simplified three-element circuit model is used to characterize the system by straightforwardly extracting the RC constant without intricate calculations of the fluidic resistance and capacitance. By utilizing a simplified three-element model, the stabilizer yields two well-fitted operational curves, demonstrating an R-square of 0.95, and provides an optimal stabilization ratio below 1%. To evaluate the system's effectiveness, unstable input flow at different working frequencies is stabilized, and droplet generation experiments are conducted and discussed. The results show that the microfluidic stabilizer system significantly reduces flow fluctuations and enhances droplet uniformity. This system provides a new avenue for microfluidic stabilization with a tunable stabilization ratio, and its plug-and-play design can be effectively applied across diverse applications to finely tune fluid flow behaviors in microfluidic devices.

***IEEE Sensors Journal* (IF 4.3)** Published: 18 July 2024

Implementing AC Signal Driving in Digital Microfluidic Chips With Active-Matrix Thin-Film Transistors.

Shaohu Zhan, Rongyue Liu, Qin Luo, Yunfei Li, Yilin Li, Zhen Liu, Mingqing Cheng and Xing Cheng

In this work, we propose a novel method for implementing ac signal driven droplets on electrowetting-on-dielectric (EWOD) chips. The electrode arrays of the EWOD chips are manufactured using active-matrix thin-film transistor (AM-TFT) technology. The ac signal used to drive droplets is achieved through a combination of five TFTs in one pixel. The metal oxide indium gallium zinc oxide (IGZO) as an active layer is used to fabricate the TFTs. Results show that the IGZO TFTs have excellent electrical characteristics, with a field-effect mobility of 8.2 cm2/V · s, a threshold voltage of 0.5 V, a subthreshold swing (SS) of 0.31 V/decade, and an on/off current ratio of greater than 107 . The simulation and experimental results indicate that the combination of five TFTs in one pixel can output stable ac signal. The droplets driven by ac signal on the EWOD chips can implement the basic manipulation, such as generation, movement, splitting, and merging. This technology improves the flexibility and configurability of droplet manipulation on AM-TFT-based EWOD chips, which is of great significance for the rapid mixing of droplets, anti-adsorption of biological macromolecules, and prevention of cross contamination.

***Nature Communications* (IF 14.7)** Published: 19 July 2024

A universal packaging substrate for mechanically stable assembly of stretchable electronics.

Yan Shao, Jianfeng Yan, Yinglin Zhi, Chun Li, Qingxian Li, Kaimin Wang, Rui Xia, Xinyue Xiang, Liqian Liu, Guoli Chen, Hanxue Zhang, Daohang Cai, Haochuan Wang, Xing Cheng, Canhui Yang, Fuzeng Ren & Yanhao Yu

Stretchable electronics commonly assemble multiple material modules with varied bulk moduli and surface chemistry on one packaging substrate. Preventing the strain-induced delamination between the module and the substrate has been a critical challenge. Here we develop a packaging substrate that delivers mechanically stable module/substrate interfaces for a broad range of stiff and stretchable modules with varied surface chemistries. The key design of the substrate was to introduce module-specific stretchability and universal adhesiveness by regionally tuning the bulk molecular mobility and surface molecular polarity of a near-hermetic elastic polymer matrix. The packaging substrate can customize the deformation of different modules while avoiding delamination upon stretching up to 600%. Based on this substrate, we fabricated a fully stretchable bioelectronic device that can serve as a respiration sensor or an electric generator with an in

vivo lifetime of 10 weeks. This substrate could be a versatile platform for device assembly.

***ACS Sensors* (IF 8.2)** Published: 23 August 2024

Response enhancement in high-temperature H2S- treated metal oxide gas sensors.

Zijun Chen, Yu Liu, Rongyue Liu, Yulong Chen, Hongjun Liu, Xing Cheng

Metal oxide gas sensors (MOGS), crucial components in monitoring air quality and detecting hazardous gases, are well known for their poisoning effects when exposed to certain gas molecules, such as hydrogen sulfide. Surprisingly, our research reveals that high-temperature H2S treatment leads to an enhancement effect rather than response decay. This study investigates the time-decaying response enhancement, being attributed to the formation of metal sulfide and metal sulfate on the metal oxide's surface, enhancing the electronic sensitization. Such an enhancement effect is demonstrated for various gases, including CO, CH3CH2OH, CH4, HCHO, and NH3. Additionally, the impacts of H2S treatment on the response and recovery time are also observed. Surface compositional analysis are conducted with X-ray photoelectron spectroscopy. A proposed mechanism for the enhancement effect is elaborated, highlighting the role of electronic sensitization and the sulfide-sulfate component. This research offers valuable insights into the potential applications of metal oxide sensors in sulfide-presented harsh environments in gas sensing, encouraging future exploration of optimized sensor materials, operation temperature, and the development of hydrogen sulfide poisoning-resistant and higher sensitivity MOGS.

***ACS Applied Materials & Interfaces* (IF 8.3)** Published: 4 September 2024

Large-scale selective micropatterning with robotics nDEP tweezers and hydrogel encapsulation.

Kaicheng Huang, Jiewen Lai, Hongliang Ren, Chunhui Wu, Xing Cheng and Henry Kar Hang Chu

Creating diverse microparticle patterns on a large scale enhances the performance and efficiency of biochemical analytics. Current techniques exhibit limitations in achieving diverse microparticle patterns on a large scale, primarily focusing on patterning particles of the same type with limited flexibility and accessibility. Moreover, accessibility to patterned particles without a fixed formation poses additional challenges. Herein, in this work, we introduce a novel robotic micropatterning system designed to address these challenges. The system facilitates the selection, batch transferring, patterning, and encapsulation of microparticles using negative dielectrophoresis (nDEP)-tweezers, enabling large-scale microparticle patterning on a hydrogel. A multielectrode chip was mounted on a micromanipulator to serve as the nDEP tweezers, and the microparticles scattering on the substrate could be trapped and displaced to different positions on a substrate with an array of holes for large-scale pattern generation. Photosensitive hydrogel was employed for microparticle pattern encapsulation. The effects of configuring different experimental parameters on the patterning efficiency were evaluated and analyzed. Experiments were conducted to explore the stability and performance of the micropatterns. Various patterns with hydrogel encapsulation were created using different color polystyrene microbeads (orange, blue, and green) with varying sizes (50, 100, and 125 μm) under the adjusted environment. Results demonstrate the successful creation of large-scale microbead patterns in a specified form and their encapsulation into an extractable hydrogel using the proposed nDEP tweezer system. The proposed system can be potentially applied to diverse bioparticles for analysis.

***Nanotechnology* (IF 2.9)** Published: 25 September 2024

A strategy to fabricate nanostructures with sub-nanometer line edge roughness.

Xin Zhuang, Yunsheng Deng, Yue Zhang, Kaimin Wang, Yulong Chen, Shiyang Gao, Jingfu Xu, Liqiu Wang * and Xing Cheng

Line edge roughness (LER) has been an important issue in the nanofabrication research, especially in integrated circuits. Despite numerous research studies has made efforts on achieving smaller LER value, a strategy to achieve sub-nanometer level LER still remains challenging due to inability to deposit energy with a profile of sub-nanometer LER. In this work, we

introduce a strategy to fabricate structures with sub-nanometer LER, specifically, we use scanning helium ion beam to expose hydrogen silsesquioxane (HSQ) resist on thin SiNx membrane (~ 20 nm) and present the 0.16 nm spatial imaging resolution based on this suspended membrane geometric construction, which is characterized by scanning transmission electron microscope (STEM). The suspended membrane serves as an energy filter of helium ion beam and due to the elimination of backscattering induced secondary electrons, we can systematically study the factors that influences the LER of the fabricated nanostructures. Furthermore, we explore the parameters including step size, designed exposure linewidth (DEL), delivered dosage and resist thickness and choosing the high contrast developer, the process window allows to fabricate lines with 0.2 nm LER is determined. AFM measurement and simulation work further reveal that at specific beam step size and DEL, the nanostructures with minimum LER can only be fabricated at specific resist thickness and dosage.

IEEE Sensors Journal **(IF 4.3)** Published: 30 September 2024

On-chip 3-D imaging and counting of particles transported in a microfluidic channel based on light-field microscopy.

Xinglong Huang, Xing Cheng, Boris Stoeber

Rapid acquisition of 3-D volumetric information and accurate counting are significant in observing and monitoring specimens moving in microfluidic channels. This study introduces a novel approach of 3-D image flow cytmetry (IFC) using light-field microscopy that images the microfluidic channel with a microlens array (MLA) and reconstructs a complete 3-D volume from a single frame. To create the custom MLA, a cost-effective method is developed, combining gray-scale photolithography, nickel electroplating, and nanoimprinting. Furthermore, a calibration procedure is devised to rectify aberrations within the imaging system prior to 3-D reconstruction. The counting process employs an algorithm based on local intensity peak identification to quantify and locate particles moving in a microchannel, achieving counting accuracies around 95%. In comparison to existing 3-D IFCs, our method offers distinct advantages, including the capability for high throughput data capture and 3-D imaging fast moving samples without necessitating complex microchannel designs.

专家简介：

委员：杜昱光 研究员



中国科学院过程工程研究所博士生导师，俄罗斯自然科学院外籍院士。国家生化工程技术研究中心（北京） 常务副主任。从事糖链合成生物学糖工程研究 30 余年，曾获香港裘搓基金会资助在香港浸会大学化学系及中药所作高访。

现兼任中国生物工程学会副秘书长、常务理事、中国生物工程学会糖生物工程专业委员会主任委员、中国化学学会甲壳素专业委员会副主任委员、中国生物化学与分子生物学会复合糖专业委员会委员、国家糖工程中心学术委员会委员、中国饲料工业协会饲料添加剂专业委员会委员及全国饲料评审委员。

主要研究方向：1. 糖链合成生物学、营养糖生物学及糖生物工程技术研究，揭示寡糖信号在体内吸收代谢及功能调控过程；研究药食同源中药材功能寡糖制备新技术，研发天然多糖/寡糖新药、糖药物先导化合物、特殊功能食品、生物农药、饲料添加剂等系列产品。2. 研发系列人类代谢器官芯片及生物安全快检技术。

RSC Advances **(IF 3.9)** Published: 29 May 2024

Automated Chemoenzymatic Modular Synthesis of Human Milk Oligosaccharides on a Digital Microfluidic Platform.

Yiran Wu, Yunze Sun, Caixia Pei, Xinlv Peng, Xianming Liu, Eika W. Qian, Yuguang Du, Jian-Jun Li

Glycans, along with proteins, nucleic acids, and lipids, constitute the four fundamental classes of biomacromolecules found in living organisms. Generally, glycans are attached to proteins or lipids to form glycoconjugates that perform critical roles in various biological processes. Automatic synthesis of glycans is essential for investigation into structure-function relationships of glycans. In this study, we presented a method that integrated magnetic bead-based manipulation and modular chemoenzymatic synthesis of human milk oligosaccharides (HMOs), on a DMF (Digital Microfluidics) platform. On the DMF platform, enzymatic modular reactions were conducted in solution, and purification of products or intermediates was achieved by using DEAE magnetic beads, circumventing the intricate steps required for traditional solid-phase synthesis. With this approach, we have successfully synthesized eleven HMOs with highest yields of up to >90% on the DMF platform. This study would not only lay the foundation for OPME synthesis of glycans on the DMF platform, but also set the stage for developing automated enzymatic glycan synthesizers based on the DMF platform.

专家简介：

委员：关一民 博士



现任上海傲睿科技董事长，上海微技术工业研究院特聘专家，上海大学微电子学院特聘导师。于 2016 年作为“国家特聘专家”回国创业，致力于智能微流控芯片技术研发及产业化。此前，关博士在美国世界 500 强公司工作了近 20 年，拥有丰富的 CMOS-MEMS 智能微流控芯片设计、研发，产品制造及市场开发经验。其团队研发的智能微流体技术及液体数字化技术在智能制造，精准医疗及检测领域有着广泛的应用前景。

关博士拥有 80 多项专利，其中包括 50 多项美国专利，曾获中科院科技进步一等奖，牵头完成国家重大专项--“核高基”专项课题（“智能微流控技术”），并承担着多项科技部及自然科学基金的重点研发课题。

Biomicrofluidics **(IF 2.6)** Published: 26 November 2024

Thermal Bubble Single-Cell Printing Chip: High-throughput, Wide-Field, and Efficient.

Bo Deng, Kun Wang, Peng Huang, Miaomiao Yang, Demeng Liu, Yimin Guan

Single-cell printing technology has arisen as a potent instrument for investigating cell biology and disease pathophysiology. Nonetheless, current single-cell printing methodologies are hindered by restricted throughput, a limited field of view, and diminished efficiency. We present an innovative single-cell printing chip that utilizes thermal inkjet technology for single-cell printing, therefore addressing these constraints. We have accomplished high-throughput, wide-field, and efficient single-cell printing by merging a high-density thermal foam-based inkjet nozzle array on a chip with high-speed cameras and computer vision technologies for optical image capture and single-cell identification training. We have shown the efficacy and adaptability of the printing chip by printing various concentrations of Chinese hamster ovary cells and human embryonic kidney 293 cells. The printing of a single 96-well plate is accomplished in 2-3 min, facilitating one-time loading and uninterrupted multi-plate paving. Our thermal bubble single-cell printing chip serves as a viable platform for high-throughput single-cell analysis applications.

Micromachines **(IF 3.0)** Published: 23 October 2024

An Automated Digital Microfluidic System Based on Inkjet Printing.

Wansheng Hu, Ming Cao, Lingni Liao, Yuanhong Liao, Yuhan He, Mengxiao Ma, Simao Wang, Yimin Guan

Cellular interactions, such as intercellular communication and signal transduction, can be enhanced within three-dimensional cell spheroids, contributing significantly to cellular viability and proliferation. This is crucial for advancements in cancer research, drug testing, and personalized medicine. The dimensions of the cell spheroids play a pivotal role in their functionality, affecting cell proliferation and differentiation, intercellular interactions, gene expression, protein synthesis, drug penetration, and metabolism. Consequently, different spheroid sizes may be required for various drug sensitivity experiments. However, conventional 3D cell spheroid cultures suffer from challenges such as size inconsistency, poor uniformity, and low throughput. To address these issues, we have developed an automated, intelligent system based on inkjet printing. This system allows for precise control of droplet volume by adjusting algorithms, thereby enabling the formation of spheroids of varying sizes. For spheroids of a single size, the printing pattern can be modified to achieve a coefficient of variation within 10% through a bidirectional compensation method. Furthermore, the system is

equipped with an automatic pipetting module, which facilitates the high-throughput preparation of cell spheroids. We have implemented a 3 × 3 spheroid array in a 24-well plate, printing a total of 216 spheroids in just 11 min. Last, we attempted to print mouse small intestinal organoids and cultured them for 7 days, followed by immunofluorescent staining experiments. The results indicate that our equipment is capable of supporting the culture of organoids, which is of great significance for high-throughput drug screening and personalized medicine.

专家简介：

委员：胡国庆 教授



浙江大学求是特聘教授，博士生导师。曾任中国科学院力学研究所非线性力学国家重点实验室副主任、研究员、中国科学院大学工程科学学院多尺度力学教研室主任、岗位教授。2000 年-2007 年间在美国、加拿大、英国、以色列等国家长期从事研究工作，目前开展微纳米尺度流体与输运机理、微纳流控芯片设计理论、纳米材料生力学/生物效应研究。主持国家自然科学基金重点项目、973 计划课题、中科院前沿科学重点研究项目、中科院 B 类先导、中科院知识创新重要方向项目等多项课题。发表 SCI 论文及专著章节 70 余篇。现任中国力学学会副秘书长、流体力学专业委员会委员、“微纳尺度流动”专业组组长、Acta Mechanica Sinica 编委、Scientific Reports 编委。

Physical Review Fluids **(IF 2.5)** Published: 9 January 2024

Front Tracking Simulation of Droplet Displacement on Solid Surfaces by Soluble Surfactant-Driven Flows.

Xinglong Shang , Zhengyuan Luo , Bofeng Bai , Long He , Guoqing Hu

We provide comprehensive numerical insights into the displacement of droplets subject to soluble surfactant-driven flows. The effects of soluble surfactants on the dynamics of moving contact lines are introduced by the surfactant-dependent generalized Navier boundary condition. We show that surfactant transport significantly influences the displacement patterns of droplets on solid surfaces, affecting both the equilibrium state of the sliding motion and the critical conditions for detachment. In particular, a linear increase in the displacement velocity of a droplet with the dimensionless adsorption depth K is observed. This rate of increase is more pronounced at higher elasticity numbers, as evidenced by a more significant increase in the advancing contact angle. The critical condition for droplet detachment depends on the surfactant's ability to swiftly adsorb from the bulk and replenish at interfaces, which is improved as the Biot number Bi or K increases. Adsorption is enhanced by an increase in Bi, resulting in a decrease in the required time td for droplet detachment. However, this enhancement effect becomes nonmonotonic at high Bi values. In contrast, consistently increasing the bulk Peclet number decreases td, eventually approaching the convection limit where the Marangoni-induced drag force ceases to increase. In addition, surfactant transfer near the moving contact line at a moderate Damkohler number restricts the motion of the advancing contact lines, promoting droplet detachment. For all detachment scenarios, we find that detachment necessitates a critical effective capillary number, and an increase in this number results in an exponential decline in td.

Analytical Chemistry **(IF 6.8)** Published: 16 January 2024

Generation of multiple concentration gradients using a two-dimensional pyramid array.

Qi Xinlei, Zhou Qin, Li Xuejin, Hu Guoqing

Concentration heterogeneity of diffusible reactants is a prevalent phenomenon in biochemical processes, requiring the generation of concentration gradients for the relevant experiments. In this study, we present a high-density pyramid array microfluidic network for the effective and precise generation of multiple concentration gradients. The complex gradient distribution in the 2D array can be adaptively adjusted by modulating the reactant velocities and concentrations at the inlets.

In addition, the unique design of each reaction chamber and mixing block in the array ensures uniform concentrations within each chamber during dynamic changes, enabling large-scale reactions with low reactant volumes. Through detailed numerical simulation of mass transport within the complex microchannel networks, the proposed method allows researchers to determine the desired number of reaction chambers within a given concentration range based on experimental requirements and to quickly obtain the operating conditions with the help of machine learning-based prediction. The effectiveness in generating a multiple concentration gradient environment was further demonstrated by concentration-dependent calcium carbonate crystallization experiments. This device provides a highly efficient mixing and adaptable concentration platform that is well suited for high-throughput and multiplexed reactions.

***Angewandte Chemie-International Edition* (IF 16.1)** Published: 8 April 2024

Increasing the accessibility of internal catalytic sites in covalent organic frameworks by introducing a bicontinuous mesostructure.

Liu Yamei, Zhou Qin, Yu Hongde, Yang Qiqi, Wang Mingchao, Huang Chuanhui, Xiang Luoxing, Li Chen, Heine Thomas, Hu Guoqing, Wang Shengyao, Feng Xinliang, Mai Yiyong

Introducing continuous mesochannels into covalent organic frameworks (COFs) to increase the accessibility of their inner active sites has remained a major challenge. Here, we report the synthesis of COFs with an ordered bicontinuous mesostructure, via a block copolymer self-assembly-guided nanocasting strategy. Three different mesostructured COFs are synthesized, including two covalent triazine frameworks and one vinylene-linked COF. The new materials are endowed with a hierarchical meso/microporous architecture, in which the mesochannels exhibit an ordered shifted double diamond (SDD) topology. The hierarchically porous structure can enable efficient hole-electron separation and smooth mass transport to the deep internal of the COFs and consequently high accessibility of their active catalytic sites. Benefiting from this hierarchical structure, these COFs exhibit excellent performance in visible-light-driven catalytic NO removal with a high conversion percentage of up to 51.4 %, placing them one of the top reported NO-elimination photocatalysts. This study represents the first case of introducing a bicontinuous structure into COFs, which opens a new avenue for the synthesis of hierarchically porous COFs and for increasing the utilization degree of their internal active sites.

***Aggregate* (IF 13.9)** Published: 15 April 2024

Spatiotemporally controlled emergence of nanoparticle microvortices under electric field.

Pan Qi, Lin Xijian, Wei Shiyuan, Su Jinghong, Zhao Hansen, Duan Xiaojie, Hu Guoqing, He Yan

Controlled assembly of nanoparticles (NPs) has garnered much interest over the past two decades. Beyond established techniques, new methods utilizing local short-range or large-scale long-range interactions remain to be explored to achieve diverse micro- and nanoscale structures. Here, we report the controlled emergence of vortex-pair arrays within monodispersed gold nanorods by applying a direct current electric field across a pair of sawtooth electrodes. By employing in situ darkfield microscopy and particle collective analysis, we elucidate the mechanism behind the formation and stabilization of the NP vortices, attributing it to the combined effects of the electrode shape, high NP density, and high solution viscosity. We further explore the controllability of the vortex-pair arrays and obtain multiple complex vortice patterns. Our findings will facilitate the investigation of efficient and controlled dynamic assembly of NPs under external fields and help manufacture next-generation optoelectronic functional materials.

***Journal of the American Chemical Society* (IF 14.5)** Published: 11 July 2024

Single-atom catalysts through pressure-controlled metal diffusion.

Al-Hilfi Samir H., Jiang Xikai, Heuer Julian, Akula Srinu, Tammeveski Kaido, Hu Guoqing, Yang Juan, Wang Hai. I.,Bonn Mischa, Landfester Katharina, Muellen Klaus, Zhou Yazhou

Single-atom catalysts (SACs) open up new possibilities for advanced technologies. However, a major complication in preparing high-density single-atom sites is the aggregation of single atoms into clusters. This complication stems from the delicate balance between the diffusion and stabilization of metal atoms during pyrolysis. Here, we present pressure-controlled metal diffusion as a new concept for fabricating ultra-high-density SACs. Reducing the pressure inhibits aggregation substantially, resulting in almost three times higher single-atom loadings than those obtained at ambient pressure. Molecular dynamics and computational fluid dynamics simulations reveal the role of a metal hopping mechanism, maximizing the metal atom distribution through an increased probability of metal-ligand binding. The investigation of the active site density by electrocatalytic oxygen reduction validates the robustness of our approach. The first realization of Ullmann-type carbon-oxygen couplings catalyzed on single Cu sites demonstrates further options for efficient heterogeneous catalysis.

***International Journal of Heat and Mass Transfer* (IF 5.0)** Published: 15 August 2024

Assessment of the heat transfer efficiency of perforated louvered fins for improved drainage.

Zhou Qin, Wang Hongyan, Liu Shengfei, Wei Huafeng, Hu Guoqing

To address the inherent drainage challenges of louvered fin and flat tube heat exchangers (LFFTHXs) when used as evaporators, this study presents an innovative louvered fin design with perforations that significantly improve drainage efficiency while reducing fin material usage. Traditional LFFTHXs, despite their superior heat exchange capacity compared to fin-and-tube heat exchangers (FTHXs), suffer from poor drainage of condensate and defrosting water, leading to problems such as metal corrosion, airflow blockage, reduced thermal comfort, and increased energy consumption. Our proposed solution, the perforated fin, especially the models with two combined holes (LF-2CH), shows a significant improvement in drainage performance compared to conventional designs, as confirmed by theoretical analysis and numerical simulations. In addition, we have systematically studied the air-side flow and heat transfer characteristics of different configurations, revealing that 18 degrees and 24 degrees louver angles in the LF-2CH models can enhance heat transfer rates by up to 20.9 % and 18.0 %, respectively, at the lowest fan power compared to conventional louvered fins. By elucidating the impact of louver angle on airflow dynamics and thermal wake patterns, we highlight the LF-2CH models as optimal for evaporator applications, combining improved thermal-hydraulic performance, efficient dewatering capacity, and reduced fin material consumption to provide a compelling advancement in heat exchanger technology.

***Micromachines* (IF 3.0)** Published: 31 August 2024

Numerical Investigation of Enhanced Heat Transfer with Micro Pin Fins in Heat Exchangers.

Xinglong Shang , Zhengyuan Luo , Bofeng Bai , Long He , Guoqing Hu

Pin-fin and flat-tube heat exchangers (PFFTHXs) offer a promising alternative to traditional louvered-fin and flat-tube heat exchangers (LFFTHXs), especially when used as evaporators. The streamlined structure of pin fins helps to effectively

remove condensate and defrost water. In this study, we conducted a numerical analysis of 60 different pin-fin configurations across three pin diameters to enhance heat transfer in PFFTHXs. Our investigation focused on how pin pitch affects both airflow and heat transfer efficiency. The results show that a closer pin pitch increases both the heat transfer rate per unit area and the pressure drop for a given airflow velocity. We evaluated the overall performance of these configurations using the heat transfer rate per unit frontal area obtained at equivalent fan power levels. The analysis identified optimal configurations for each pin diameter, with the 0.2 mm diameter configuration demonstrating the highest heat transfer efficiency—this was on par with louvered fins but used fewer resources. This makes it an ideal choice for evaporative applications in PFFTHXs.

***Nature Nanotechnology* (IF 38.1)** Published: September 2024

Direct cytosolic delivery of siRNA via cell membrane fusion using cholesterol-enriched exosomes.

Zhuo Yan, Luo Zhen, Zhu Zhu, Wang Jie, Li Xiang, Zhang Zhuan, Guo Cong, Wang Bingqi, Nie Di, Gan Yong, Hu Guoqing, Yu Miaorong

Efficient cytosolic delivery is a significant hurdle when using short interfering RNA (siRNA) in therapeutic applications. Here we show that cholesterol-rich exosomes are prone to entering cancer cells through membrane fusion, achieving direct cytosolic delivery of siRNA. Molecular dynamics simulations suggest that deformation and increased contact with the target cell membrane facilitate membrane fusion. In vitro we show that cholesterol-enriched milk-derived exosomes (MEs) achieve a significantly higher gene silencing effect of siRNA, inducing superior cancer cell apoptosis compared with the native and cholesterol-depleted MEs, as well as conventional transfection agents. When administered orally or intravenously to mice bearing orthotopic or subcutaneous tumours, the cholesterol-enriched MEs/siRNA exhibit antitumour activity superior to that of lipid nanoparticles. Collectively, by modulating the cholesterol content of exosome membranes to facilitate cell entry via membrane fusion, we provide a promising approach for siRNA-based gene therapy, paving the way for effective, safe and simple gene therapy strategies.

***Nature Communications* (IF 14.7)** Published: 27 September 2024

Selective regulation of macrophage lipid metabolism via nanomaterials' surface chemistry.

Wu Junguang, Bai Xuan, Yan Liang, Baimanov Didar, Cong Yalin, Quan Peiyu, Cai Rui, Guan Yong, Bu Wei, Lin Binhua, Wang Jing, Yu Shengtao, Li Shijiao, Chong Yu, Li Yang, Hu Guoqing, Zhao Yuliang, Chen Chunying, Wang Liming

Understanding the interface between nanomaterials and lipoproteins is crucial for gaining insights into their impact on lipoprotein structure and lipid metabolism. Here, we use graphene oxide (GOs) nanosheets as a controlled carbon nanomaterial model to study how surface properties influence lipoprotein corona formation and show that GOs have strong binding affinity with low-density lipoprotein (LDL). We use advanced techniques including X-ray reflectivity, circular dichroism, and molecular simulations to explore the interfacial interactions between GOs and LDL. Specifically, hydrophobic GOs preferentially associate with LDL's lipid components, whereas hydrophilic GOs tend to bind with apolipoproteins. Furthermore, these GOs distinctly modulate a variety of lipid metabolism pathways, including LDL recognition, uptake, hydrolysis, efflux, and lipid droplet formation. This study underscores the importance of structure analysis at the nano-biomolecule interface, emphasizing how nanomaterials' surface properties critically influence cellular lipid metabolism. These insights will inspire the design and application of future biocompatible nanomaterials and nanomedicines.

Journal of Chemical Physics **(IF 3.1)** Published: 7 November 2024

Neural network-assisted model of interfacial fluids with explicit coarse-grained molecular structures.

Ma Shuhao, Li Dechang, Li Xuejin, Hu Guoqing

Interfacial fluids are ubiquitous in systems ranging from biological membranes to chemical droplets and exhibit a complex behavior due to their nonlinear, multiphase, and multicomponent nature. The development of accurate coarse-grained (CG) models for such systems poses significant challenges, as these models must effectively capture the intricate many-body interactions, both inter- and intramolecular, arising from atomic-level phenomena, and account for the diverse density distributions and fluctuations at the interface. In this study, we use advanced machine learning techniques incorporating force matching and diffusion probabilistic models to construct a robust CG model of interfacial fluids. We evaluate our model through simulations in various settings, including the water-air interface, bulk decane, and dipalmitoylphosphatidylcholine monolayer membranes. Our results show that our CG model accurately reproduces the essential many-body and interfacial properties of interfacial fluids and proves effective across different CG mapping strategies. This work not only validates the utility of our model for multiscale simulations, but also lays the groundwork for future improvements in the simulation of complex interfacial systems.

Cell Reports Physical Science **(IF 7.9)** Published: 12 November 2024

Raising Enzymatic Stability During Biocatalysis with Hierarchically Hollow Two-Dimensional MOF Nanocapsules.

Mengfan Mao, Shengfei Liu, Xiaolong Zhong, Yue Lin, Cuiying Lin, Guoqing Hu, Kang Liang, Chuanhui Huang, Zhenyu Lin

Metal-organic frameworks (MOFs) have emerged as promising platforms for enzyme immobilization. Nevertheless, conventional MOF carriers encounter challenges, including restricted catalytic activity and inadequate acid stability, thereby limiting their applicability in oncological contexts. Here, glucose oxidase and ZIF-8 (a common MOF carrier) are chosen as models. Hierarchically hollow twodimensional conjugated MOF (Zn-HHTP [zinc 2,3,6,7,10,11-hexahydroxytriphenylene]) nanocapsules are constructed by a mild ZIF-8to-Zn-HHTP transformation at room temperature to boost the ex vivo and in vivo biocatalytic activity and stability of enzymes. The hierarchical Zn-HHTP nanocapsules feature hollow nanostructures and mesoporous-microporous structures (4.2 and 1.2 nm), which are beneficial for enhanced biocatalytic activity and maintaining enzyme conformation. Glucose oxidase@Zn-HHTP exhibits 2.5 times higher catalytic activity than that of glucose oxidase@ZIF-8. Importantly, nanocapsules exhibit higher acid stability than the parental ZIF-8, allowing them to stably traverse the acidic microenvironment of a tumor and achieve intracellular glucose detection to discriminate normal and cancerous cells.

Acta Mechanica Sinica **(IF 3.8)** Published: 4 December 2024

Novel method for assessment of thermal performance of louvered fin and flat tube heat exchangers.

Qin Zhou, Shengfei Liu, Guoqing Hu

This study presents a simplified numerical approach for evaluating the thermal performance of louvered fin and flat tube heat exchangers (LFFTHXs), which are critical in many thermal management applications but difficult to model due to their complex geometries. The proposed method uses an equivalent convective heat transfer coefficient to represent the fins, significantly reducing the computational requirements of the simulations. Validation against the effectiveness-number of transfer units (NTU) method showed average deviations of 4.4% for the novel louvered fin with two combined holes

(LF-2CH) and 9.5% for conventional configurations, confirming the accuracy of the method. Further application to two-phase refrigerant scenarios using experimental data demonstrated the robustness of the method and its suitability for practical design and optimization of LFFTHXs. The approach not only improves the feasibility of thermal analysis in industrial applications, but also provides a foundation for future research into more efficient heat exchanger designs.

专家简介：

委员：孔继烈 教授



复旦大学化学系教授， 博士生导师，1987、1990、1993 年分别获复旦大学本科、硕士和博士学位，后分别在美国肯州路易威尔大学和康州州立大学做博士后。先后主持国家“863“项目、“973“子课题、基金委重点及面上项目、教育部人才项目及上海市科委专项等多项课题研究，研究领域及兴趣包括功能光电功能材料及器件、生物分子光电化学分析、电化学生物传感器、芯片微分析系统、中草药及海洋药物分析等。已在国外 SCI 学术刊物发表论文 70 余篇，编著三本，获 6 项国家发明专利授权。担任《分析科学学报》、《电化学》、《化学传感器》等刊物编委，《科学通报》特约编辑，中国仪器仪表学会化学传感器专业委员会委员，任复旦大学化学系分析化学研究所所长，电分析化学研究室负责人。研究领域：微纳生化分析、微分析仪器、疾病分子诊断新方法新技术。

Advanced Materials **(IF 27.4)** Published: 30 January 2024

Electro-Optical Multiclassification Platform for Minimizing Occasional Inaccuracy in Point-of-Care Biomarker Detection.

Changhao Dai, Huiwen Xiong, Rui He, Chenxin Zhu, Pintao Li, Mingquan Guo, Jian Gou, Miaomiao Mei, Derong Kong, Qiang Li, Andrew Thye Shen Wee, Xueen Fang, Jilie Kong, Yunqi Liu, Dacheng Wei

On-site diagnostic tests that accurately identify disease biomarkers lay the foundation for self-healthcare applications. However, these tests routinely rely on single-mode signals and suffer from insufficient accuracy, especially for multiplexed point-of-care tests (POCTs) within a few minutes. Here, this work develops a dual-mode multiclassification diagnostic platform that integrates an electrochemiluminescence sensor and a field-effect transistor sensor in a microfluidic chip. The microfluidic channel guides the testing samples to flow across electro-optical sensor units, which produce dual-mode readouts by detecting infectious biomarkers of tuberculosis (TB), human rhinovirus (HRV), and group B streptococcus (GBS). Then, machine-learning classifiers generate three-dimensional (3D) hyperplanes to diagnose different diseases. Dual-mode readouts derived from distinct mechanisms enhance the anti-interference ability physically, and machine-learning-aided diagnosis in high-dimensional space reduces the occasional inaccuracy mathematically. Clinical validation studies with 501 unprocessed samples indicate that the platform has an accuracy approaching 99%, higher than the 77%–93% accuracy of rapid point-of-care testing technologies at 100% statistical power (>150 clinical tests). Moreover, the diagnosis time is 5 min without a trade-off of accuracy. This work solves the occasional inaccuracy issue of rapid on-site diagnosis, endowing POCT systems with the same accuracy as laboratory tests and holding unique prospects for complicated scenes of personalized healthcare.

Nature Communications **(IF 14.7)** Published: 2 March 2024

Long-term monitoring of ultratrace nucleic acids using tetrahedral nanostructure-based NgAgo on wearable microneedles.

Bin Yang, Haonan Wang, Jilie Kong, Xueen Fang

Real-time and continuous monitoring of nucleic acid biomarkers with wearable devices holds potential for personal health management, especially in the context of pandemic surveillance or intensive care unit disease. However, achieving high sensitivity and long-term stability remains challenging. Here, we report a tetrahedral nanostructure-based Natronobacterium gregoryi Argonaute (NgAgo) for long-term stable monitoring of ultratrace unamplified nucleic acids (cell-free DNAs and RNAs) in vivo for sepsis on wearable device. This integrated wireless wearable consists of a flexible circuit board, a microneedle biosensor, and a stretchable epidermis patch with enrichment capability. We comprehensively investigate the recognition mechanism of nucleic acids by NgAgo/guide DNA and signal transformation within the Debye distance. In vivo experiments demonstrate the suitability for real-time monitoring of cell-free DNA and RNA with a sensitivity of 0.3 fM up to 14 days. These results provide a strategy for highly sensitive molecular recognition in vivo and for on-body detection of nucleic acid.

***Biosensors and Bioelectronics* (IF 10.7)** Published: 15 August 2024

Rapid and Simultaneous Detection of Common Childhood Diarrhea Viruses by Microfluidic-Fen1-assisted Isothermal Amplification with Ultra-High Specificity and Sensitivity.

Xin Ye, Linlin Fan, Lei Zhang, Dan Wang, Yanfen Ma, Jilie Kong, Wenjie Fang, Jian Hu, Xiaoqin Wang

Rapid and accurate diagnostic methods are crucial for managing viral gastroenteritis in children, a leading cause of global childhood morbidity and mortality. This study introduces a novel microfluidic-Flap endonuclease 1 (FEN1)-assisted isothermal amplification (MFIA) method for simultaneously detecting major viral pathogens associated with childhood diarrhea—rotavirus, norovirus, and adenovirus. Leveraging the specificity-enhancing properties of FEN1 with a universal dspacer-modified flap probe and the adaptability of microfluidic technology, MFIA demonstrated an exceptional detection limit (5 copies/μL) and specificity in the simultaneous detection of common diarrhea pathogens in clinical samples. Our approach addresses the limitations of current diagnostic techniques by offering a rapid (turn around time <1 h), cost-effective, easy design steps (universal flap design), and excellent detection performance method suitable for multiple applications. The validation of MFIA against the gold-standard PCR method using 150 actual clinical samples showed no statistical difference in the detection performance of the two methods, positioning it as a potential detection tool in pediatric diagnostic virology and public health surveillance. In conclusion, the MFIA method promises to transform pediatric infectious disease diagnostics and contribute significantly to global health efforts combating viral gastroenteritis.

***Journal of Chemical Education* (IF 2.5)** Published: 5 September 2024

A Novel General Chemistry Experiment for Freshmen: Transgenic Soybean Detection Based on Microfluidic Molecular Fluorescence Spectroscopy Analysis.

Pintao Li, Min Gu, Ghazala Ashraf, Huiwen Xiong, Fei Cun, Xuting Chen, Jilie Kong, Xueen Fang

In this experiment, we present a microfluidic-based molecular fluorescence spectroscopy method for analyzing nucleic acids to identify transgenic soybeans. This method is integrated into a General Chemistry Experiment course tailored for freshmen. The primary goals of this course are to deepen student's understanding of some important knowledge points of general chemistry, introduce students to experimental techniques at the micro- and nanoscale, help students understand the principles of molecular fluorescence spectroscopy and enzyme reaction kinetics, elucidate the relationship between chemistry and its practical applications, stimulate their interest in chemistry, and provide multidisciplinary perspectives and thinking. Over the period from 2021 to 2023, more than 180 freshmen enrolled in this course, and over 30 universities in China have initiated the advancement of this course. Most students successfully completed the experiment, achieving high completion rate and promising results. Participating students improved their practical skills and the ability to work collaboratively in a laboratory setting, which led to numerous innovative ideas and insights in related areas. Positive feedback from the students confirmed that the predetermined learning objectives were successfully achieved.

Advanced Science (IF 14.3) Published: 9 December 2024

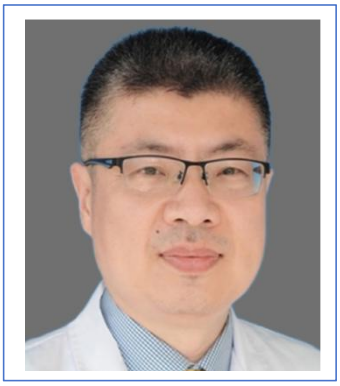
An Alternating Current Electroosmotic Flow-Based Ultrasensitive Electrochemiluminescence Microfluidic System for Ultrafast Monitoring, Detection of Proteins/miRNAs in Unprocessed Samples.

Huiwen Xiong, Chenxin Zhu, Changhao Dai, Xin Ye, Yuanyuan Li, Pintao Li, Shuang Yang, Ghazala Ashraf, Dacheng Wei, Hui Chen, Huali Shen, Jilie Kong, Xueen Fang

Early diagnosis of acute diseases is restricted by the sensitivity and complex process of sample treatment. Here, an ultrasensitive, rapid, and portable electrochemiluminescence-microfluidic (ECL-M) system is described via sandwich-type immunoassay and surface plasmonic resonance (SPR) assay. Using a sandwich immunoreaction approach, the ECL-M system employs cardiac troponin-I antigen (cTnI) as a detection model with a Ru@SiO2 NPs labeled antibody as the signal probe. For miR-499-5p detection, gold nanoparticles generate SPR effects to enhance Ru(bpy)32+ ECL signals. The system based on alternating current (AC) electroosmotic flow achieves an LOD of 2 fg mL−1 for cTnI in 5 min and 10 aM for miRNAs in 10 min at room temperature. The point-of-care testing (POCT) device demonstrated 100% sensitivity and 98% specificity for cTnI detection in 123 clinical serum samples. For miR-499-5p, it exhibited 100% sensitivity and 97% specificity in 55 clinical serum samples. Continuous monitoring of these biomarkers in rats' saliva, urine, and interstitial fluid samples for 48 hours revealed observations rarely documented in biotic fluids. The ECL-M POCT device stands as a top-performing system for ECL analysis, offering immense potential for ultrasensitive, rapid, highly accurate, and facile detection and monitoring of acute diseases in POC settings.

专家简介：

委员：刘大渔 研究员



华南理工大学附属第二医院微流控体外诊断研究室 PI，广东省微流控芯片医学诊断工程技术研究中心负责人。博士期间于中科院大连化学物理研究所从事微流控芯片体外诊断研究，博士后期间于香港科技大学机械工程系从事微分析系统研究。现为研究员、博士生导师，广州市重点医学人才。曾主持和参与多项国家自然科学基金和科技部重点研发专项。在一系列国际主流学术期刊发表研究论文 60 余篇，获得专利 20 余项，并参与了《微流控芯片实验室》、《现场快速检测新进展》等书籍的撰写。

Interdisciplinary Medicine Published: 8 January 2024

Programmable Droplet Microfluidics for Complex Multistep Bioassays.

Enqi Huang, Yu Wang, Dongyang Cai, Dayu Liu

Programmable droplet microfluidics (PDM) refers to a microfluidic device that integrates the functionality of a series of droplets with distinct spatial locations in a designated temporal order. PDM streamlines the intricate workflow of complex bioassays by enabling programmable and macroscopic droplet displacements, in which the droplets serve as reservoirs for reagents, microvalves for liquid insulation, and in some cases micropumps for mass transportation. As these droplets are intangible structures, the need for expensive microfabrication procedures is eliminated. Furthermore, the parallelization of the droplet series provides flexibility in controlling the throughput of the microfluidic analysis system. This paper provides a comprehensive review of PDMs enabled by various microfluidic mechanisms, including magnetism actuation, relative liquid displacement, capillary suction and sequential microdisplacement. Additionally, important applications of PDM systems for nucleic acid detection, immunoassay, drug testing, and sample recovery are also introduced. In conclusion, PDM demonstrates its potential as a highly advantageous tool for executing intricate multistep bioassays on a microfluidic platform. These technologies have exhibited superiority over their traditional counterparts in terms of size reduction, automation, and low sample/reagent consumption.

Lab on a Chip (IF 7.5) Published: 12 March 2024

Selective Expansion of Renal Cancer Stem Cells Using Microfluidic Single-Cell Culture Arrays for Anticancer Drug Testing.

Xiaogang Wang, Tao He, Zihe Chen, Jueming Chen, Yanzhang Luo, Dongguo Lin, Xiancheng Li, Dayu Liu

The suboptimal prognosis associated with drug therapy for renal cancer can be attributed to the presence of stem-cell-like renal cancer cells. However, the limited number of these cells prevents conventional drug screening assays from effectively assessing the response of renal cancer stem cells to anti-cancer agents. To address this issue, the present study employed microfluidic single-cell culture arrays to expand renal cancer stem cells by exploiting the anti-apoptosis and self-renewal properties of tumor stem cells. A microfluidic chip with 18 000 hydrophilic microwells was designed and fabricated to establish the single-cell culture array. Over a 7 day culture, the large-scale single-cell culture yielded a limited quantity of single-cell-derived tumorspheres. The sphere formation rates for Caki-1, 786-O, and ACHN cells were determined to be 8.74 +/- 0.53%, 12.02 +/- 1.43%, and 4.98 +/- 1.68%, respectively. The expanded cells exhibited stemness characteristics, as indicated by immunofluorescence, flow cytometry, serial passaging, and in vitro differentiation assays. Additionally, the comparative transcriptomic analysis showed significant differences in the gene expression patterns of the expanded cells

compared to the differentiated renal cancer cells. The drug testing indicated that renal cancer stem cells exhibited reduced sensitivity towards the tyrosine kinase inhibitors sorafenib and sunitinib, compared to differentiated renal cancer cells. This reduced sensitivity can be attributed to the elevated expression levels of tyrosine kinase in renal cancer stem cells. This present study provides evidence that the utilization of microfluidic single-cell culture arrays for selective cell expansion can facilitate drug testing of renal cancer stem cells. Selective single-cell expansion on a microfluidic chip facilitates drug testing of renal cancer stem cells.

ACS Biomaterials Science and Engineering (IF 5.4) Published: 12 August 2024

Forming Single-Cell-Derived Colon Cancer Organoid Arrays on a Microfluidic Chip for High Throughput Tumor Heterogeneity Analysis.

Zihe Chen, Jueming Chen, Dongguo Lin, Hui Kang, Yanzhang Luo, Xiaogang Wang, Lihui Wang, Dayu Liu

Single-cell-derived tumor organoids (STOs) possess a distinct genetic background, making them valuable tools for demonstrating tumor heterogeneity. In order to fulfill the high throughput demands of STO assays, we have developed a microfluidic chip containing 30 000 microwells, which is dedicated to a single cell culture approach for selective expansion and differential induction of cancer stem cells. The microwells are coated with a hydrophilic copolymer to eliminate cell adhesion, and the cell culture is supported by poly(ethylene glycol) (PEG) to establish a nonadhesive culture environment. By utilizing an input cell density of 7 × 103·mL-1, it is possible to construct a 4000 single cell culture system through stochastic cell occupation. We demonstrate that the addition of 15% PEG10000 in the cell culture medium effectively prevents cell loss while facilitating tumor stem cell expansion. As were demonstrated by HCT116, HT29, and SW480 colon cancer cells, the microfluidic approach achieved a STO formation rate of ~ 20%, resulting in over 800 STOs generated from a single culture. Comprehensive analysis through histomorphology, immunohistochemistry, drug response evaluation, assessment of cell invasion, and biomarker detection reveals the heterogeneity among individual STOs. Specifically, the smaller STOs exhibited higher invasion and drug resistance capabilities compared with the larger ones. The developed microfluidic approach effectively facilitates STO formation and offers promising prospects for investigating tumor heterogeneity, as well as conducting personalized therapy-focused drug screening.

Analytical Chemistry (IF 6.7) Published: 17 July 2024

Rapid Detection of Uropathogens Using an Integrated Multiplex Digital Nucleic Acid Detection Assay Powered by a Digital-to-Droplet Microfluidic Device.

Yang Xie, Zhenhua Chen, Dongyang Cai, Dezhi Huang, Enqi Huang, Xiao Yang, Ting Zhang, Hongting Wen, Yu Wang, Meng Zhao, Dayu Liu, Banglao Xu

The digital nucleic acid detection assay features the capability of absolute quantitation without the need for calibration, thereby facilitating the rapid identification of pathogens. Although several integrated digital nucleic acid detection techniques have been developed, there are still constraints in terms of automation and analysis throughput. To tackle these challenges, this study presents a digital-to-droplet microfluidic device comprising a digital microfluidics (DMF) module at the bottom and a droplet microfluidics module at the top. Following sample introduction, the extraction of nucleic acid and the dispensation of nucleic acid elution for mixing with the multiple amplification reagents are carried out in the DMF module. Subsequently, the reaction droplets are transported to the sample inlet of the droplet microfluidic module via a liquid outlet, and then droplet generation in four parallel units within the droplet microfluidics module is actuated by negative pressure generated by a syringe vacuum. The digital-to-droplet microfluidic device was employed to execute an integrated multiplex digital droplet nucleic acid detection assay (imDDNA) incorporating loop-mediated isothermal amplification (LAMP). This assay was specifically designed to enable simultaneous detection of four uropathogens, namely, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Enterococcus faecalis. The entire process of the imDDNA is completed within 75 min, with a detection range spanning 5 orders of magnitude (9.43 × 10-2.86 × 104 copies

μL-1). The imDDNA was employed for the detection of batched clinical specimens, showing a consistency of 91.1% when compared with that of the conventional method. The imDDNA exhibits simplicity in operation and accuracy in quantification, thus offering potential advantages in achieving rapid pathogen detection.

Analytical Chemistry **(IF 6.7)** Published: 5 August 2024

Automated Droplet Ejection from a Digital Microfluidics Sample Pretreatment Device Enables Batch-Mode Chemiluminescence Immunoassay.

Dezhi Huang, Enqi Huang, Dongyang Cai, Zhenhua Chen, Hongting Wen, Yu Wang, Dachuan Ma, Yao Lu, Xianming Liu, Dayu Liu

Digital microfluidics (DMF) features programmed manipulation of fluids in multiple steps, making it a valuable tool for sample pretreatment. However, the integration of sample pretreatment with its downstream reaction and detection requires transferring droplets from the DMF device to the outside world. To address this issue, the present study developed a modified DMF device that allows automated droplet ejection out of the chip, facilitated by a tailor-designed interface. A double-layered DMF microchip with an oil-filled medium was flipped over, with a liquid infusion port and a liquid expulsion port accommodated on the top working PCB plate and the bottom grounded ITO plate, respectively, to facilitate chip-to-world delivery of droplets. Using chemiluminescent immunoassay (CLIA) as an illustrative application, the sample pretreatment was programmed on the DMF device, and CLIA droplets were ejected from the chip for signal reading. In our workflow, CLIA droplets can be ejected from the DMF device through the chip-to-world interface, freeing up otherwise occupied electrodes for more sample pretreatment and enabling streamlined droplet microreactions and batch-mode operation for bioanalysis. Integrated with these interfacing portals, the DMF system achieved a single-channel throughput of 17 samples per hour, which can be further upscaled for more productive applications by parallelizing the DMF modules. The results of this study demonstrate that the droplet ejection function that is innovated in a DMF sample pretreatment microsystem can significantly improve analytical throughput, providing an approach to establishing an automated but decentralized biochemical sample preparation workstation for large-scale and continuous bioanalysis.

专家简介：

委员：李刚 教授



重庆大学光电工程学院，教授，博士生导师。南开大学，理学学士；清华大学，理学硕士；中国科学院大学，微电子学与固体电子学专业，工学博士。主要从事生物微机电系统（BioMEMS）和微流控技术方面的研究，研究内容包括 BioMEMS 工艺、器件和系统以及微流控技术及应用等，近年来研究重点聚焦于基于微流控技术的简易低成本微型诊疗设备、蛋白质结晶微系统和基于 MEMS 技术的神经-电子接口器件等三方面。自 2005 年以来，先后主持和参与了国家 973 计划课题 2 项、863 目标导向项目子课题 1 项、863 前沿探索项目 1 项、中科院科研装备研制项目 2 项、国家自然科学基金面上项目 3 项、上海市科委项目 4 项、重庆市科委项目 2 项，项目总经费近二千万元。至今共发表研究论文 100 余篇（其中 SCI 一区 14 篇）， 申请发明专利 52 项（其中授权 35 项），参编教材一部、专著一部。

Biosensors **(IF 4.9)** Published: 21 February 2024

Complete prevention of bubbles in PDMS-based digital PCR chip with a dual-function cavity.

Shiyuan Gao, Tiegang Xu, Lei Wu, Xiaoyue Zhu, Xuefeng Wang, Ying Chen, Gang Li, Xinxin Li

In a chamber-based digital PCR (dPCR) chip fabricated with polydimethylsiloxane (PDMS), bubble generation in the chambers at high temperatures is a critical issue. Here, we found that the main reason for bubble formation in PDMS chips is the too-high saturated vapor pressure of water at an elevated temperature. The bubbles should be completely prevented by reducing the initial pressure of the system to under 13.6 kPa to eliminate the effects of increased-pressure water vapor. Then, a cavity was designed and fabricated above the PCR reaction layer, and Parylene C was used as a shell covering the chip. The cavity was used for the negative generator in sample loading, PDMS degassing, PCR solution degassing in the digitization process and water storage in the thermal reaction process. The analysis was confirmed and finally achieved a desirable bubble-free, fast-digitization, valve-free and no-tubing connection dPCR.

ACS Applied Materials & Interfaces **(IF 8.3)** Published: 8 May 2024

Controllable Fabrication of Highly Ordered Spherical Microcavity Arrays by Replica Molding of In Situ Self-Emulsified Droplets.

Xue Han, Qi Zhang, Guoyuan Zhang, Bangyong Sun, Lei Wu, Gang Li

Ordered spherical hollow micro- and nanostructures hold great appeal in the fields of cell biology and optics. However, it is extremely challenging for standard lithography techniques to achieve spherical micro-/nanocavities. In this paper, we describe a simple, cost-effective, and scalable approach to fabricate highly ordered spherical microcavity arrays by replica molding of in situ self-emulsified droplets. The in situ self-emulsion involves a two-step process: discontinuous dewetting-induced liquid partition and interfacial tension-driven liquid spherical transformation. Subsequent replica molding of the droplets creates spherical microcavity arrays. The shapes and sizes of the microcavities can be easily modulated by varying the compositions of the droplet templates or utilizing an osmotically driven water permeation. To demonstrate the utility of this method, we employed it to create a spherical microwell array for the mass production of embryoid bodies with high viability and minimal loss. In addition, we also demonstrated the optical functions of the

generated spherical microcavities by using them as microlenses. We believe that our proposed method will open exciting avenues in fields ranging from regenerative medicine and microchemistry to optical applications.

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 11 June 2024

A syringe-driven PicoArray device for rapid isolation and quantification of foodborne Salmonella.

Sa Yang , Tianbao Hu , Qi Zhang , Bangyong Sun , Zhiyou Qin , Kaiyuan Zheng , Yanwu Liu , Gang Li

Rapid and accurate detection of pathogenic in food and environmental sources is of paramount importance to protect public health from salmonellosis. However, most current assays are labor-intensive, time-consuming, and require expensive instruments and experienced operators. In this work, we developed a PicoArray-based colony-forming unit (CFU) quantification system for rapid and ultrasensitive detection. To enable on-site detection, we employed syringe-vacuum-assisted sample loading and oil-induced sample digitization to stochastically confine single bacteria in the picoliter-level wells of the PicoArray device (containing 40,233 wells). Such a single bacterial confinement enables the isolation and characterization of individual bacteria from a large population. In addition, the confinement of bacteria in small volumes allows rapid accumulation of metabolites, thereby eliminating the pre-incubation step and reducing the time required to detect bacteria. By combining it with a selective medium for the isolation of and a fluorescent redox indicator (, resazurin) to facilitate the detection of individual microcolonies, the PicoArray device can rapidly and precisely detect . As a proof-of-concept, we demonstrated the ability of our platform for rapid, sensitive, and specific detection of in spiked milk samples. Our platform offers the possibility of close monitoring of pathogens in food or drinks at the consumer end because it allows a non-trained operator to detect foodborne pathogens in the clinically relevant range in the home setting.

Sensors and Actuators A: Physical **(IF 4.2)** Published: 16 October 2024

A handheld, wide-range pressure pump for portable microfluidic applications.

Bai, Yansong; Yu, Xingjiang; Han, Xue; Liu, Yanwu; Li, Gang

Pumping is an indispensable operation in microfluidic applications. Numerous simple pumps have been developed to improve the portability of microfluidic systems, but they generally have poor controllability, short duration working time, and narrow pressure range, which compromises the functionality of portable microdevices. To address these limitations, we present a novel handheld, wide-range pressure pump that utilizes a disposable mini gas cylinder as a pressure source and a porous PDMS film as a flow-rate regulator. Specifically, by incorporating a set of parallel porous PDMS films with varying porosity, sectional area, and thickness into the pump system, and selectively switching between the branch flow circuits containing these porous PDMS films, we are able to finely regulate the flow rate of air released from the mini gas cylinder. This capability enables precise control of the pumping pressure applied to microfluidic devices over a wide range, thereby governing the fluid flow rate to accommodate different applications. The compact and lightweight nature of our pressure source renders this pump system particularly advantageous for field-portable microfluidic applications. Additionally, we demonstrate its capabilities through the performance of well-established microfluidic experiments, including concentration gradient generation and emulsion droplet production. We firmly believe that the compactness, operational simplicity, and disposability of our pump will greatly facilitate the widespread adoption of microfluidic technologies, particularly in point-of-care diagnostics and resource-limited settings.

专家简介：

委员：骆广生 教授



清华大学化学工程系教授，教育部长江学者，清华微化工技术方向创始人和分离科学与技术学术带头人，长期从事微尺度流动化学、微化工技术、分离科学与技术、多相流动与传递、粉体材料制备等研究。致力于微化工理论体系构建和微化工技术从概念到工业应用的突破，揭示界面力、粘性力等对多相微分散体系的调控机制，发展基于剪切力调控的微分散方法和设备，分析微分散过程中动态界面张力的变化规律，研究探索微尺度混合、传递和反应基本规律并建立数学模型，发展分离和反应过程强化新方法，提出微设备放大和微化工系统集成理论与方法，发明微槽式、微滤膜式、多重孔径微筛孔式、微筛孔阵列式、微元件组合式等多种微化工设备，突破多项微化工技术产业应用的重大难题，在国际上率先实现微化工技术在万吨级湿法磷酸净化、酸团萃取、纳米碳酸钙制备、溴化丁基橡胶合成、橡胶促进剂合成等的产业化应用。在核心刊物上发表论文 420 余篇，获授权发明专利 100 余项，获国家技术发明二等奖和科技进步二等奖各 1 项、以及省部委科技奖励 9 项。任中国化工学会和中国颗粒学会常务理事，国务院学位委员会学科评议组化学工程与技术组成员，入选英国皇家化学会会士、中国化工学会会士、国际标准委员会微气泡分委会成员、国际微反应技术会议学术委员、国际溶剂萃取委员会国际委员。任 CJChE 执行主编和 Particuology、《化工学报》、《中国科学－化学》、Chemical Engineering Journal、Reaction Chemistry and Engineering、Separation and Purification Technology、Journal of Flow Chemistry 等多个杂志的编委。

Nature Communications **(IF 14.7)** Published: 29 January 2024

Efficient Conversion of Propane in a Microchannel Reactor at Ambient Conditions.

Chunsong Li , Haochen Zhang , Wenxuan Liu , Lin Sheng , Mu-Jeng Cheng , Bingjun Xu , Guangsheng Luo , Qi Lu

The oxidative dehydrogenation of propane, primarily sourced from shale gas, holds promise in meeting the surging global demand for propylene. However, this process necessitates high operating temperatures, which amplifies safety concerns in its application due to the use of mixed propane and oxygen. Moreover, these elevated temperatures may heighten the risk of overoxidation, leading to carbon dioxide formation. Here we introduce a microchannel reaction system designed for the oxidative dehydrogenation of propane within an aqueous environment, enabling highly selective and active propylene production at room temperature and ambient pressure with mitigated safety risks. A propylene selectivity of over 92% and production rate of 19.57 mmol mCu−2 h−1 are simultaneously achieved. This exceptional performance stems from the in situ creation of a highly active, oxygen-containing Cu catalytic surface for propane activation, and the enhanced propane transfer via an enlarged gas-liquid interfacial area and a reduced diffusion path by establishing a gas-liquid Taylor flow using a custom-made T-junction microdevice. This microchannel reaction system offers an appealing approach to accelerate gas-liquid-solid reactions limited by the solubility of gaseous reactant.

Chemical Engineering Science **(IF 4.1)** Published: 5 March 2024

Hydrodynamics of gas-liquid microfluidics: A review.

Lin Sheng , Yu Chang , Junjie Wang , Jian Deng , Guangsheng Luo

Gas-liquid multiphase process occupies a significant part in the chemical industry, and the emerging gas–liquid microfluidic technology provides a highly efficient and controllable tool for gas–liquid systems such as chemical product synthesis, gas separation, and environmental protection. To point out the microscale gas–liquid multiphase process from the fundamental study to its utilization, this review mainly focuses on advances in the hydrodynamics of the gas–liquid microdispersion and microflow for the design of the gas–liquid microfluidic device. The progress of the gas–liquid flow pattern is first introduced, and then the microdispersion in both single-channel and multi-channel are summarized from the bubble size prediction model and operating conditions. Besides, the microflow characteristic of bubble movement velocity and pressure drop in a single-channel and flow distribution in multi-channels for scaling-up are presented, and the design procedure of gas–liquid microreactors is proposed. Finally, a summary and perspective are provided.

Synthesis **(IF 2.04)** Published: 6 March 2024

Gas–Liquid Microchemical Oxidation for Continuous Synthesis Processes: A Short Review.

Yu Chang, Yuyang Xing, Jian Deng, Zifei Yan, G. Luo

Gas–liquid oxidation processes, despite their wide application in the chemical industry, still pose considerable safety concerns. Microchemical technology has received high recognition for its intrinsic safety performance and process-intensification capability in hazardous reactions. This Short Review offers a comprehensive summary on how microchemical technology can be employed to achieve gas–liquid oxidation processes for continuous synthesis of chemicals in a safe, efficient, and controlled manner. Herein, we discuss the key aspects of gas–liquid dispersion and hydrodynamics, as well as mass transfer characteristics on microscale, and present representative gas–liquid oxidation cases in microflow reactors. Finally, the current challenges in industrial applications and potential academic research directions are presented.1 Introduction2 Microbubble Generation Technology for Gas–Liquid Oxidation Reactions3 Hydrodynamic and Mass-Transfer Characteristics of Gas–Liquid Oxidation Microreactors4 Gas–Liquid Oxidation Reactions in Microreactors5 Conclusion and Outlook.

Chemical Engineering Journal **(IF 13.3)** Published: 3 May 2024

Continuous Synthesis of Calcium Hydrogen Phosphate Dihydrate (DCPD) in an Annular Rotating Flow Loop Reactor.

Tianyao Tang , Jiaxin Tian , Jian Deng , Guangsheng Luo

The synthesis of calcium hydrogen phosphate dihydrate (DCPD) involves a gas–liquid-solid three-phase slurry system that poses challenges for precise control using traditional batch reactors to produce crystals with controlled morphologies and particle sizes. In this study, an annular rotating flow loop reactor (ARLR) was developed to continuously synthesize DCPD. The unique internal loop and annular rotating flow field of the reactor delivered exceptional plug-flow characteristics, ensuring that the obtained DCPD exhibited a controlled morphology and particle size. The morphology of DCPD was adjusted to be bowknot-shaped (BS) agglomerate crystals, reaching a length of 120 μm and a D50 size of 70 μm. The ARLR can achieve long-term stable operation with high-solid holdup slurries, outputting up to 125 g/h by maintaining precise and controllable flow and mixing conditions. Notably, ARLR marked a significant advancement in processing high-solid-holdup slurries, offering the adaptability to adjust the geometric design for various slurry systems and forecasting promising prospects.

Separation and Purification Technology **(IF 8.1)** Published: 26 June 2024

A Microsystem Based on Micro-Capillary Jetting for Intensifying Countercurrent Extraction with High Phase Ratio.

Qichen Shang , Yu Chang , Junjie Wang , Daiwei Gu , Jian Deng , Chencan Du , Guangsheng Luo

Liquid-liquid extraction can be greatly intensified in microchannel devices. Unfortunately, countercurrent flow is hard to realize at microscale. Meanwhile the microdroplet extraction efficiency is still low when the phase ratio is high. Micro-capillary jetting as a new technology for microdispersion can produce microdroplets with narrow size distribution without the restriction of phase ratio. In this work, an integrated microsystem of the micro-capillary jetting for microdroplet generation with the liquid–liquid countercurrent flow in a millimeter column has been developed, and the countercurrent extraction based on microdroplet under high phase ratio was successfully realized. More than 3 theoretical stages within 40 cm were achieved under the phase ratio of 50 ~ 90 for H2O2 extraction. This paper systematically reports the microdispersion, flow characteristics and extraction performances of the microsystem. It means a lot for future intensification of the countercurrent extraction with high phase ratio.

Chemical Engineering Journal **(IF 13.3)** Published: 3 August 2024

Liquid-liquid Addition Reaction of Ethylene Oxide with Hydrazine Hydrate in Microreactors: Kinetics and Process Optimization.

Haiyun Ma , Lixia Yang , Chaoqun Yao , Shuainan Zhao , Fengjun Jiao , Guangsheng Luo , Guangwen Chen

The addition reaction of ethylene oxide (EO) and hydrazine hydrate (N2H4·H2O) to β-hydroxyethyl hydrazine (HEH) is an important process for the synthesis of hydrazine-derived monopropellant in the aerospace industry. Due to the complexity of this reaction mechanism, it is difficult to reduce the formation of byproducts and efficiently obtain pure HEH. Hence it is necessary to investigate process behavior and establish kinetic network for further optimization. Here a continuous microflow system was developed to systematically investigate the synthesis of HEH under high pressure in the liquid–liquid form. A simple and effective pre-column derivatization method was applied to characterize and quantify the product. Subsequently, a thorough optimization of parameters, including N2H4·H2O concentration, molar ratio (N2H4·H2O/EO), temperature and reaction time, was conducted. Additionally, response surface methodology was employed to optimize the reaction conditions, illuminating the intricate interactions among the specified variables and achieving a high HEH yield of 96.97 %. Finally, a kinetic model was established, and the activation energies for the main reaction and side reaction were measured to be 38.31 kJ·mol−1 and 44.94 kJ·mol−1, respectively. This kinetic model can enable the accurate determination of kinetic parameters and provide guidance for the process intensification of this EO addition reaction.

Industrial & Engineering Chemistry Research **(IF 4.3)** Published: 14 August 2024

Controllable Synthesis of Porous 1T-Mos2 with Large Surface Area Via Continuous Hydrothermal System.

Zhiyuan Yu, Tianyi Huang, Shafqat Ullah, Yujun Wang, Guangsheng Luo

1T-phase MoS2, a versatile two-dimensional transition-metal dichalcogenide, is typically synthesized using a one-pot hydrothermal method. However, inadequate control of the sulfurization, reduction, and crystallization processes in the autoclave leads to multilayer 1T-MoS2 with high crystallinity, a small surface area, and few defects. Considering the aforementioned issues, a two-stage microreactor continuous hydrothermal flow synthesis (CHFS) system coupled with accurate control and rapid processing is used to prepare 1T-MoS2 with abundant voids and a large surface area under 250 °C and 4.0–4.5 MPa. And density functional theory calculations reveal that nitrogenous species, acting as reductants and electron donors, lower the energy of 1T-MoS2 by intercalation and surface adsorption, facilitating its swift synthesis within the presulfurization stage for 10 min and reduction stage for 24 min. The precisely controlled synthesis of porous 1T-MoS2, originating from prenucleation clusters, results in a large surface area of 201.5 m2/g, concentrated mesopores of 2–5 nm, and a pore volume of 0.58 cm3/g. Moreover, a significant transformation from the 1T to the 2H phase is prevented by rapid cooling downstream of the CHFS system.

Chemical Engineering Journal (IF 13.3) Published: 21 August 2024

Large-scale Production of Cefazolin in a Microreactor with a Low Impurity Content and High Yield.

Yongqi Pan , Shenyuan Zhao , Lijie Wang , Libin Zhang , Mengde Yang , Baojun Wei , Guogang Hu , Shafqat Ullah , Yujun Wang , Guangsheng Luo

Cefazolin is crucial in the field of healthcare because of its efficacy against bacterial diseases, but trace amounts of polymer impurities produced during synthesis may cause severe allergic reactions. In this work, an efficient system based on a membrane dispersion microreactor was designed for scalable cefazolin production with a high yield and low impurity content. At a production scale of 200 kg, the yield could reach 90 %, and the polymer impurity content could reach <0.008 %. Density functional theory calculations were used to investigate the formation mechanisms of the polymer impurities. The results revealed that the activation energy of cefazolin ring-opening and substitution reactions decreased by 22.4 kJ/mol and 6.4 kJ/mol respectively under alkaline conditions, resulting in increased polymer content. Computational fluid dynamics simulation indicates that the organic base in the substrate can be rapidly dispersed in the membrane dispersion microreactor, thus avoiding excessive local base concentration. In conclusion, the development of a membrane dispersion microreactor system offers a scalable and efficient method for cefazolin production with significantly lower polymer impurity content, thereby addressing a critical challenge in antibiotic synthesis and ensuring safer and more reliable healthcare applications.

Chemical Engineering Journal (IF 13.3) Published: 1 September 2024

A Micro-Capillary Jetting Technology for Liquid-Liquid Microdispersion with Narrow Size Distribution.

Qichen Shang, Lin Sheng, Daiwei Gu, Jian Deng, Guangsheng Luo

Liquid-liquid microdispersion is one of the key foundations for chemical process intensification. However, liquidliquid microdispersion at the conditions of high phase ratio and high volume flow rate remains a problem and new microdispersion technology is highly required. Based on the microscale effect of the liquid jet, we developed the micro-capillary jetting technology. It can produce microdroplets (250-500 mu m) with narrow size distribution (CV approximate to 10-20 %) in a wide range of physical properties with large capacity and little cost without the restriction of phase ratio. This paper reports the laws of the micro-capillary jetting technology. The liquid-liquid flow patterns and mechanism are studied, and a precise quantitative model to distinguish different jetting patterns is provided for the first time based on the energy analysis in the microscale. Then important factors including physical properties, dispersion mode and structural parameters are investigated. Accordingly, a mathematical model for the prediction of the average droplet size is established and the energy utilization in the jetting dispersion process is calculated.

Fuel (IF 6.7) Published: 7 September 2024

The Structure Activity Relationship of Promoted La Doped Ni-CeO_2 Catalysts Prepared by Continuous-Flow Microreactor for Low Temperature CO_2 Methanation.

Shafqat Ullah , Yongqi Pan , Qiangqiang Xue , Tianyi Huang , Yizhi Hu , Runping Ye , Yujun Wang , Guangsheng Luo

CO_2 methanation has emerged as a key strategy for its potential uses and ability to alleviate climate change by reducing CO_2 emissions. Herein, we present a controllable and continuous improved coprecipitation catalyst preparation method employing a T-junction microreactor to investigate La doped Ni-CeO_2 catalysts. A series of catalysts was systematically synthesized, with Ni/CeLa (5:5) emerging as the most promising candidate, exhibiting 76 % CO_2 conversion at 250 degrees C and 60.5 mmol/gcat.h space-time yield of methane. Different structural characterization techniques, including in-situ Raman, Quasi in-situ XPS, in-situ DRIFTS, and DFT calculations were employed to unravel the structure activity mechanisms contributing to the enhanced catalytic performance. The findings indicate that the introduction of La as a

dopant reduces particle size, promotes Ni dispersion, and increases interfacial sites. These enriched interfacial sites contribute a pivotal role in facilitating the adsorption and hydrogenation of bicarbonate species, ultimately leading to improved methanation performance. This study not only highlights the efficiency of the La doped Ni-CeO_2 catalyst, but it also gives valuable insights for chemical strategy to improve structure activity relationships and mechanism studies for efficient CO_2 methanation performance.

Chemical Engineering Journal **(IF 13.3)** Published: 12 September 2024

Hierarchically Self-Supporting Porous Ultrathin Films with Aligned Photothermal Nanosheets for Ultrafast Uranium Extraction from Seawater.

Jiayi Ai , Lijuan Feng , Jiacheng Zhang , Xuewen Cao , Guangsheng Luo , Yihui Yuan , Ning Wang

Seawater is the world’ s largest reservoir of uranium and, hence, uranium in seawater is one of the most sustainable sources of nuclear fuel. Poly(amidoxime) (PAO)-based adsorbents hold promise for uranium extraction from seawater but have not been industrialized because of their insufficient uranium extraction efficiency. Herein, hierarchically porous ultrathin PAO films with aligned graphene oxide nanosheets were prepared by Marangoni flow‐driven superspreading and evaluated as adsorbents for uranium extraction from seawater efficiently. The best-performing film exhibited high photothermal conversion, short uranium diffusion path, and excellent salt-shrinkage resistance. These features endow the film with a high uranium adsorption capacity of 10.4 mg g−1 for natural seawater after 10 days, with an ultrafast rate of 1.04 mg g−1 day−1 exceeding those of previously reported recoverable AO-based adsorbents. Given the upscalability of the film fabrication method and regenerability of the developed films, the present study paves the way for uranium of extraction from seawater efficiently.

Chinese Journal of Chemical Engineering **(IF 3.7)** Published: 16 September 2024

A General Pressure Drop Model Based on Liquid Holdup of Gas-Liquid Flow in Micro-Packed Beds.

Junjie Wang, Lin Sheng, Jiang Deng, Guangsheng Luo

The understanding of the gas−liquid flow characteristics in a micro-packed bed reactor is still immature, especially for many gas−organic working systems commonly used in industry. Accordingly, this study proposes a platform to investigate the gas–liquid flow characteristics in a micro-packed bed reactor and presents a unified expression for these characteristics of both organic and aqueous liquid phase. The influence of two-phase flow rate, working solution viscosity, and packing particle size on the liquid holdup and pressure drop were studied. The gas-organic working systems results show that the liquid holdup ranges between 0.5 and 0.8 and pressure drop ranges from 50 to 350 kPa·m–1. In particular, a strong correlation between the two flow characteristics parameters (liquid holdup and pressure drop) was proposed for the first time. Finally, a general pressure drop mathematical prediction model in micro-packed bed were developed.

Chemical Engineering Journal **(IF 13.3)** Published: 15 October 2024

High-throughput Generation of Monodisperse Double Emulsions Via Controllable Symmetric Splitting in Y-shaped Microchannels.

Lin-Ling Fan , Wei Wang , Xiao-Jie Ju , Zhuang Liu , Rui Xie , Jianhong Xu , Guangsheng Luo , Da-Wei Pan , Liang-Yin Chu

To achieve high-throughput generation of monodisperse double emulsions via controllable symmetric splitting, the splitting dynamics of double emulsions in Y-shaped microchannels are systematically investigated by the combination of experimental study and numerical simulation. Four distinct breakup flow patterns of double emulsions splitting are initially identified, namely non-breakup, once uneven breakup, twice uneven breakup and twice even breakup, and the underlying hydrodynamic mechanisms of each flow pattern are further elucidated through the flow field structures and pressure

distributions. The results show that the upstream pressure created by the flow obstruction of continuous phase governs the stable and symmetric splitting of double emulsions in Y-shaped microchannels. Effects of the flowrates of continuous phase, the outer and inner diameters of double emulsions, the physical properties of all the inner, middle and outer fluids as well as the angle of Y-shaped microchannel on the flow pattern transition laws are systematically clarified, and the corresponding universal flow pattern diagrams for predicting the critical boundary for the transition of flow patterns are established. Based on controllable symmetric splitting of double emulsions, three-level splitting microfluidic networks are rationally designed to achieve high-throughput generation of monodisperse double emulsions as well as monodisperse microcapsules via template synthesis. The results in this study not only advance the deep understanding of the breakup dynamics of double emulsions in Y-shaped microchannels, but also offer valuable guidance for the rational design of microfluidic devices for mass production of monodisperse double emulsions, thus providing a significant contribution to the fields of micro-chemical engineering and droplet microfluidics.

***Separation and Purification Technology* (IF 8.1)** Published: 30 October 2024

Process Intensification of Chemical Phosphorus Removal in a Microreaction System.

Qingchuan Chen , Jian Deng , Guangsheng Luo

Serious problems including excessive ferric salt dose, high effluent phosphorus concentration and long handling time are encountered for chemical phosphorus removal by ferric salt in batch processes due to poor mixing performance. In this work, we develop a microreaction system to intensify phosphorus removal process using ferric chloride by achieving rapid mixing. Phosphorus residual is remarkably reduced by optimizing mixing-related factors, including flow rate, contacting mode, device structures and flow rate ratio which is justified by CFD simulation. The results show that phosphorus removal performance is not sensitive to flow rate ratio. Phosphorus residual can be lower than 0.20 mg/L at [P]0 = 6 mg/L, pH = 6.0, Fe/P = 1.8 and residence time = 42.8 s. Compared with batch processes, the microreaction system has several advantages including much lower phosphorus residual, lower ferric salt dose, shorter processing time and larger handling capacity. Moreover, a machine learning model is established to predict the device performance with high accuracy.

***Chinese Journal of Chemical Engineering* (IF 3.7)** Published: 2 November 2024

Controllable synthesis of hydrogen-bonded organic framework encapsulated enzyme for continuous production of chiral hydroxybutyric acid in a two-stage cascade microreactor.

Danyang Zhao, Qiangqiang Xue, Yujun Wang, Guangsheng Luo

Constructing a framework carrier to stabilize protein conformation, induce high embedding efficiency, and acquire low mass-transfer resistance is an urgent issue in the development of immobilized enzymes. Hydrogen-bonded organic frameworks (HOFs) have promising application potential for embedding enzymes. In fact, no metal involvement is required, and HOFs exhibit superior biocompatibility, and free access to substrates in mesoporous channels. Herein, a facile in situ growth approach was proposed for the self-assembly of alcohol dehydrogenase encapsulated in HOF. The micron-scale bio-catalytic composite was rapidly synthesized under mild conditions (aqueous phase and ambient temperature) with a controllable embedding rate. The high crystallinity and periodic arrangement channels of HOF were preserved at a high enzyme encapsulation efficiency of 59%. This bio-composite improved the tolerance of the enzyme to the acid-base environment and retained 81% of its initial activity after five cycles of batch hydrogenation involving NADH coenzyme. Based on this controllably synthesized bio-catalytic material and a common lipase, we further developed a two-stage cascade microchemical system and achieved the continuous production of chiral hydroxybutyric acid (R-3-HBA).

***AIChE Journal* (IF 3.5)** Published: 13 November 2024

General Prediction Models for Void Fraction and Specific Surface Area of Gas–liquid Microflows.

Lin Sheng, Chenglin Zheng, Yu Chang, Jian Deng, Guangsheng Luo

The flow characteristics of void fraction and specific surface area are important to predict the mass transfer and reaction performances in gas-liquid microreactors. However, the models and trends for the two parameters in different flow patterns remain ununified and insufficient. Accordingly, this work first time studies the void fraction and specific surface area in a very wide flow pattern range (Taylor, short bubble, bubbly, and bubble swarm flow). The results show that at the same gas-liquid flow rates, the void fraction decreases with bubble size in Taylor and short bubble flow but is totally opposite in bubbly and bubble swarm flow. Importantly, the variation of specific surface area with bubble size is independent of the flow pattern and decreases with bubble size. Finally, based on bubble size, two general models for the two parameters are developed. This work provides a new direction for the unification of flow characteristics.

***Industrial & Engineering Chemistry Research* (IF 3.8)** Published: 19 November 2024

A Gas Kinetic Energy Based Strategy for the Accurate Regulation of Taylor Bubble Length in Flow-Focusing Microchannels.

Lin Sheng, Junjie Wang, Jian Deng, Guangsheng Luo

Accurate regulation of the bubble length determines the microchannel reaction performance, but the existing methods focus on the construction of complex bubble generation structures with high operating requirements. Accordingly, for the flow-focusing microchannel, this study proposes a convenient method that varies the gas inlet kinetic energy to adjust the bubble length. The results show that the gas inlet kinetic energy can be easily regulated by changing the gas channel width, and the bubble size is markedly reduced via expanding the gas channel width, which for the first time breaks the traditional cognition that the bubble size becomes large with the gas inlet width in the T-junction. Besides, the reason behind the formation of smaller bubbles in the flow-focusing with a wider gas channel is jointly revealed by analyzing the two-phase interface behaviors in flow-focusing and T-junction microchannels. Especially, a new variable (the liquid equivalent residence time) is proposed to describe the interaction between the two phases, and the design criterion for the gas inlet size is proposed to reach the minimal bubble length in flow-focusing microchannels. Finally, considering the gas inlet kinetic energy effect, a universal bubble length model containing the ratio of Weber numbers for gas and liquid and capillary number for liquid is developed, which shows its excellent performance for the flow-focusing microchannels used in this work and other studies.

***Biomicrofluidics* (IF 2.6)** Published: 20 November 2024

Data-driven Models for Microfluidics: A Short Review.

Yu Chang, Qichen Shang, Zifei Yan, Jian Deng, Guangsheng Luo

Microfluidic devices have many unique practical applications across a wide range of fields, making it important to develop accurate models of these devices, and many different models have been developed. Existing modeling methods mainly include mechanism derivation and semi-empirical correlations, but both are not universally applicable. In order to achieve a more accurate and general modeling process, the use of data-driven modeling has been studied recently. This review highlights recent advances in the application of data-driven modeling techniques for simulating and designing microfluidic devices. First, it introduces the application of traditional modeling approaches in microfluidics; subsequently, through different database sources, it reviews studies on data-driven modeling in three categories; and finally, it raises some open issues that require further investigation.

***Industrial & Engineering Chemistry Research* (IF 3.8)** Published: 28 November 2024

Fast Reliable Determination of Gas-Liquid Mass Transfer in Micropacked Beds Via In-line Direct Measuring of Pressure Drop.

Junjie Wang, Lin Sheng, Jian Deng, Guangsheng Luo

Current methods for determining gas-liquid mass transfer or reaction performance in micropacked bed reactors (μ PBRs) are inefficient and complex, hindering their application in high throughput screening, process optimization, and online monitoring. New fast determining technology is highly required. This study introduced an innovative soft measurement technology for reliable determining of gas – liquid mass transfer by directly correlating pressure drop with mass transfer coefficients through online measurement. We systematically analyzed the effect of various factors, including two-phase flow rate, packing particle size, front-end predispersion, gas composition, and liquid concentration on gas – liquid flow pressure drop and mass transfer in μ PBRs. A predictive mathematical model for mass transfer coefficients was successfully established, and its capacity was successfully validated in the hydrogenation experiments within the Riedl – Pfleiderer process. This technology offers a fast, reliable, and real-time online approach for process monitoring, process optimization, and rapid catalyst screening within μ PBRs.

Chemical Engineering Science **(IF 4.1)** Published: 30 November 2024

Laminar Jet Flow at the Microscale: the Characteristic Sizes and the Wave Development.

Qichen Shang, Daiwei Gu, Lin Sheng, Yu Chang, Jian Deng, Guangsheng Luo

Laminar jet flow is an underlying phenomenon used to generate droplets efficiently. However, its hydrodynamics at the microscale remains unknown. This work focuses on the scale effect. We innovatively propose the difference between the jet at the microscale and that at the regular scale is not in the wave development but in the regime of flow pattern, and it's much more stable at the microscale. The characteristic effect at the microscale due to the intensified gas/liquid/solid–liquid interaction is first reported. The variations of characteristic sizes and hydrodynamics with the kinetic energy, physical property, and structural size at the microscale are analyzed by introducing two key parameters − wave velocity and wave numbers, which are first proposed. The result shows that the kinetic energy determines the hydrodynamics. Viscosity and interfacial tension significantly affect the microscale laminar jet. Using wave numbers, Tyler's equation is modified, guiding the design of effective microdroplet-generation devices.

Chemical Engineering Science **(IF 4.1)** Published: 5 December 2024

Gas-liquid Countercurrent Flow Characteristics in a Microbubble Column Reactor.

Yu Chang, Qichen Shang, Lin Sheng, Jian Deng, Guangsheng Luo

Countercurrent flow mode is widely utilized in many chemical unit operations due to its effective enhancement of mass transfer driving force. While the microbubble column reactor has garnered attention for its substantial gas–liquid specific surface area and fast mass transfer rate under the concurrent flow condition, countercurrent flow microbubble column reactors remain relatively underexplored. Consequently, in this study a novel microbubble generator device featuring gas–liquid co-crossing a microfiltration membrane was developed. This device could generate microbubbles with narrow size distribution, and proved suitable for integration into the countercurrent microbubble column reactor. Further investigation ensued to elucidate the operational principles of this dispersion method. Finally, the hydrodynamic behavior of the countercurrent microbubble column reactor was examined. Remarkably, a gas–liquid-specific surface area 2300 m2/m3 was reached, surpassing that of conventional bubble column reactors by a significant margin. New gas–liquid chemical processes and process intensification technologies could be developed accordingly.

Chemical Engineering and Industrial Chemistry **(IF 5.9)** Published: 9 December 2024

Chat-Microreactor: A Large-Language-Model-Based Assistant for Designing Continuous Flow Systems.

Yongqi Pan, Qinfan Xiao, Fangyu Zhao, Zhenhao Li, Jianyang Liu, Shafqat Ullah, Kang Hui Lim, Tianyi Huang, Zhiyuan

Yu, Claudia Li, Dingyan Zhang, Qiangqiang Xue, Qiang Chen, Sibudjing Kawi, Yujun Wang, Guangsheng Luo

Continuous flow in microchannels play pivotal roles in advancing automated chemical synthesis. However, frequent multiphase reactions pose key challenges for designing reactors that efficiently disperse phases. Although effort has been directed toward automating development processes, the unique nature of each existing study offers limited opportunities for generalization; consequently applying this knowledge to new microreactor designs is difficult. In this study, we introduce a self-optimizing workflow that uses large language models (LLMs) to extract key microreactor-system parameters, such as density, velocity, and Capillary number, from the literature. Minimal training led to a reduction in extraction time from 24 to 16 s, with the collected data processed by ensemble learning models delivering F1 scores greater than 70% when classifying flow patterns. Through interpretability analysis, we confirmed the machine learning model's alignment with human expertise. We then applied the model to an oil-water dispersion system for controlled alumina microsphere preparation and a piperacillin synthesis system, achieving accuracy rates of 83% and 94%, respectively. This study offers synthetic chemists an LLM-based tool for the development of microreactor systems, thereby pioneering the use of machine learning in literature-sparse fields.

***Separation and Purification Technology* (IF 8.1)** Published: 25 December 2024

Asymmetric Flow-Focusing: A Novel Microreactor Operation Procedure for Making Smaller Microbubbles.

Lin Sheng, Junjie Wang, Jian Deng, Guangsheng Luo

Production of smaller bubbles benefits the promotion of the mass transfer performance in microreactors, but the existing methods mainly focus on designing complex structures. This work proposes a novel asymmetric operation procedure of the flow-focusing microreactor to directly prepare smaller microbubbles without the structure modification. It shows that under a given total liquid volumetric flux, the microbubble size could be obviously reduced with the increase in the liquid volumetric flux deviation between two side inlets. Importantly, the microbubble size can be decreased by 1 fold and the minimal bubble diameter is lower to 25% of the channel width, which breaks the microbubble size bottleneck from the standard symmetric operation procedure of the flow-focusing microreactor. Besides, the inherent reason behind the excellent performance of the asymmetric operation procedure is revealed from the velocity field profile and the interface evolution behavior. Finally, semi-empirical prediction models are proposed for the bubble size. This work breaks the symmetric operation procedure of the flow-focusing microreactor that lasted for two decades and provides a new process intensification strategy for the microbubble preparation.

***AIChE Journal* (IF 3.5)** Published: 26 December 2024

V-shaped Pressure Drop Curve of Microbubble Swarm Flow in a Microchannel.

Lin Sheng, Junjie Wang, Chenglin Zheng, Jian Deng, Guangsheng Luo

Precise prediction of the pressure drop in a gas–liquid microreactor is significant for reactor design; however, the understanding on the pressure drop in the microbubble swarm flow in microreactors is limited. Accordingly, this is the first study in which the rules for the pressure drop in the microbubble swarm flow over a wide range of void fractions are investigated. At a given gas flow rate, the pressure drop first decreases with the liquid flow rate and then gradually increases and almost occurs at a void fraction of 0.20; this is named as the V-shaped pressure drop curve of microbubble swarm flow. In addition, the microbubble size, specific surface area, and void fraction are tested to reveal the mechanism underlying this new phenomenon. Finally, the two regions of separated and homogeneous flows are divided, and semi-empirical prediction models are developed to quantify the pressure drop in the microbubble swarm flow.

专家简介：

委员：刘宏 教授



东南大学青年首席教授，生物电子学国家重点实验室副主任。入选国家“万人计划”中青年科技创新领军人才、国家“青年千人”、江苏省“双创人才”、“双创团队”领军人才、“六大人才高峰”和南京市高层次创业人才引进计划。担任中国电子学会标准化工作委员会委员以及生物医学电子学分会副秘书长。2009 年本硕毕业于南京大学，后获得美国德克萨斯大学奥斯汀分校全额奖学金资助，并于 2012 年获得博士学位。长期从事现场快速检测（POCT）方法和器件的基础与应用研究，着眼于医疗器械领域“卡脖子”的关键技术问题。

Sensors and Actuators B: Chemical (IF 8.0) Published: 15 December 2024

Wearable microfluidic electrochemical sensor integrated with iontophoresis for non-invasive sweat ketone monitoring.

Yixin Shen , Gangsheng Chen , Yi Chen , Yakun Gao , Chao Hou , Kylin Liao , Biao Ma , Hong Liu

The detection of β-hydroxybutyrate (β-HB) is crucial for the rapid diagnosis of diabetic ketoacidosis and health management. However, daily monitoring of dynamically changing β-HB concentrations is challenging and still limited to laboratory settings or painful and invasive measurements. Herein, we report a wearable electrochemical sensor integrated with iontophoresis for non-invasive monitoring of sweat β-HB. This device can actively stimulate the skin to induce sweat by iontophoresis, and the sweat is controllably collected and transported to the sensing area through the microfluidic channel. The sweat β-HB was measured through an electrochemical oxidation reaction mediated by the generated nicotinamide adenine dinucleotide, which can achieve fast response analysis of sweat β-HB within 40 sec and a low detection limit of 10 μM. We also used this sensor to monitor the sweat β-HB levels in a volunteer experiencing the ketogenic diet and the sweat and blood β-HB levels exhibited high correlation. We believe this wearable sensor capable of on-demand and noninvasive detection of sweat β-HB shows a wide application prospect in clinical medicine and home healthcare.

专家简介：

委员：林建涵 教授



中国农业大学信息与电气工程学院教授、博导、副院长，于 2001、2004 和 2007 年在中国农业大学分别获得电子工程学士学位、农业工程硕士学位和农业工程博士学位。2007 年 10 月至 2009 年 5 月，在美国阿肯色大学做博士后，从事生物传感器研究。2009 年 6 月至 2011 年 6 月，继续在阿肯色大学担任助理研究员。2011 年 7 月，受聘于美英特生物仪器公司，担任技术总监。2012 年 9 月，以高层次人才引进到中国农业大学工作至今。2017 年 12 月，晋升教授。

在科研方面，林建涵教授长期从事病原微生物快速检测技术与装备研究，研究方向主要包括生物传感器、微流控芯片、免疫磁分离等。近 5 年，以唯一通信作者在工程、化学、生物、医学、食品、兽医等专业领域国际顶级期刊发表高水平 SCI 论文 70 余篇，其中 1 篇自然指数，42 篇 ESI 前 10%（22 篇 IF>10）,11 篇前 20%，2 篇高被引，3 篇封面，累计他引超过 2 千次，并授权发明专利十余项。

Chemical Engineering Journal **(IF 13.3)** Published: 18 January 2024

A Digital Platform for One-Pot Signal Enhanced Foodborne Pathogen Detection Based on Mesophilic Argonaute-Driven Polydisperse Microdroplet Reactors and Machine Learning.

Junping Wen , Minjie Han , Niu Feng , Guoxun Chen , Feng Jiang , Jianhan Lin , Yiping Chen

Foodborne pathogens endanger human health. Therefore, sensitive and accurate detection assays are key for their prevention and control. Microdroplet digital nucleic acid platforms can achieve single-molecule sensitivity in the presence of specialized instrumentation for generating homogenized monodisperse droplets, expensive thermal cyclers, high temperature-resistant reagents, and time-consuming multistep operations in the lab. Argonaute (Ago), an emerging next-generation gene editing tool, can be used for the detection of pathogen genetic information. Current reports mainly adopt the high temperature-dependent thermophilic Ago in stepwise nucleic acid detection, which hinders its applications in ultrasensitive digital detection. Here, we expressed and purified the mesophilic Clostridium butyricum Argonaute (CbAgo) and developed a polydisperse microdroplet reactors-assist asymmetric recombinase polymerase amplification driven CbAgo report digital detection platform (DRAGON). It realized the signal-enhanced nucleic acid amplification and CbAgo report compatibility in novel low-cost and ultrafast-prepared polydisperse microdroplet reactors. The microdroplet reactor area and fluorescence intensity were combined to establish a dual parameter-based random forest machine learning model, which achieved high sensitivity (1 CFU/mL) and efficiency (<45 min) for detecting pathogens. This is the first time that mesophilic Ago was used to achieve true sensitive one-step and one-pot low-temperature digital nucleic acid detection. Our system accomplished multiplex detection in one-step and one-pot with a single nuclease which is impossible for CRISPR/Cas system and thermophilic Ago-based stepwise platforms. DRAGON represents the next-generation platform for pathogen detection based on gene editing tools and intelligent digital nucleic acid detection system.

Biosensors and Bioelectronics **(IF 10.7)** Published: 1 February 2024

Deep Learning Enhanced Multiplex Detection of Viable Foodborne Pathogens in Digital Microfluidic Chip.

Han Quan, Siyuan Wang, Xinge Xi, Yingchao Zhang, Ying Ding, Yanbin Li, Jianhan Lin, Yuanjie Liu

Culture plating is worldwide accepted as the gold standard for quantifying viable foodborne pathogens. However, it is time-consuming (1-2 days) and requires specialized laboratory and personnel. This study reported a deep learning enhanced

digital microfluidic platform for multiplex detection of viable foodborne pathogens. The new method used a Time-Lapse images driven EfficientNet-Transformer Network (TLENTNet) to type and quantify the bacteria through spatiotemporal features of bacterial growth and digital enumeration of bacterial culture. First, the bacterial sample was prepared with LB medium and injected into a pre-vacuumed microfluidic chip with an array of 800 microwells to encapsulate at most one bacterium in each well. Then, a programmed sliding microscopic platform was used to scan all microwells every 15 min, capturing time-lapse images of bacterial growth within each microwell. Finally, the TLENTNet was used to facilitate bacterial typing and quantification. Under optimal conditions, this platform was able to detect four bacterial species (S.typhimurium, E. coli O157:H7, S. aureus and B. cereus) with an average accuracy of 97.72% and a detection limit of 63 CFU/mL in 7 h.

Lab on a Chip **(IF 6.1)** Published: 14 April 2024

Multiplex nanozymatic biosensing of Salmonella on a finger-actuated microfluidic chip.

Nana Jin, Fan Jiang, Fengzhen Yang, Ying Ding, Ming Liao, Yanbin Li, Jianhan Lin

A colorimetric biosensor was elaboratively designed for fast, sensitive and multiplex bacterial detection on a single microfluidic chip using immune magnetic nanobeads for specific bacterial separation, immune gold@platinum palladium nanoparticles for specific bacterial labeling, a finger-actuated mixer for efficient immunoreaction and two coaxial rotatable magnetic fields for magnetic nanobead capture (outer one) and magnet-actuated valve control (inner one). First, preloaded bacteria, nanobeads and nanozymes were mixed through a finger actuator to form nanobead-bacteria-nanozyme conjugates, which were captured by the outer magnetic field. After the inner magnetic field was rotated to successively wash the conjugates and push the H2O2-TMB substrate for resuspending these conjugates, colorless TMB was catalyzed into blue TMBox products, followed by color analysis using ImageJ software for bacterial determination. This simple biosensor enabled multiplex Salmonella detection as low as 9 CFU per sample in 45 min.

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 15 April 2024

An eco-friendly and ultrasensitive micro-orifice resistance assay for the detection of Listeria monocytogenes based on calcium carbonate signal probes harvested from discarded eggshells.

Liangqiong Ren, Feng Hong, Niu Feng, Jianhan Lin, Jianlong Wang, Shilong Ruan, Yiping Chen

The development of eco-friendly analytical methods for the detection of foodborne pathogens is of great importance for protecting human health and alleviating environmental pressure. Here, we demonstrate that a material (CaCO3 microparticles) prepared from discarded eggshells can be used as signal probes for micro-orifice resistance assay (MORA) and can be combined with ligation-mediated branching hybridization chain reaction (LB-HCR)-based signal-amplification technique (e-LMORA) for high sensitivity detection of Listeria monocytogenes. This strategy used LB-HCR-induced aggregation of streptavidin-modified CaCO3 microparticles, which were recognized by the particle counter for quantitative analysis of the target DNA. Compared with traditional MORA using polystyrene microspheres as signal probes, CaCO3 microparticles prepared from waste eggshells are more environmentally friendly. The combination of DNA-recognition probe, signal probes, and enzyme-free signal-amplification strategy not only reduces the cost synergistically, but also enables the biosensor to attain high sensitivity (limit of detection = 21 CFU/mL) due to its efficient signal amplification.

Food Chemistry **(IF 8.5)** Published: 22 July 2024

A Multimetallic Nanozyme Enhanced Colorimetric Biosensor for Salmonella Detection on Finger-Actuated Microfluidic Chip.

Fan Jiang, Nana Jin, Lei Wang, Siyuan Wang, Yanbin Li Jianhan Lin

Salmonella screening is essential to avoid food poisoning. A simple, fast and sensitive colorimetric biosensor was

elaborately developed for Salmonella detection on a microfluidic chip through limiting air chambers for precise air control, switching rotary valves for accurate fluid selection, a convergence-and-divergence passive micromixer and an extrusion-and-suction active micromixer for efficient fluid mixing, and immune gold@platinum palladium nanocatalysts for effective signal amplification. The mixture of bacteria, immune magnetic nanobeads and nanocatalysts was first rapidly mixed to form nanobead-bacteria-nanocatalyst conjugates and magnetically separated for enrichment. After washing with water, the conjugates were used to catalyze colorless substrate and blue product was finally analyzed using ImageJ for quantifying bacterial concentration. The finger-actuated microfluidic chip enabled designated control of designated fluids in designated places towards designated directions by simple press-release operations on designated air chambers without any external power. Under optimal conditions, this sensor could detect Salmonella at 45 CFU/mL in 25 min.

Lab on a Chip **(IF 6.1)** Published: 31 July 2024

An all-in-one microfluidic SlipChip for power-free and rapid biosensing of pathogenic bacteria.

Li Xue, Ming Liao, Jianhan Lin

Point-of-care testing of pathogens is becoming more and more important for the prevention and control of food poisoning. Herein, a power-free colorimetric biosensor was presented for rapid detection of Salmonella using a microfluidic SlipChip for fluidic control and Au@PtPd nanocatalysts for signal amplification. All the procedures, including solution mixing, immune reaction, magnetic separation, residual washing, mimicking catalysis and colorimetric detection, were integrated on this SlipChip. First, the mixture of the bacterial sample, immune magnetic nanobeads (IMBs) and immune Au@PtPd nanocatalysts (INCs), washing buffer and H2O2-TMB chromogenic substrate were preloaded into the sample, washing and catalysis chambers, respectively. After the top layer of this SlipChip was slid to connect the sample chamber with the separation chamber, the mixture was moved back and forth through the asymmetrical split-and-recombine micromixer by using a disposable syringe to form the IMB-Salmonella-INC sandwich conjugates. Then, the conjugates were captured in the separation chamber using a magnetic field, and the top layer was slid to connect the washing chamber with the separation chamber for washing away excessive INCs. Finally, the top layer was slid to connect the catalysis chamber with the separation chamber, and the colorless substrate was catalyzed by the INCs with peroxidase-mimic activity to generate color change, followed by using a smartphone app to collect and analyze the image to determine the bacterial concentration. This all-in-one microfluidic biosensor enabled simple detection of Salmonella as low as 101.2 CFU mL-1 within 30 min and was featured with low cost, straightforward operation, and compact design.

Food Chemistry **(IF 8.5)** Published: 4 December 2024

A Press-Actuated Slidable Microfluidic Colorimetric Biosensor for Salmonella Detection Utilizing Nickel Mesh Sheet and MIL-88@Pd/Pt Nanoparticles.

Jing Yuan, Lei Wang, Hong Duan, Siyi Ye, Ying Ding, Yanbin Li, Jianhan Lin

A press-actuated slidable microfluidic colorimetric biosensor was designed for rapid, sensitive and multi-channel detection of Salmonella. The nickel mesh sheet (NMS) modified with capture antibodies was employed for capturing target bacteria, and metal organic frameworks decorated with palladium (Pd) and platinum (Pt) nanoparticles (MIL-88@Pd/Pt NPs) modified with detection antibodies were used for amplifying colorimetric signals. The capture efficiency of the immune NMS reached 83 %, and the detection limit of this colorimetric biosensor was 35 CFU/mL in 20 min. The average recoveries for Salmonella in spiked chicken meats ranged from 92.2 % to 102.5 % with a variation from 3.7 % to 7.2 %. The press-actuated slidable microfluidic chip was elaboratively developed with multiple functions, including mixing, separation, washing, catalysis and detection.

Current Opinion in Food Science (IF 8.9) Published: 22 December 2024

Novel Microfluidic Chips Integrated with Smart Devices for In-Situ Detection of Foodborne Pathogenic Bacteria.

Ruibin Hu, Wen Wang, Qingfeng Zheng, Jianhan Lin, Hua Yang

The in-situ detection of foodborne pathogens at the early stages of infection is crucial for preventing the further spread of pathogens. Currently, integrated microfluidic biosensors, combined with new materials and technologies, are widely used for the rapid detection of various pathogens in point-of-care-testing setting. Herein, we summarize recent advances in microfluidics-based biosensors for in-situ detection of foodborne pathogens, with a focus on sample preprocessing, signal amplification, and the automation and intelligence of devices to improve detection sensitivity and performance. Furthermore, the future outlook of microfluidic biosensor-based assays for foodborne pathogens is also considered. The integrated microfluidic biosensors with convenient, rapid, sensitive and cost-effective can provide a promising platform for early prevention and control of foodborne pathogen contamination.

Journal of Analysis and Testing (IF 5.5) Published: 24 December 2024

Lab-on-a-Syringe Biosensing of Salmonella Using Magnetic Grid Separation with Nanozyme Signal Amplification.

Lei Wang, Meixuan Li, Ai Xu, Yanbin Li & Jianhan Lin

This work aimed to use a syringe as an experimental platform, and Salmonella typhimurium as a research model to develop a simple, cheap, rapid, and disposable optical biosensor. First, an elaborate separator with multiple fluidic channels and high-gradient magnetic fields, consisting of permanent magnets, was 3D printed and installed inside a 10 mL syringe. Then, the mixture of bacterial samples, immune magnetic nanoparticles and immune gold@platinum nanozymes was repeatedly pulled and pushed by the syringe to realize sufficient mixing and immunoreaction for the formation of nanoparticle-bacteria-nanozyme conjugates, which were subsequently captured in the fluidic channels. After washing with skim milk and ultrapure water, colorless TMB substrate was drawn into the fluidic channels and catalyzed by the nanozymes to produce blue TMBox catalysate. Finally, a self-developed smartphone APP was employed to analyze the image of catalysate for Salmonella detection. The biosensor could detect as low as 87 CFU/mL Salmonella in 25 min with a linear range of 1.08 × 102–1.08 × 106 CFU/mL.

专家简介：

委员：林玲 教授



北京工商大学博士生导师，国家优秀青年基金获得者。2016 年博士毕业于日本东京大学，2017-2020 年在国家纳米科学中心担任助/副研究员从事科研工作，2021 年加入北京工商大学开展独立科研工作。主要从事微流控生命分析研究，解决细胞代谢过程中超微量组分检测等科学问题。主持国家自然科学基金优青、面上、青年项目，入选北京市科技新星、北京市高层次留学人项目。研究成果以通讯或第一作者发 SCI 及国际学术会议论文 50 余篇，包括 Chem. Soc. Rev. Angew. Chem. Int. Ed., Matter, Chem. Eng. J., Chem. Sci., Anal. Chem.等，授权发明专利 8 项；参与撰写微流控细胞分析相关中英文书籍 4 部。担任《Chinese Chemical Letters》青年编委会委员、中国生物物理学会微流控系统学会分会委员、中国药学会药物分析专业委员会委员等。

Chinese Chemical Letters (IF 9.4) Published: 6 January 2024

A Microfluidic Biosensor for Multiplex Immunoassay of Foodborne Pathogens Agitated by Programmed Audio Signals.

Gaowa Xing , Yuting Shang , Xiaorui Wang , Zengnan Wu , Qiang Zhang , Jiebing Ai , Qiaosheng Pu , Ling Lin

Foods are often contaminated by multiple foodborne pathogens, which threatens human health. In this work, we developed a microfluidic biosensor for multiplex immunoassay of foodborne bacteria with agitation driven by programmed audio signals. This agitation, powered by the vibration of a speaker cone during music playing, accelerated the mass transport in the incubation process to form bacterial complexes within 10 min. Immunoassay reagents of the two target bacteria (O157:H7 and) were preloaded into the corresponding fore-vacuum storage chamber on the chip, and released to participate in the subsequent immune analysis process by piercing the chambers. All the detection processes were integrated into a single microfluidic chip and controlled by a smartphone through Bluetooth. Under selected conditions, wide linear ranges and low limits of detection (LODs < 2 CFU/mL) were obtained, and real food samples were successfully determined within 30 min. This biosensing method can be extended to wide-ranging applications by loading different recognizing reagents.

Chemical Engineering Journal (IF 15.1) Published: 1 February 2024

On-microparticle construction of endothelialized liver microtissues for drug testing.

Zengnan Wu, Yajing Zheng, Jin-Ming Lin, Yuxuan Li, Yongning Lin, Xiaorui Wang, Ling Lin

With the advantage of uniformity and customizability, hydrogel microparticles are widely used to establish in vitro organoid modeling for drug testing. However, the practical values of current strategies are limited by the lack of near-physiological structures and functions. In this work, microparticle-based liver models with biomimetic endothelial barriers are engineered using a simple, biocompatible, and high-throughput method for the application of drug testing. The hepatocyte-laden hydrogel microparticles with a rough surface are prepared using a microfluidic spraying technique, and their surfaces allow for customized protein modifications. Under the action of topological texture and matrigel modifications, the microparticle surface can induce endothelial cell adhesion, extension, and junction, thus generating a continuous, tight monolayer endothelial barrier. Semi-permeability of endothelial barrier and enhanced liver function was demonstrated in the constructed microparticle tissue models. Finally, these models were utilized to reproduce a sensitive inhibitory action of the endothelial barrier on the biotransformation of prodrugs (i.e., tegafur). Overall, microparticle-based endothelialized liver models achieved not only heterotypic cell co-culture but also tissue morphogenesis, which is anticipated to accelerate

comprehensive evaluations of the drug biotransformation and improve the translatability of drug testing results from in vitro to in vivo.

Sensors and Actuators B: Chemical **(IF 8.0)** Published:1 February 2024

Microfluidic Chip-Based Microbial Metabolism-Indexed BOD Sensor for Rapid Determination of Biochemical Oxygen Demand.

Haifeng Lin,Ning Xu,Gaowa Xing,Yuting Shang,Xiaorui Wang,Ling Lin

Reliance on five-day biochemical oxygen demand (BOD5) as an indicator of water quality has inhibited the development of efficient process control due to the associated uncertainty and lag time. In the work, we proposed a novel strategy for rapid on-site BOD5 determination by a microfluidic chip-based microbial metabolism-indexed BOD sensor (MCB-MMI BOD sensor). The rapid on-site BOD5 detection was achieved by quantifying the equilibrium concentration of tryptophan involved in aerobic biodegradation for alternating the traditional 5-day monitoring of dissolved oxygen variation. The regulated metabolized tryptophan was identified by fluorescence spectrum and converted into BOD5 value. The prominent performance for MCB-MMI BOD sensor BOD5 determination was accessible in the field application, such as decreasing detection time from 5 days to 10 min, lowering sample volume from 250 mL to 2.5 mL, diminishing the working area, extending the detection range (without dilution) from 6 mg/L to 27 mg/L, featured with 83% accuracy, and free-labor automation, which exhibited the infinite potential for MCB-MMI BOD sensor on rapid on-site BOD5 monitoring. We believe the MCB-MMI BOD sensor would broaden its practical applications in BOD5-contained multiple-parameters water quality sensing, and would favorably supply a new tool for sewage-treatment process control, environmental monitoring, and aquaculture.

Small **(IF 12.96)** Published: 20 April 2024

Fabrication and performance of bubble-containing multicompartmental particles: Novel self-orienting carriers.

Zengnan Wu, Yajing Zheng, Ling Lin,* Yongning Lin, Tianze Xie, Jiaxu Lin, Gaowa Xing, and Jin-Ming Lin

In this work, a class of bubble-containing multicompartmental particles with self-orienting capability is developed, where a single bubble is enclosed at the top of the super-segmented architecture. Such bubbles, driven by potential energy minimization, cause the particles to have a bubble-upward preferred orientation in liquid, enabling efficient decoding of their high-density signals in an interference-resistant manner. The particle preparation involves bubble encapsulation via the impact of a multicompartmental droplet on the liquid surface and overall stabilization via rational crosslinking. The conditions for obtaining these particles are systematically investigated. Methodological compatibility with materials is demonstrated by different hydrogel particles. Finally, by encapsulating cargoes of interest, these particles have found broad applications in actuators, multiplexed detection, barcodes, and multicellular systems.

Analytical Chemistry **(IF 6.7)** Published: 3 July 2024

Real-Time pH Sensor in Bacterial Microenvironments Using Liquid Crystal Core–Shell Microspheres.

Yaoshuang Xie, Yuxuan Li , Haifeng Lin, Xiaorui Wang, Wenjun Liao , Zeyang Liu, Ling Lin

It is well-known that the bacterial microenvironment imposes restrictions on the growth and behavior of bacteria. The localized monitoring of microenvironmental factors is appreciated when consulting bacterial adaptation and behavior in the presence of chemical or mechanical stimuli. Herein, we developed a novel liquid crystal (LC) biosensor in a microsphere configuration for real-time 3D monitoring of the bacteria microenvironment, which was implemented by a microfluidic chip. As a proof of concept, a LC gel (LC-Gel) microsphere biosensor was prepared and employed in the localized pH changes of bacteria by observing the configuration change of LC under polarized optical microscopy. Briefly, the microsphere

biosensor was constructed in core–shell configuration, wherein the core contained LCE7 (a nematic LC) doped with 4-pentylbiphenyl-4′-carboxylic acid (PBA), and the shell encapsulated the bacteria. The protonation of carboxyl functional groups of the PBA induced a change in charge density on the surface of LCE7 and the orientation of E7 molecules, resulting in the transitions of the LC nucleus from axial to bipolar. The developed LC-Gel microspheres pH sensor exhibited its dominant performance on localized pH real-time sensing with a resolution of 0.1. An intriguing observation from the prepared pH biosensor was that the diverse bacteria impelled distinct acidifying or alkalizing effects. Overall, the facile LC-Gel microsphere biosensor not only provides a versatile tool for label-free, localized pH monitoring but also opens avenues for investigating the effects of chemical and mechanical stimuli on cellular metabolism within bacterial microenvironments.

Analytical Chemistry **(IF 6.7)** Published: 16 August 2024

Microfluidic Engineering of Addressable Multicompartmental Microspheres for Multicellular Systems.

Yongning Lin, Zengnan Wu, Yajing Zheng, Xiaorui Wang, Jin-Ming Lin, Ying Hou, Nan Li, Gaowa Xing, Ling Lin.

With the advantages of high-throughput manufacturing and customizability, on-microsphere construction of in vitro multicellular analytical systems has garnered significant attention. However, achieving a precise, biocompatible cell arrangement and spatial signal analysis in hydrogel microspheres remains challenging. In this work, a microfluidic method is reported for the biocompatible generation of addressable supersegmented multicompartmental microspheres. Additionally, these microspheres are developed as novel label-free multicellular systems. In the microfluidic approach, controllable microfluidics is used to finely tune the internal microstructure of the microspheres, and the gas ejector ensures the biocompatibility of the preparation process. As a proof of concept, six- and twenty-compartment microspheres were obtained without the addition of any biohazardous reagents. For microsphere decoding, the visualization of two basic compartments can provide clues for identifying label-free cells due to the structural regularity of the microspheres. Finally, by encapsulating cells of different types, these microspheres as multicellular systems were successfully used for cell coculture and drug testing. These biocompatible, scalable, and analyzable microspheres will open up new prospects for biomedical analysis.

Analytical Chemistry **(IF 6.7)** Published: 28 August 2024

Robust Long-Nanowire Fabrication by Clean-Phase-Assisted Micro Chemical Pen for Enhanced Bioassay Sensitivity.

Haifeng Lin, Ning Xu, Sifeng Mao, Hizuru Nakajima, Jin-Ming Lin, Katsumi Uchiyama, Nahoko Kasai, Ling Lin

Accurate assessment of phenotypic and genotypic characteristics of bacteria can facilitate comprehensive cataloguing of all the resistance factors for better understanding of antibiotic resistance. However, current methods primarily focus on individual phenotypic or genotypic profiles across different colonies. Here, a Digital microfluidic-based automated assay for whole-genome sequencing of single-antibiotic-resistant bacteria is reported, enabling Genotypic and Phenotypic Analysis of antibiotic-resistant strains (Digital-GPA). Digital-GPA can efficiently isolate and sequence antibiotic-resistant bacteria illuminated by fluorescent D-amino acid (FDAA)-labeling, producing high-quality single-cell amplified genomes (SAGs). This enables identifications of both minor and major mutations, pinpointing substrains with distinctive resistance mechanisms. Digital-GPA can directly process clinical samples to detect and sequence resistant pathogens without bacterial culture, subsequently provide genetic profiles of antibiotic susceptibility, promising to expedite the analysis of hard-to-culture or slow-growing bacteria. Overall, Digital-GPA opens a new avenue for antibiotic resistance analysis by providing accurate and comprehensive molecular profiles of antibiotic resistance at single-cell resolution.

Matter **(IF 17.3)** Published: 2 October 2024

Open aerosol microfluidics enable orthogonal compartmentalized functionalization of hydrogel particles.

Zengnan Wu, Yajing Zheng, Ling Lin, Yongning Lin, Tianze Xie, Wenjun Liao, Shiyu Chen, Yingrui Zhang, Jin-Ming Lin

Compartmentalized hydrogel microparticles are promising for applications in chemical, biological, and biomedical fields, owing to their customizability. However, simultaneous tailoring of the functionalities in both internal and surface compartments remains challenging. Here, an open aerosol microfluidic (OAMF) approach is reported to fabricate compartmentalized hydrogel particles, achieving orthogonal (independent and non-interfering) control over both internal and surface functionalization. The OAMF method utilizes microfluidic networks for shaping internal compartment layouts and employs reactive aerosols for precise surface engineering. As a proof of concept, particles featuring intricate internal and surface designs were created. In addition, the broad material versatility of particle customization is demonstrated by different hydrogels. Finally, potential applications of particles were explored as novel cell carriers. As exemplars, patterned cell cultures can be established both on the surface and inside of the particles. The proposed approach enables flexible design of engineered particles, advancing tissue engineering, drug screening, and cell therapeutic applications.

Advanced Materials Technologies **(IF 6.4)** Published:12 December 2024

Non-Invasive Ammonia Detection on Cancer Cell Surfaces Using Liquid Crystal Elastomer.

Mashooq Khan, Weiwei Li, Qiongzheng Hu, Jin-Ming Lin, Ling Lin

Delving into the intricate world of cancer cells requires a profound understanding of the signaling molecules released from the cells. In this contribution, ammonia (NH_3) is monitored, a small signaling molecule and potential cancer biomarker, on the cell surfaces through liquid crystal elastomer microspheres (LCEM) at the single-cell level. The LCEM are synthesized from molecular building blocks, 7-octenoic acid (7OAc) and 2-methyl-1,4-phenylene bis(4-((acryloyloxy)hexyl)oxy) benzoate (RM82) and adorned on the surfaces of healthy human umbilical vein endothelial cells (HUVEC), and cancerous, human primary glioblastoma (U87), human colon carcinoma (CaCo-2), and human breast adenocarcinoma (MCF7) cells, cultured within microfluidic channels. The ethereal release of NH_3 from living cells is monitored through a radial-to-concentric transfiguration of LCEM. The cellular heterogeneity among cancerous cell populations is unraveled by mapping the LCEM morphology on 100 cells of each cell line. The LCEM paves the way for designing probes that offer selective, simplistic, and label-free monitoring of the biochemical processes unfurling on the surfaces of living cells, which are challenging to measure through other analytical techniques.

Chemical Engineering Journal **(IF 15.1)** Published: 15 December 2024

Thermo-responsive Microparticle Swimmer As a Remote Tool for Cell Delivery in Tissue Engineering.

Zengnan Wu, Yajing Zheng, Jin-Ming Lin, Gaowa Xing, Tianze Xie, Yongning Lin, Jiaxu Lin, Ling Lin

Developing biocompatible and flexible cell manipulation tools is crucial for effective cell delivery in tissue engineering. Herein, thermo-responsive microparticle swimmers, composed of an alginate core and a rough gelatin surface, are developed as a tool for remote cell manipulation and the construction of patterned cell models. The microparticles are fabricated using a novel bio-friendly surface assembly strategy, which leverages morphology-induced gelatin adsorption combined with temperature-cycling crosslinking to deposit multiple gelatin layers onto microfluidic-derived rough microparticles. Gelatin molecules can adsorb onto the rough surface at 25 °C and become cross-linked at 4 °C to form a stable coating layer while preserving the coarse morphology for additional assembly cycles. The gelatin layers remain intact at room temperature for cell loading and transport, but rapidly dissipate at 37 °C, enabling cell release. Moreover, complex manipulations of living cell populations, such as remote tweezing, can be achieved by the introduction of magneto-responsive moieties. These versatile microparticles provide an efficient tool for the in vitro construction of flexible

and dynamic patterned cell models, with promising applications in tissue engineering, drug screening, and organoid development.

专家简介：

委员：刘婷姣 教授



口腔医学博士、三级教授、博士研究生导师， 复旦大学口腔医学院口腔基础医学系主任及学科带头人、口腔组织病理学教研室主任、上海市口腔医院病理科主任，以项目负责人获得国家自然基金委面上项目 6 项和多项省部级项目，在 PNAS、Molecular cancer、International Journal of Oral Science、Advanced Science、Advanced Functional Materials 等国际主流学术杂志上发表 SCI 收录论文 50 余篇，以第一发明人获授权发明专利 4 项，以第一完成人获省级科技进步二等奖 1 项、三等奖 1 项。

Biosensors and Bioelectronics **(IF 10.7)** Published: 17 April 2024

Vortexing-generated High Throughput Single-Cell Droplets for Facile Analysis of Multiplexed Microrna Dynamic Secretion.

Fengjiao Zhu, Yangyang Long, Weiwei Shi, Bin Li, Yahui Ji, Xue Bai, Xianming Liu, Dongyuan Qi, Bo Sun, Fuyin Zhang, Tingjiao Liu, Bingcheng Lin, Yao Lu

Discriminating secretory phenotypes provides a direct, intact, and dynamic way to evaluate the heterogeneity in cell states and activation, which is significant for dissecting non-genetic heterogeneity for human health studies and disease diagnostics. In particular, secreted microRNAs, soluble signaling molecules released by various cells, are increasingly recognized as a critical mediator for cell-cell communication and the circulating biomarkers for disease diagnosis. However, single-cell analysis of secreted miRNAs is still lacking due to the limited available tools. Herein, we realized three-plexed miRNA secretion analysis over four time points from single cells encapsulated in picoliter droplets with extreme simplicity, coupling vortexing-generated single-cell droplets with multiplexed molecular beacons. Notably, our platform only requires pipetting and vortexing steps to finish the assay setup within 5 min with minimal training, and customized software was developed for automatic data quantification. Applying the platform to human cancer cell lines and primary cells revealed previously undifferentiated heterogeneity and paracrine signaling underlying miRNA secretion. This platform can be used to dissect secretion heterogeneity and cell-cell interactions and has the potential to become a widely used tool in biomedical research.

Advanced Functional Materials **(IF 18.5)** Published: 14 June 2024

An Engineered Anisotropic Skeletal Muscle Organoid-on-a-Chip for Deciphering Muscle Response under Intermittent Hypoxia.

Jiao Li,Weihua Zhang,Anqi Liu,Yun Lu,Liming Yu,Xue Liu,Liangyan Sun,Bingjiao Zhao,Xianqin Tong,Tingjiao Liu,Yuehua Liu

Generating highly organized skeletal muscle tissues that mimics the cellular alignment, maturation, and contraction of native skeletal muscle remains a challenge in disease modeling and regenerative therapies. Existing methodologies are constrained by complexity in fabrication and difficulty in achieving aligned 3D myofibers. Here, a functional skeletal muscle organoid-on-a-chip (SMO) is engineered by establishing mechanical boundary constraints at either end of the cell-laden extracellular matrix hydrogel within polydimethylsiloxane microstructures to promote the formation of an anisotropic biophysical microenvironment in tissues. The linearly aligned tissue, featuring multinucleated myofibers with distinct cross-striations, exhibited a positive force-frequency relationship and stable calcium transients under electrical

stimulation. SMOs applicability is demonstrated by systematically evaluating muscle response to varying degrees of intermittent hypoxia. Murine- or human-derived SMOs revealed that, with increasing hypoxia severity, muscles transitioned from a compensatory phase-characterized by enhanced contractile function, vacuolation and hypertrophic-like changes in myofibers, fiber type switching, and metabolic shift, to a decompensatory stage, paralleling in vivo muscle responses and highlighting interspecies differences. Human-derived SMOs are also utilized to assess self-repair capabilities and pharmaceuticals protective effects on damaged muscle. Together, the platform, with its simplicity of operation and reliable phenotypic readouts, demonstrates significant potential for future disease modeling and regenerative therapies.

专家简介：

委员：陆瑶 研究员



中国科学院大连化学物理研究所博士生导师，国家高层次青年人才。2010 年毕业于中国科学院大连化学物理研究所，获分析化学博士学位；2010-2015 年在美国耶鲁大学生物医学工程系从事博士后研究；2015 年 9 月底回所工作。主要研究方向为微流控芯片单细胞分析技术发展及其在生物医学中的应用研究。发展的喷蜡打印制造纸基质微流控芯片技术成为相关领域最主要制备技术，被广泛采用；发展的单细胞分泌蛋白分析技术被广泛用于肿瘤免疫治疗、细胞治疗药品开发及临床测试，被 The Scientist 杂志评为 2017 年度十大医疗技术发明首位。相关研究工作以第一/通讯作者发表于 PNAS, Science Signaling, Advanced Science, Analytical Chemistry, Biofabrication 等期刊，单篇最高他引近 500 次。申请/授权中国、国际专利十余件。参与主编中文(科学出版社，2019）、英文（Elsevier，2021）专著各一部。；获 2017 年国际分析科学大会青年报告奖；获中国科学院青年创新促进会优秀会员、大连化物所张大煜青年学者、辽宁省百千万人才工程（万）、大连市青年科技之星等荣誉称号。

Nature Communications **(IF 14.7)** Published: 17 April 2024

Monolithically integrated micro-supercapacitors with high areal number density produced by surface adhesive-directed electrolyte assembly.

Sen Wang, Shuanghao Zheng, Xiaoyu Shi, Pratteek Das, Linmei Li, Yuanyuan Zhu, Yao Lu, Xinliang Feng & Zhong-Shuai Wu

Accurately placing very small amounts of electrolyte on tiny micro-supercapacitors (MSCs) arrays in close proximity is a major challenge. This difficulty hinders the development of densely-compact monolithically integrated MSCs (MIMSCs). To overcome this grand challenge, we demonstrate a controllable electrolyte directed assembly strategy for precise isolation of densely-packed MSCs at micron scale, achieving scalable production of MIMSCs with ultrahigh areal number density and output voltage. We fabricate a patterned adhesive surface across MIMSCs, that induce electrolyte directed assembly on 10,000 highly adhesive MSC regions, achieving a 100 μm-scale spatial separation between each electrolyte droplet within seconds. The resultant MIMSCs achieve an areal number density of 210 cells cm−2 and a high areal voltage of 555 V cm−2. Further, cycling the MIMSCs at 190 V over 9000 times manifests no performance degradation. A seamlessly integrated system of ultracompact wirelessly-chargeable MIMSCs is also demonstrated to show its practicality and versatile applicability.

Biosensors and Bioelectronics **(IF 10.7)** Published: 17 April 2024

Vortexing-generated High Throughput Single-Cell Droplets for Facile Analysis of Multiplexed Microrna Dynamic Secretion.

Fengjiao Zhu, Yangyang Long, Weiwei Shi, Bin Li, Yahui Ji, Xue Bai, Xianming Liu, Dongyuan Qi, Bo Sun, Fuyin Zhang, Tingjiao Liu, Bingcheng Lin, Yao Lu

Discriminating secretory phenotypes provides a direct, intact, and dynamic way to evaluate the heterogeneity in cell states and activation, which is significant for dissecting non-genetic heterogeneity for human health studies and disease diagnostics. In particular, secreted microRNAs, soluble signaling molecules released by various cells, are increasingly recognized as a critical mediator for cell-cell communication and the circulating biomarkers for disease diagnosis. However, single-cell analysis of secreted miRNAs is still lacking due to the limited available tools. Herein, we realized three-plexed miRNA secretion analysis over four time points from single cells encapsulated in picoliter droplets with extreme simplicity,

coupling vortexing-generated single-cell droplets with multiplexed molecular beacons. Notably, our platform only requires pipetting and vortexing steps to finish the assay setup within 5 min with minimal training, and customized software was developed for automatic data quantification. Applying the platform to human cancer cell lines and primary cells revealed previously undifferentiated heterogeneity and paracrine signaling underlying miRNA secretion. This platform can be used to dissect secretion heterogeneity and cell-cell interactions and has the potential to become a widely used tool in biomedical research.

Biosensors and Bioelectronics **(IF 10.7)** Published: 17 April 2024

Braiding Three-Dimensional Paper-Based Microfluidic Devices.

Cuiyun Jia, Bin Li, jie Pan, Fengjiao Zhu, Xue Bai, Xianming Liu, Bingcheng Lin, Yahong Chen*, Yao Lu*

Three-dimensional paper-based microfluidic devices have shown great potential in various applications, including point-of-care diagnostics, environmental monitoring, and tissue engineering. However, their fabrication is still limited to stacking and origami methods. Inspired by the art of bamboo braiding in China, we developed a novel fabrication technique based on the braiding concept to create three-dimensional paper-based microfluidic devices with PDMS-impregnated paper substrate as the building units. The resulting three-dimensional paper device brings unique advantages, including compactness, facile disassembly, and real-time flow visualization. The multiplexed glucose analysis with a braided device integrated with 16-switchable valves for flow control was further fabricated to demonstrate the device‘s applicability. We envision braiding-based fabrication technology opening new possibilities and bringing broad applications for three-dimensional paper microfluidic devices.

Analytical Chemistry **(IF 6.7)** Published: 5 August 2024

Automated Droplet Ejection from a Digital Microfluidics Sample Pretreatment Device Enables Batch-Mode Chemiluminescence Immunoassay.

Dezhi Huang, Enqi Huang, Dongyang Cai, Zhenhua Chen, Hongting Wen, Yu Wang, Dachuan Ma, Yao Lu, Xianming Liu, Dayu Liu

Digital microfluidics (DMF) features programmed manipulation of fluids in multiple steps, making it a valuable tool for sample pretreatment. However, the integration of sample pretreatment with its downstream reaction and detection requires transferring droplets from the DMF device to the outside world. To address this issue, the present study developed a modified DMF device that allows automated droplet ejection out of the chip, facilitated by a tailor-designed interface. A double-layered DMF microchip with an oil-filled medium was flipped over, with a liquid infusion port and a liquid expulsion port accommodated on the top working PCB plate and the bottom grounded ITO plate, respectively, to facilitate chip-to-world delivery of droplets. Using chemiluminescent immunoassay (CLIA) as an illustrative application, the sample pretreatment was programmed on the DMF device, and CLIA droplets were ejected from the chip for signal reading. In our workflow, CLIA droplets can be ejected from the DMF device through the chip-to-world interface, freeing up otherwise occupied electrodes for more sample pretreatment and enabling streamlined droplet microreactions and batch-mode operation for bioanalysis. Integrated with these interfacing portals, the DMF system achieved a single-channel throughput of 17 samples per hour, which can be further upscaled for more productive applications by parallelizing the DMF modules. The results of this study demonstrate that the droplet ejection function that is innovated in a DMF sample pretreatment microsystem can significantly improve analytical throughput, providing an approach to establishing an automated but decentralized biochemical sample preparation workstation for large-scale and continuous bioanalysis.

Biosensors and Bioelectronics **(IF 10.7)** Published: 4 December 2024

Digital microfluidics with integrated Raman sensor for high-sensitivity in-situ bioanalysis.

Wenbo Dong, Rongxin Fu, Nan Zhang, Jing Zhao, Yudan Ma, Han Cui, Jiangjiang Zhang, Zipeng Zhao, Hang Li, Yunxia Zhao, Yao Lu, Zhizhong Chen, Tianming Xu, Huikai Xie, Qian Yu, Shuailong Zhang

This study introduces an advanced bioanalytical platform that combines digital microfluidics (DMF) with Raman spectroscopy, effectively addressing common issues in bioanalysis such as sample contamination, excessive consumption of samples and reagents, and manual handling. Our innovative system is engineered to handle diverse sample types and enables both sample preparation and in-situ analysis on a single device, utilizing less than 5 μL of samples and reagents. It incorporates a Translucent Raman Enhancement Stack (TRES) sensor, which boosts the detection signal, and includes droplet-driving functionality for automated processing of complex samples in a compact setting. The hydrophilic surface of the TRES sensor draws analytes into the detection zone, expediting sample attachment and enhancing the surface-enhanced Raman scattering (SERS). Moreover, the TRES sensors are cost-effective, straightforward to manufacture, and scalable, making them suitable for widespread production and single-use bioanalytical applications. This integrated and automated approach streamlines the sample preparation and analysis processes, enhances detection efficiency, and achieves high sensitivity, excellent linearity, and effective detection of different biochemical analytes. We validate the system's accuracy through on-device enrichment and analysis of exosomes from serum, demonstrating its capability for real-time, on-site analysis of complex biological samples.

专家简介：

委员：罗勇 教授



大连理工大学化工学院药学系副教授，中科院过程所生化工程国家重点实验室客座研究员，深圳老年医学研究所客座研究员，辽宁省肾脏病及血液净化临床医学协同创新联盟常务理事，辽宁省心率失常临床医学协同创新联盟理事，Editor, Journal of 3D printing and applications，中国机械工程学会生物制造分会会员，中国毒理协会会员，南开大学化学系学士，中科院大连化学物理研究所博士，美国能源部 Ames Lab 访问学者，专注于微流控器官芯片和微流控 POCT 芯片，发表论文五十余篇，被引用八百余次，授权专利二十项，出版《器官芯片》（科学出版社），主持国家自然科学基金面上项目和科技部重大新药创制项目，科技部重大仪器专项和重点研发计划项目骨干，关于肾器官芯片的研究收录于科技部《2019 生命科学与生物技术发展报告》，获 2007 年辽宁省科学技术奖励一等奖和大连市学术论文二等奖，2014 年英国皇家化学会 Top 1%高引用学者，2019 年中国中西医学会科学技术二等奖。

Lab on a Chip **(IF 6.1)** Published: 12 March 2024

Integrated phase separation in microliter droplets for ultratrace-enriching biomarker analysis.

Qihao Zha, Yong Luo, Conghui Liu, Tailin Xu

Ultratrace-enriching biomarker analysis is an effective method for achieving highly accurate and enhanced sensitive detection. In this study, we have developed an enrichment detection platform by combining a minipillar array with an aqueous two-phase system (ATPS) for ultratrace enriching biomarker analysis. After optimizing the enrichment conditions of ATPS, target miRNAs at ultratrace levels specifically accumulate in the DEX-rich phase, which significantly increases the target miRNA concentration-related fluorescence intensity. Compared to non-enriched miRNA in the single-phase PEG solution, the detection limit of ATPS-enriched miRNA had improved more than 200-fold. The ATPS-based enrichment detection strategy offers a novel and convenient approach for the simultaneous detection of biomarkers with ultratrace.

Methods in molecular biology **(IF 8.5)** Published: 23 June 2024

Ultrasound-Induced Enrichment of Ultra-Trace miRNA Biosensing in Nanoliter Samples.

Yong Luo, Tailin Xu

The rapid and accurate analysis of micro-samples is a crucial foundation for precision medicine, particularly for early screening and monitoring of cancer, where it holds significant importance. Ultrasound-based multifunctional biocompatible manipulation techniques have been extensively applied in a variety of biomedical fields, providing insights for the development of rapid, cost-effective, and accurate biomarker detection strategies. In this chapter, we combine ultrasound-based gradient pressure fields with functionalized microsphere enrichment to develop a biosensing method for ultra-trace miRNA enrichment in nanoliter samples without PCR. This system relies on inexpensive capillaries, enabling simultaneous visual imaging and trace sample detection.

Research **(IF 8.5)** Published: 24 July 2024

Integrated Mini-pillar Platform for Wireless Real-time Cell Monitoring.

Yong Luo, Yongchao Song, Jing Wang, Tailin Xu, Xueji Zhang

Cell culture as the cornerstone of biotechnology remains a labor-intensive process requiring continuous manual oversight and substantial time investment. In this work, we propose an integrated mini-pillar platform for in situ monitoring of multiple cellular metabolism processes, which achieves media anchoring and cell culture through an arrayed mini-pillar

chip. The assembly of polyaniline (PANI)/dendritic gold-modified microelectrode biosensors exhibits high sensitivity (63.55 mV/pH) and excellent interference resistance, enabling real-time acquisition of biosensing signals. We successfully employed such integrated devices to real-time measuring pH variations in multiple cells and real-time monitoring of cell metabolism under drug interventions and to facilitate in situ assisted cultivation of 3-dimensional (3D) cell spheroids. This mini-pillar array-based cell culture platform exhibits excellent biosensing sensitivity and real-time monitoring capability, offering considerable potential for the advancement of biotechnology and medical drug development.

***Advanced Materials* (IF 27.4)** Published: 6 August 2024

A Fully Integrated Conformal Wearable Ultrasound Patch for Continuous Sonodynamic Therapy.

Faxing Zou,Yong Luo,Wenxuan Zhuang,Tailin Xu

Cancer treatment is a continuous process, that the current therapy cannot meet the requirement well, including radiotherapy and chemotherapy. Wearable ultrasound device has the potential for continuous sonodynamic therapy due to its portability. However, the miniaturization of ultrasonic probe, system integration of device, and the strategy of continuous treatment are still urgent issues to be addressed. Herein, a portable wearable antitumor system is introduced, which utilizes a custom-developed multiplexed ultrasonic patch array (CWUS Patch) to accurately focus ultrasound on the lesion site and controllably stimulate sonosensitizer to produce a large amount of toxic reactive oxygen species (ROS). The system enables dynamic control of the ultrasound patches and allows real-time adjustments to optimize their performance in various applications, providing greater flexibility and precision in healthcare technology. Furthermore, the excellent penetration property of ultrasound into tumor tissues that induce synchronous apoptosis of tumor cells from the inside out is verified through a mouse model of breast cancer. This fully integrated conformal wearable ultrasound system provides a promising approach to noninvasively, continuously, and efficiently treat deep tumors.

***Chemical Engineering Journal* (IF 13.3)** Published: 16 November 2024

Algae-based Flexible Localized Oxygen Control Around Cells: an Approach Leading to More Biomimetic Microphysiological Systems.

Yuangui Liu, Yueyang Qu, Youlong Yang, Quanfeng Deng, Yong Luo, Xiuli Zhang

Oxygen levels are crucial in the cellular microenvironment, affecting cellular function. Controlling pericellular oxygen is essential for understanding cell-oxygen interactions, disease mechanisms, and developing therapies. In this study, an algae strain was engineered as a biological oxygen-control material, integrated with a light-controlled microphysiological system to regulate pericellular oxygen. This technique could provide different oxygen levels and varying profiles for different locations within one microphysiological system. Additionally, the pericellular oxygen dynamics were faster than those achieved by other methods. By utilizing this algae-integrated microfluidic chip, mesenchymal stem cells differentiated into adipocytes with improved phenotypic characteristics, including increased numbers and sizes of lipid droplets, under 21-day stage-specific oxygen concentrations. Furthermore, this technique effectively mitigated the need to vent significant amounts of oxygen or nitrogen into the laboratory during long-term or virus-infested experiments, thereby enhancing both safety and practicality. The algae-integrated microfluidic chip also served as a platform for constructing a stroke-related vascular-on-chip model, enabling the evaluation of the protective effects of oxygen therapy on endothelial injury induced by oxygen-glucose deprivation/reperfusion (OGD/R). The results indicated that waving hyperoxic dynamics were most effective in safeguarding vascular tissue against OGD/R compared to other hyperoxic dynamics. This finding can guide the clinical oxygen inhalation mode during stroke management. All the aforementioned results demonstrated that the algae-light microphysiological system offered a technical platform capable of precise, dynamic pericellular oxygen control across the disciplines of biology and pharmaceutics. Moreover, The cost-effective cultivation of algae on a large scale made this method suitable for wider use.

专家简介：

委员：牟颖 教授



浙江大学教授，生物化学与分子生物学/控制科学与工程/电子信息专业跨学科博士生导师。1997 年于白求恩医科大学获得博士学位，2000-2006 年任职吉林大学生命科学学院副教授/教授，2004-2005 年多伦多大学访问学者，2006 年至今任职浙江大学教授。承担十余项国家及省部级科研项目，公开发表学术论文 200 余篇，授权国家发明专利 16 项，转让 1 项。目前主要从事微流控系统及生命科学新技术、新仪器研究。

Biosensors (IF 4.8) Published: 24 January 2024

Digital PCR for Single-Cell Analysis.

Weibo Fang, Xudong Liu, Mariam Maiga, Wenjian Cao, Ying Mu, Qiang Yan, Qiangyuan Zhu

Single-cell analysis provides an overwhelming strategy for revealing cellular heterogeneity and new perspectives for understanding the biological function and disease mechanism. Moreover, it promotes the basic and clinical research in many fields at a single-cell resolution. A digital polymerase chain reaction (dPCR) is an absolute quantitative analysis technology with high sensitivity and precision for DNA/RNA or protein. With the development of microfluidic technology, digital PCR has been used to achieve absolute quantification of single-cell gene expression and single-cell proteins. For single-cell specific-gene or -protein detection, digital PCR has shown great advantages. So, this review will introduce the significance and process of single-cell analysis, including single-cell isolation, single-cell lysis, and single-cell detection methods, mainly focusing on the microfluidic single-cell digital PCR technology and its biological application at a single-cell level. The challenges and opportunities for the development of single-cell digital PCR are also discussed.

Sensors and Actuators B: Chemical (IF 8.0) Published: 15 April 2024

A fully automatic dPCR microfluidic system for detection of large-volume and low-abundance bacteria sample.

Kai Hu, Weihong Yin, Yu Wang, Liping Xia, Yiwen Bai, Qiangyuan Zhu, Juxin Yin, Ying Mu, W. Jin

Digital polymerase chain reaction (dPCR) has become a key technology for bacteria detection with superior sensitivity and accuracy, enabling in reducing the spread of waterborne disease. However, the current systems lack a complete dPCR detection workflow for low-abundance bacteria water sample in large-volume, including bacteria enrichment, nucleic acid (NA) extraction and digital arrays generation. In this work, a fully automated workflow system has been developed for dPCR detection. A preprocessing cartridge designed for single-use has been fabricated to realize the bacterial capture (~ 98%), NA absorption (~ 81%), mixing and heating. A PDMS-based microfluidic chip and a vacuum cover are employed for the generation of digital arrays without the pre-degas of PDMS. The proposed system exhibits a good linear relationship of Escherichia coli (E. coli) detection within the range from 2.5 × 101 CFU/mL to 2.5 × 104 CFU/mL, with a limit of detection ~ 2.5 CFU/mL when enrich 5 mL sample. Furthermore, the dPCR detection results of four actual water samples are comparable to those obtained by the gold standard method plate counting, demonstrating its potential as a point-of-care testing (POCT) tool for accurate quantification of large-volume and low-abundance bacteria samples.

Talanta (IF 5.6) Published: 5 June 2024

Concanavalin A-assisted multiplex digital PCR assay for rapid capture and accurate quantification detection of foodborne pathogens.

Liping Xia, Yehong Gui, Rui Yin, Na Li, Min Yue, Ying Mu

Multiplex, sensitive, and rapid detection of pathogens is crucial for ensuring food safety and safeguarding human health, however, it remains a significant challenge. This study proposes a oncanavalin -assisted ultiplex igital mplification (CAMDA) assay for simultaneous quantitative detection of multiple foodborne bacteria. The CAMDA assay enables the simultaneous detection of six foodborne pathogens within 1.1 h and the limit of detection is 10 CFU/mL. Furthermore, the CAMDA assay exhibits high specificity, with a rate of 97 % for and 100 % for other pathogens tested in this study. Moreover, practical application validation using eight milk powder samples demonstrates that the accuracy of the CAMDA assay reaches 100 % when compared to qPCR results. Therefore, our developed CAMDA assay holds great potential for accurate and rapid detection of multiple pathogens in complex food matrices while also promoting the utilization of microfluidic chips in food investigation.

Biomicrofluidics (IF 2.6) Published: 7 June 2024

Microfluidic technologies for advanced antimicrobial susceptibility testing.

Wenshuai Wu, Ying Mu

Antimicrobial resistance is getting serious and becoming a threat to public health worldwide. The improper and excessive use of antibiotics is responsible for this situation. The standard methods used in clinical laboratories, to diagnose bacterial infections, identify pathogens, and determine susceptibility profiles, are time-consuming and labor-intensive, leaving the empirical antimicrobial therapy as the only option for the first treatment. To prevent the situation from getting worse, evidence-based therapy should be given. The choosing of effective drugs requires powerful diagnostic tools to provide comprehensive information on infections. Recent progress in microfluidics is pushing infection diagnosis and antimicrobial susceptibility testing (AST) to be faster and easier. This review summarizes the recent development in microfluidic assays for rapid identification and AST in bacterial infections. Finally, we discuss the perspective of microfluidic-AST to develop the next-generation infection diagnosis technologies.

Biosensors (IF 4.8) Published: 28 July 2024

CRISPR-Based Biosensors for Medical Diagnosis: Readout from Detector-Dependence Detection Toward Naked Eye Detection.

Kai Hu, Weihong Yin, Yunhan Bai, Jiarui Zhang, Juxin Yin, Qiangyuan Zhu, Ying Mu

The detection of biomarkers (such as DNA, RNA, and protein) plays a vital role in medical diagnosis. The CRISPR-based biosensors utilize the CRISPR/Cas system for biometric recognition of targets and use biosensor strategy to read out biological signals without the employment of professional operations. Consequently, the CRISPR-based biosensors demonstrate great potential for the detection of biomarkers with high sensitivity and specificity. However, the signal readout still relies on specialized detectors, limiting its application in on-site detection for medical diagnosis. In this review, we summarize the principles and advances of the CRISPR-based biosensors with a focus on medical diagnosis. Then, we review the advantages and progress of CRISPR-based naked eye biosensors, which can realize diagnosis without additional detectors for signal readout. Finally, we discuss the challenges and further prospects for the development of CRISPR-based biosensors.

Lab on a Chip (IF 6.1) Published: 26 August 2024

Fast and Sensitive Detection of Viable Escherichia Coli O157:H7 Using a Microwell-Confined and Propidium Monoazide-Assisted Digital CRISPR Microfluidic Platform.

Weihong Yin, Kai Hu, Bingwen Yu, Tao Zhang,Haohua Mei, Bowen Zhang, Zheyu Zou, Liping Xia,Yehong Gui, Juxing Yin,Wei Jin,Ying Mu

Escherichia coli O157:H7 is a major foodborne pathogen that poses a significant threat to food safety and human health. Rapid and sensitive detection of viable Escherichia coli O157:H7 can effectively prevent food poisoning. Here, we developed a microwell-confined and propidium monoazide-assisted digital CRISPR microfluidic platform for rapid and sensitive detection of viable Escherichia coli O157:H7 in food samples. The reaction time is significantly reduced by minimizing the microwell volume, yielding qualitative results in 5 min and absolute quantitative results in 15 min. With the assistance of propidium monoazide, this platform can eliminate the interference from 99% of dead Escherichia coli O157:H7. The direct lysis method obviates the need for a complex nucleic acid extraction process, offering a limit of detection of 3.6 × 101 CFU mL−1 within 30 min. Our results demonstrated that the platform provides a powerful tool for rapid detection of Escherichia coli O157:H7 and provides reliable guidance for food safety testing.

Analytical Chemistry (IF 6.7) Published: 31 October 2024

A Propidium Monoazide-Assisted Digital CRISPR/Cas12a Assay for Selective Detection of Live Bacteria in Sample.

Weihong Yin, Kai Hu, Yunxing Yang, Jianjian Zhuang, Zheyu Zou, Yuanjie Suo, Liping Xia, Jiale Li, Yehong Gui, Haohua Mei, Juxin Yin, Tao Zhang, Ying Mu

Escherichia coli O157:H7 (E. coli O157:H7) is a prominent pathogenic bacterium that poses serious risks to food safety and public health. Rapid and accurate detection of live E. coli O157:H7 is of great importance in food quality monitoring and clinical diagnosis. Here, we report a propidium monoazide-assisted nonamplification digital CRISPR/Cas12a assay for sensitive and rapid detection of live E. coli O157:H7. The incorporation of propidium monoazide into the method enables the selective detection of live bacteria by eliminating 98% of interference from the dead bacterial nucleic acid. Implemented on microfluidic digital chips, this method can achieve absolute quantification of nonamplified nucleic acid. The entire detection process of live bacteria can be completed within 120 min without the need for establishing a standard curve, and the sensitivity of the method reaches 1.2 × 103 CFU/mL. The method was validated using various samples, yielding results consistent with the plate counting method (Pearson's r = 0.9490). Consequently, this method holds significant potential for applications in fields requiring live bacterial detection.

专家简介：

委员：邢婉丽 研究员



现任清华大学医学院医学系统生物学研究中心教授、博士生导师、研究员，生物芯片北京国家工程研究中心常务副主任，生物芯片北京国家工程研究中心暨博奥生物集团常务副主任，北京博奥晶典生物技术有限公司董事长。中国医药生物技术协会生物芯片分会常委，国家生物芯片标准化技术委员会秘书长，第七届国家卫生标准委员会临床检验标准专业委员会委员，中国高科技产业化研究会生物医药产业化工作委员会，副主任委员。2007 年获科技部“十一五”八六三重点项目支持。 实验室的主要研究方向：生物芯片研究及其应用。 实验室承担“十一五”八六三重点项目一项（课题负责人）。

团队主要从事 DNA 芯片、蛋白芯片、细胞芯片和芯片缩微实验室的研究开发和在健康管理、疾病诊断、食品安全检测、药物开发中的应用研究，以及依托互联网大数据和人工智能的大健康管理相关研究。

Analyst **(IF 3.6)** Published: 25 July 2024

A Pumpless Liver-on-a-chip for Drug Hepatotoxicity Analysis.

Dian Jiao , Lan Xie, Wanli Xing

This study presents the development and validation of an innovative microfluidic liver-on-a-chip device utilizing gravity-driven perfusion for the evaluation of drug hepatotoxicity. This research involved the construction of a hydrogel-based coculture chip that integrates liver parenchymal and stellate cells within a tri-channel configuration. The assembly and operation of the liver-on-a-chip and its accompanying custom rocker were straightforward. The cells in the chip maintained high viability and continuously synthesized liver albumin over extended culture durations. Acetaminophen (APAP), a hepatic injury-inducing drug, was utilized as a positive control in hepatic toxicity assays on the chip. The liver chip exhibited hepatotoxic responses comparable to those observed in 2D models. Furthermore, in this study we evaluated the effects of two plant-derived natural compounds, aristolochic acid I (AA) and its analog aristolactam AII (AL), in both 2D cell models and the liver-on-a-chip system. AA, known for its hepatorenal toxicity, was observed to cause hepatotoxicity in both the 2D models and on the chip. The flow cytometry and mRNA sequencing results confirmed the propensity of these compounds to induce liver cell apoptosis. Notably, AL, previously considered nontoxic, provoked a significant decrease in the hepatic functionality marker albumin exclusively in the liver chip but not in 2D models, indicating the liver chip's enhanced sensitivity to toxic substances. In summary, this pumpless liver-on-a-chip is a simple yet powerful tool for drug hepatotoxicity studies.

专家简介：

委员：徐健 研究员



中国科学院青岛生物能源与过程所研究员、生物能源研究室主任、单细胞中心主任、基因组工程团队负责人；山东省能源生物遗传资源重点实验室主任。1997 年北京大学生物技术学士；2003 年华盛顿大学（WUSTL）计算机科学硕士和生物化学博士；2004-08 年于华盛顿大学遗传学系和基因组研究院任基因型组装和分析团队负责人。2008 年入选中科院人才计划并全职加入中科院青岛生物能源与过程所。论文发表于 Science、Cell Host Microbe、Nature Commu. 、Science Adv. 等 170 余篇，被引约 15000 次，入选爱思唯尔“中国高被引学者”（H-index 57）。主持国家重大科学仪器研制、科技部重点研发计划、国家基金委重点、重大研究计划重点支持等项目。获首届中组部人才计划、国家杰出青年基金（2014）、中国青年科技奖（2015）、科技部人才计划、中源协和生命医学创新突破奖（2016）、山东省人才计划、“科技领军人才工作室”（山东省科技厅）等荣誉。

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 1 May 2024

A microfluidics-free centrifugally-driven nano-liquid pipetting system (CNPS) for single-cell whole genome amplification.

Chunyu Li, Yanhai Gong, Fei Wu, Jian Xu, Bo Ma

We developed a microfluidics-free centrifugally-driven nano-liquid pipetting system (CNPS) for single-cell whole genome amplification. The capillary tube and the collection vessel (PCR tube or 96-well PCR plate), both of which are easily accessible, make up the basic components of the system. Unlike microfluidic chips that need a clean room and special skills to fabricate, the CNPS can be assembled in the typical biology laboratory without any special training. Centrifugation is used to directly pipette the nanoliter-volume liquid into the collection tube, which eliminates the requirement for extra equipment. The CNPS, which is compatible with the standard handheld pipette, allows for a smooth transition between the micro and macro worlds, thereby overcoming the problem of retrieving nanoliter-volume products. We further demonstrated the feasibility of the CNPS for nanoliter-volume single-cell multiple displacement amplification. Based on the sequencing results, the mapped reads cover on average 95.23%, 95.15%, and 80.94% for Saccharomyces cerevisiae, Escherichia coli, and Staphylococcus epidermidis, respectively. In sum, the CNPS has the potential to become an alternative powerful platform for single-cell genome sequencing with the ability to manipulate ultra-small volumes, as well as to enhance precision and sophistication by significantly minimizing sample losses and reducing amplification bias.

Analytical Chemistry **(IF 6.7)** Published: 12 November 2024

Ultrafast Evolution of Bacterial Antimicrobial Resistance by Picoliter-Scale Centrifugal Microfluidics.

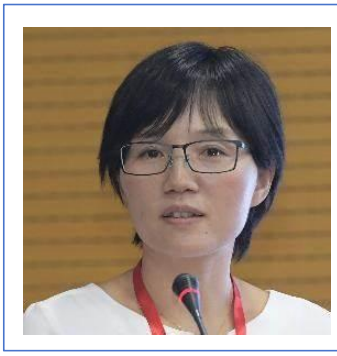
Teng Xu, Yajie Dai, Anle Ge, Xueqian Chen, Yanhai Gong, Tze Hau Lam, Kelvin Lee, Xiao Han, Yuetong Ji, Wei Shen, Jiquan Liu, Luyang Sun, Jian Xu, Bo Ma

Experimental evolution is a powerful approach for scrutinizing and dissecting the development of antimicrobial resistance; nevertheless, it typically demands an extended duration to detect evolutionary changes. Here, a centrifugal microfluidics system is designed to accelerate the process. Through a simple step of on-chip centrifugation, a highly condensed bacterial matrix of ~ 1012 cells/mL at the enrichment tip of the chip channel is derived, enabling bacteria encapsulated to survive in

antimicrobial concentrations several times higher than the minimum inhibitory concentration (MIC) and rapidly develop resistance in the first 10 h. After 48 h of on-chip evolution, the E. coli strain demonstrated a 64 to 128-fold reduction in sensitivity to disinfectants (triclosan) as well as antibiotics (ciprofloxacin and amikacin), a rate substantially swifter compared to conventional continuous inoculation-based experimental evolution. The speed and simplicity of this microfluidic system suggest its broad application for uncovering resistance mechanisms and identifying targets of biocides and antibiotics.

专家简介：

委员：曾湖烈 研究员



博士，复旦大学青年研究员，第九批上海市特聘研究员入选者，博士生导师。2006 年中国科学院生态环境研究中心获得博士学位（导师：林金明教授），2006-2008 年日本东京都立大学博士后研究员（合作导师：Katsumi Uchiyama 教授），2008-2010 年加拿大滑铁卢大学博士后研究员（合作导师：Carolyn Ren 教授和 Janusz Pawliszyn 教授），2011-2019 年日本东京都立大学助理教授。2019 年 3 月加入复旦大学药学院。主要研究领域包括生物及药物微量分析方法及仪器开发，药物活体在线分析方法。在分析仪器高效化、便携化及小型化，药物及生物标志物等的在线分析传感等方面取得了系列研究成果。 已在 ACS Appl. Mater. Interfaces, Anal. Chem., Sens. Actuators B Chem., J. Mater. Chem. C 等学术期刊上发表论文 50 余篇；获批专利 3 项，其中 1 项获批国际专利及多国专利。研究成果得到国内外同行及学者的认可和关注。

Biosensors and Bioelectronics (IF 10.7) Published: 15 February 2024

Dynamic tissue model in vitro and its application for assessment of microplastics-induced toxicity to air-blood barrier (ABB).

Anchen Fu, Sifeng Mao, Nahoko Kasai, Haiyan Zhu, Hulie Zeng

The replication of the hominine physiological environment was identified as an effectual strategy to develop the physiological model in vitro to perform the intuitionistic assessment of toxicity of contaminations. Herein, we proposed a dynamic interface strategy that accurately mimicked the blood flow and shear stress in human capillaries to subtly evaluate the physiological damages. To proof the concept, the dynamic air-blood barrier (ABB) model in vitro was developed by the dynamic interface strategy and was utilized to assess the toxicity of polyethylene terephthalate microplastics (PET-MPs). The developed dynamic ABB model was compared with the static ABB model developed by the conventional Transwell® system and the animal model, then the performance of the dynamic ABB model in evaluation of the PET-MPs induced pulmonary damage via replicating the hominine ABB. The experimental data revealed that the developed dynamic ABB model in vitro effectively mimicked the physiological structure and barrier functions of human ABB, in which more sophisticated physiological microenvironment enabled the distinguishment of the toxicities of PET-MPs in different sizes and different concentrations comparing with the static ABB model constructed on Transwell® systems. Furthermore, the consistent physiological and biochemical characters adopted dynamic ABB model could be achieved in a quick manner referring with that of the mouse model in the evaluation of the microplastics-induced pulmonary damage. The proposed dynamic interface strategy supplied a general approach to develop the hominine physiological environment in vitro and exhibited a potential to develop the ABB model in vitro to evaluate the hazards of inhaled airborne pollutants.

Analytical Chemistry (IF 6.7) Published: 20 April 2024

Microsphere-Enhanced Fluorescence-Lightened Solid-Phase Hybridization Assay: the Strategy to Highly Selective Detection of Micro Ribonucleic Acids.

Ziheng Wei, Xiaoli Yang, Lingrui Xu, Lamu Benma, Danhong Wu, Hulie Zeng

The detection of low-abundance microribonucleic acid (miRNA) frequently adopted nucleic acid sequence-based amplification detection, which was found to have poor selectivity for the nonspecific amplification of template-dependent ligation in enzyme-mediated cascade reactions. Here, a highly selective detection of miRNAs was developed that combined microsphere-enhanced fluorescence (MSEF) and solid-phase base-paired hybridization. The target miRNA could be accurately and quantitatively identified through the solid-phase hybridization assay on the surface of an optical microsphere,

while the detected fluorescence signal could be physically amplified by MSEF. Hereinto, the optical microsphere acted as the fluorescence amplifier and whose surface supplied the space to carry out base-paired hybridization to recognize the target miRNA via the immobilized capture DNA sequence. The detected fluorescence signal of the single-base mismatched miRNA-21 sequence was just around 12% of that of the target miRNA-21 sequence in the measurement of model miRNA-21, while the limit of detection of miRNA-21 could be 1.0 fM. The developed detection of miRNA on an optical microsphere was demonstrated to be an excellent physically amplified method to selectively and sensitively detect the target miRNA and magnificently avoid the nonspecific amplification and false-positive results, which is expected to have wide applications in pathematology, pharmacology, clinic diagnosis, and on-site screening fields as well.

Microchemical Journal (IF 4.9) Published: 22 May 2024

Highly Precisive Digital Polymerase Chain Reaction Based on Inkjet Printer.

Xinning He , Beilu Weng , Lamu Benma , Yan Zou , Hizuru Nakajima , Hulie Zeng

To eliminate the indeterminate droplet partitions that highly obfuscate the distinguishment of the positive and the negative partitions in digital polymerase chain reaction (dPCR), the highly precisive droplets array of dPCR was developed via the inkjet printer coupled with the X-Y stage. The highly precisive droplets could be generated by the inkjet printer and the droplets array would be arranged by the movable X-Y stage at the same time. The highly precisive droplets array in a volume of at least 20,000 droplets could be obtained with a coefficients of variation (CV) of 1.57 % for the decided droplets in a diameter of 145.16 μm. The CV of the fluorescence intensities of droplets in array could be lowered to 3.17 % for the droplets of 5 μM fluorescein sodium solution, which guaranteed the clear identification of the positive droplets in the absolute quantification of dPCR. In addition, the thermal amplification in dPCR was designed to implement at the same sheet to avoid the delivery of the droplet partitions. The highly precisive dPCR was demonstrated through the wide linear range of more than 10 in the measurement of the model GAPDH gene with a low limitation of detection (LOD) of 0.60 copies/μL. Finally, the practicality of developed dPCR was confirmed by the measurement of the human mammaglobin (hMAM) gene in MCF-7 cell as well. The successful development of the highly precisive droplet array through the inkjet printer coupled with X-Y stage eliminated the indeterminate positive droplet partitions in dPCR. It paved a way to develop the compact and highly sensitive dPCR.

Analytical Chemistry (IF 6.7) Published: 2 October 2024

Dynamic Liver Chip Based on Well-Coupled Microfluidics: An Accurate NASH Model for Drug Evaluation.

Mingyang Chang, Anchen Fu, Bingqian Liu, Yongxiang Wang, Hulie Zeng

The convenient liver model in vitro recapitulating the hepatic functions, metabolism, and even steatohepatitis to perform the accurate drug evaluation is still challenging because of the unattainable hominine physiological microenvironment in vitro. Here, the progressed stages of nonalcoholic steatohepatitis (NASH) disease were precisely modeled to accurately evaluate the performance of antilipemic based on the dynamic liver chip adopting the well-coupled microfluidics, which well recapitulated the normal and steatohepatitis of liver in vitro. In brief, the mild nutrient flow and sufficient oxygen supply for parenchymal liver cells could be well supplied through the endothelial cells layer that mimicked the real physiological barrier of endothelium, while the loading of drugs might be obtained by directly adding drug into the running nutrient flow to mimic the intravenously administrable. The progressed degree of steatohepatitis could be directly reflected by the amount of intramyocellular lipid content (IMLC) of the HepG2 cell hepatocyte layer in wells that were induced by different concentrations of free fatty acids (FFA). To prove the concept of the liver chip in drug evaluation, an accurate assessment of the performance of firsocostat, the acetyl-CoA carboxylase (ACC) inhibitor of hepatic mitochondria of hepatocytes, was carried out. The subtle time dependence of firsocostat treatment to different progressed stages of NASH was clearly figured out. Therefore, we prospect the liver chip that adopted well-coupled microfluidics could be an accurate and standard liver model in vitro to carry out the antilipemic evaluation and screening, which significantly enlightens the drug evaluation by

liver on chip in vitro.

专家简介：

委员：钟润涛 教授



分析化学专业博士，大连海事大学环境系统生物学研究所成员。武汉大学化学系，理学学士，中国科学院研究生院博士，2009-2012 年在美国加州大学河滨分校进行博士后工作。主要从事微流控技术开发和生物标志物检测方面的教学和研究工作。研究方向为微流控系统开发和生物标志物微全分析，实现生物标志物实时现场检测，用于特殊环境（空间、远洋、野外等）下的生物医学研究、环境监测、健康检测等，为环境或健康风险评估提供基础数据和技术支撑。目前的研究重点是基于微流控芯片的核酸微全分析、免疫标志物多指标现场快速检测、模式生物（如线虫）自动化培养与监测等。已参与国家级科研项目近 10 项，发表学术论文和会议论文 20 余篇，参与编写微流控芯片专著 2 部，已授权专利近 10 项，目前申请专利近 10 项（含美国专利 1 项）。

Lab on a Chip (IF 7.5) Published: 10 July 2024

WormSpace μ-TAS enabling automated on-chip multi-strain culturing and multi-function imaging of Caenorhabditis elegans at the single-worm level on the China Space Station.

Qianqian Yang, Runtao Zhong*, Wenbo Chang, Kexin Chen, Mengyu Wang, Shuqi Yuan, Zheng Liang, Wei Wang, Chao Wang, Guanghui Tong, Tao Zhang, Yeqing Sun*

As a model organism for space biology experiments, Caenorhabditis elegans (C. elegans) has low demand for life support and strong resistance to unfavorable environments, making experimentation with C. elegans relatively easy and cost-effective. Previously, C. elegans has been flown in several spaceflight investigations, but there is still an urgent need for analytical platforms enabling on-orbit automated monitoring of multiple phenotypes of worms, such as growth and development, movement, changes of biomarkers, etc. To solve this problem, we presented a fully integrated microfluidic system (WormSpace μ-TAS) with an arrayed microfluidic chip (WormChip-4.8.1) and a replaceable microfluidic module (WormChip cartridge), which was compatible with the experimental facility on the China Space Station (CSS). By adopting technologies of programmed fluid control based on liquid medium CeMM as well as multi-function imaging with a camera mounted on a three-dimensional (3D) transportation stage, automated and long-term experimentation can be performed for on-chip multi-strain culturing and bright-field and fluorescence imaging of C. elegans at the single-worm level. The presented WormSpace μ-TAS enabled its successful application on the CSS, achieving flight launch of the sample unit (WormChip cartridge) at low temperature (controlled by a passive thermal case at 12 °C), automated 30-day cultivation of 4 strains of C. elegans, on-orbit monitoring of multiple phenotypes (growth and development, movement, and changes of fluorescent protein expression) at the single worm-level, on-chip fixation of animals at the end of the experiment and returning the fixed samples to earth. In summary, this study presented a verified microfluidic system and experimental protocols for automated on-chip multi-strain culturing and multi-function imaging of C. elegans at the single-worm level on the CSS. The WormSpace μ-TAS will provide a novel experimental platform for the study of biological effects of space radiation and microgravity, and for the development of protective drugs.

专家简介：

委员：张涛 教授



张涛博士，浙江大学副教授，博士生导师，浙江大学求是青年学者，中国生物物理学会微流控系统学分会委员。主要从事微流控芯片、生物传感器及分析仪器技术研究，主持国家重大科学仪器设备开发专项课题、国家自然科学基金、浙江省重大科技专项计划项目等省部级以上项目 10 余项，在 Lab on a Chip、Analytical Chemistry、Chemical Science 等期刊上发表学术论文 30 余篇，获授权发明专利 10 余项。

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 15 January 2024

Photofabricated Channel-Digital Microfluidics (pcdmf): A Promising Lab-on-a-chip Platform for Fully Integrated Digital PCR.

Yu He , Zefan Lu , Ke Liu , Lan Wang , Qiudi Xu , Hongliang Fan , Chong Liu , Tao Zhang

Microfluidics-based digital PCR (dPCR) is a potent technique capable of absolute quantification of nucleic acids with ultrahigh sensitivity. However, an indispensable process, nucleic acid extraction (NAE) remains hard to be integrated with dPCR into a monolithic device, because both of them involve complicated processes and exquisite fluid manipulation. An ideal solution to this issue is to integrate the two main microfluidic platforms, channel-based microfluidics (CMF) and digital microfluidics (DMF), which, however, remains very challenging. To address these challenges, we herein develop a photofabricated channel-digital microfluidic chip (pCDMF) with significant advantages including: the fabrication of pCDMF is very convenient due to the flexible material choices of photocuring, without tedious process of hydrophobic coating; a parallel-plate configuration can be easily formed, enabling all basic functions of DMF; various channels and microstructures can be freely designed, allowing for fluidic functions of CMF. It is therefore the first example of full integration of DMF and CMF as a monolithic device, with capabilities to precisely handle both discrete droplets and continuous fluids. Finally, an all-in-one device for sample-to-answer digital PCR has been successfully demonstrated. We also envisioned that the pCDMF may open an alternative route toward the fully integrated lab-on-a-chip for various biological applications.

Lab on a Chip **(IF 6.1)** Published: 9 May 2024

Laser-induced graphene-based digital microfluidics (gDMF): a versatile platform with sub-one-dollar cost.

Ke Liu, Yu He, Zefan Lu, Qiudi Xu, Lan Wang, Zhongxuan Liu, Jeremy Khou, Jiaming Ye, Chong Liu, Tao Zhang

Digital microfluidics (DMF), is an emerging liquid-handling technology, that shows promising potential in various biological and biomedical applications. However, the fabrication of conventional DMF chips is usually complicated, time-consuming, and costly, which seriously limits their widespread applications, especially in the field of point-of-care testing (POCT). Although the paper- or film-based DMF devices can offer an inexpensive and convenient alternative, they still suffer from the planar addressing structure, and thus, limited electrode quantity. To address the above issues, we herein describe the development of a laser-induced graphene (LIG) based digital microfluidics chip (gDMF). It can be easily made (within 10 min, under ambient conditions, without the need of costly materials or cleanroom-based techniques) by a computer-controlled laser scribing process. Moreover, both the planar addressing DMF (pgDMF) and vertical addressing

DMF (vgDMF) can be readily achieved, with the latter offering the potential of a higher electrode density. Also, both of them have an impressively low cost of below $1 ($0.85 for pgDMF, $0.59 for vgDMF). Experiments also show that both pgDMF and vgDMF have a comparable performance to conventional DMF devices, with a colorimetric assay performed on vgDMF as proof-of-concept to demonstrate their applicability. Given the simple fabrication, low cost, full function, and the ease of modifying the electrode pattern for various applications, it is reasonably expect that the proposed gDMF may offer an alternative choice as a versatile platform for POCT.

Sensors and Actuators B: Chemical **(IF 8.0)** Published: 4 November 2024

Digital microfluidic chip with photopatterned reactive sites for direct biomolecules immobilization and magnetic beads-free immunoassay.

Qiudi Xu, Ke Liu, Yu He, Lan Wang, Zefan Lu, Zhongxuan Liu, Tao Zhang

Digital microfluidics (DMF), as an emerging liquid-handling technology, is widely recognized as an ideal platform for enzyme-linked immunosorbent assay (ELISA). However, current DMF-based ELISA methods are highly dependent on magnetic beads (MBs), which usually involves tedious modification of MBs, complex peripherals for MBs control, and impairs the parallel processing capability of DMF. To address these issues, we herein developed a photopatterned reactive sites-integrated DMF chip (PRS-DMF) for MBs-free immunoassay. By taking advantage of click chemistry between N-(allyloxycarbonyloxy) succinimide and thiol-ene substrate, the preparation of PRS is very simple, and leaves the reactive N-hydroxysuccinimide (NHS) ester groups on the surface. This enables direct biomolecules immobilization without any surface modification/activation processes. Moreover, the patterned micropillar array can notably increase the specific surface area, and promote the liquid mixing and immunoreaction. As a consequence, highly sensitive and MBs-free ELISA can be readily achieved on PRS-DMF, with a proof-of-concept H5N1 assay having been successfully demonstrated herein, which offers a low limit of detection (LOD) of 147 pg/mL. This also avoids the use of complex magnetic peripherals, and thus, contributing to the instrument miniaturization into a very compact form. It is therefore reasonably expected that the proposed PRS-DMF may serve as a promising platform for a variety of biological and biomedical applications, especially in the field of point-of-care testing (POCT).

专家简介：

委员：张秀莉 教授



2019 年加入苏州大学药学院，任特聘教授。目 前主要研究方向为发展器官芯片、类器官、3D 生物打印等仿生技术，解决天然产物在药效和毒效评价中面临的问题。总计发表 SCI 文章 99 篇，H-index 为 30，参与撰写英文专著的一章，中文专著的二章。作为发明人已授权 20 项中国专利和 1 项美国专利。发表的文章曾获“第一届中国百篇最具影响优秀国际学术论文”和“辽宁省自然科学学术成果学术论文”二、三等奖，曾承担了科技部国际合作、自然科学基金面上项目等多个项目。

Frontiers in Pharmacology **(IF 4.4)** Published: 30 May 2024

Assessing immune hepatotoxicity of troglitazone with a versatile liver-immune-microphysiological-system.

Quanfeng Deng, Youlong Yang, Yuangui Liu, Mengting Zou, Guiyuan Huang, Shiqi Yang, Lingyu Li, Yueyang Qu, Yong Luo, Xiuli Zhang

Drug-induced liver injury is a prevalent adverse event associated with pharmaceutical agents. More significantly, there are certain drugs that present severe hepatotoxicity only during the clinical phase, consequently leading to the termination of drug development during clinical trials or the withdrawal from the market after approval. The establishment of an evaluation model that can sensitively manifest such hepatotoxicity has always been a challenging aspect in drug development. In this study, we build a liver-immune-microphysiological-system (LIMPS) to fully demonstrate the liver injury triggered by troglitazone (TGZ), a drug that was withdrawn from the market due to hepatotoxicity. Leveraging the capabilities of organ-on-chip technology allows for the dynamic modulation of cellular immune milieu, as well as the synergistic effects between drugs, hepatocytes and multiple immune cells. Through the LIMPS, we discovered that 1) TGZ can promote neutrophils to adhered hepatocytes, 2) the presence of TGZ enhances the crosstalk between macrophages and neutrophils, 3) the induction of damage in hepatocytes by TGZ at clinically relevant blood concentrations not observed in other in vitro experiments, 4) no hepatotoxicity was observed in LIMPS when exposed to rosiglitazone and pioglitazone, structurally similar analogs of TGZ, even at the higher multiples of blood drug concentration levels. As an immune-mediated liver toxicity assessment method, LIMPS is simple to operate and can be used to test multiple drug candidates to detect whether they will cause severe liver toxicity in clinical settings as early as possible.

Chemical Engineering Journal **(IF 13.3)** Published: 26 November 2024

Algae-based Flexible Localized Oxygen Control Around Cells: an Approach Leading to More Biomimetic Microphysiological Systems.

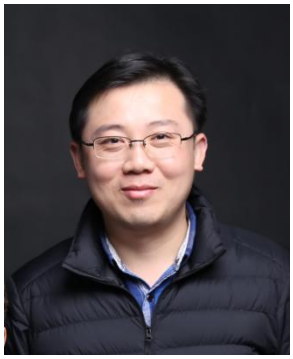
Yuangui Liu, Yueyang Qu, Youlong Yang, Quanfeng Deng, Yong Luo, Xiuli Zhang

Oxygen levels are crucial in the cellular microenvironment, affecting cellular function. Controlling pericellular oxygen is essential for understanding cell-oxygen interactions, disease mechanisms, and developing therapies. In this study, an algae strain was engineered as a biological oxygen-control material, integrated with a light-controlled microphysiological system to regulate pericellular oxygen. This technique could provide different oxygen levels and varying profiles for different locations within one microphysiological system. Additionally, the pericellular oxygen dynamics were faster than those achieved by other methods. By utilizing this algae-integrated microfluidic chip, mesenchymal stem cells differentiated into

adipocytes with improved phenotypic characteristics, including increased numbers and sizes of lipid droplets, under 21-day stage-specific oxygen concentrations. Furthermore, this technique effectively mitigated the need to vent significant amounts of oxygen or nitrogen into the laboratory during long-term or virus-infested experiments, thereby enhancing both safety and practicality. The algae-integrated microfluidic chip also served as a platform for constructing a stroke-related vascular-on-chip model, enabling the evaluation of the protective effects of oxygen therapy on endothelial injury induced by oxygen-glucose deprivation/reperfusion (OGD/R). The results indicated that waving hyperoxic dynamics were most effective in safeguarding vascular tissue against OGD/R compared to other hyperoxic dynamics. This finding can guide the clinical oxygen inhalation mode during stroke management. All the aforementioned results demonstrated that the algae-light microphysiological system offered a technical platform capable of precise, dynamic pericellular oxygen control across the disciplines of biology and pharmaceutics. Moreover, The cost-effective cultivation of algae on a large scale made this method suitable for wider use.

专家简介：

委员：赵远锦 教授



赵远锦，教授，博导，国家“万人计划”科技领军人才，国家优青，江苏省杰青，英国皇家化学会(RSC) Fellow。于 2006 年获得东南大学临床医学学士学位；2009 年到 2010 年到哈佛大学 David A. Weitz 教授（美国三院院士）团队学习；2011 年毕业于东南大学，获工学博士学位。2012 年破格晋升为副研究员；2013 年入选教育部“新世纪优秀人才支持计划”、江苏省“六大人才高峰”资助计划；2014 年获“江苏省杰出青年基金”；2015 年破格晋升为研究员、特聘教授，获“国家优秀青年基金”、“中国化学会青年化学奖”；2016 年入选“江苏省 333 高层次人才培养工程”；2017 年入选“中国新锐科技人物”；2018 年入选英国皇家化学会(RSC)的 Fellow、科技部中青年科技领军人才；2019 年入选国家“万人计划”科技创新领军人才；2020 年获“中国化学会-杰出青年科学家奖”。

现在的主要研究方向有生物材料与组织工程、仿生器官与器官芯片、微流控等。已发表 SCI 论文 220 余篇，其中 80 余篇发表于 IF 大于 10 的国际权威期刊，论文 IF 之和约 2000，被引用 7700 余次（H 因子为 46）；第一作者/通讯作者论文包括 7 篇 Nature / Science 子刊、4 篇 PNAS、16 篇 Adv.Mater. / JACS / Angew、以及 Chem.Rev. / Chem.Soc.Rew. / Accounts 等；研究成果共申请专利 102 项，获授权 41 项，转让 2 项。

Nature Chemical Engineering **(IF 13.9)** Published: 1 January 2024

Flexible hemline-shaped microfibers for liquid transport.

Chaoyu Yang , Yunru Yu , Luoran Shang , Yuanjin Zhao

Directional liquid transport is important in both fundamental studies and industrial applications. Most existing strategies rely on the use of predesigned surfaces with sophisticated microstructures that limit the versatility and universality of the liquid transport. Here we present a platform for liquid transport based on flexible microfluidic-derived fibers with hemline-shaped cross-sections. These microfibers have periodic parallel microcavities along the axial direction, with sharp edges and wedge corners that enable unilateral pinning and capillary rise of liquids. This structure enables directional liquid transport along hydrophilic substrates with the use of a single fiber. Alternatively, a pair of fibers enables directional liquid transport along hydrophobic substrates or even without any additional substrate; the directional transport behavior applies to a wide range of liquids. We demonstrate the use of these fibers in open microfluidics, water extraction and liquid transport along arbitrary three-dimensional paths. Our platform provides a facile and universal solution for directional liquid transport in a range of different scenarios.

Aggregate **(IF 13.9)** Published: 4 March 2024

Bio-inspired temporospatial catalytic cascades systems based on ultrasound-triggered multicomponent piezoelectric microparticles.

Danqing Huang, Jinglin Wang, Xiao Fu, Yuanjin Zhao, Lingyun Sun

Reactive oxygen species (ROS) have certain effect in cancer treatment, thus many studies have been focused on developing functional systems to generate ROS in tumor. Here, inspired by the multi-enzyme biocatalysis in organisms, novel ultrasound-triggered temporospatial catalytic cascades systems are presented based on barium titanate (BTO) and platinum (Pt) co-loaded multi-component microparticles (Pt/BTO@MCMPs) to successively achieve oxygen and ROS production for tumor sonodynamic therapy. By using a customized capillary microfluidic device, the Pt/BTO@MCMPs are fabricated with Pt nanoparticles located in their core part and BTO nanocubes located in their peripheral part, alternating with blank porous hydrogel components for increasing interaction areas between the encapsulated nanomaterials and the ambient substrates. In

the microparticles, the Pt can catalyze hydrogen peroxide from the tumor microenvironment to generate O2 and H2O serving as substrates for piezoelectric catalytic reactions, contributing to additional generation of ROS under US activation. Based on the system, it is demonstrated that the Pt/BTO@MCMPs are featured with excellent biocompatibility under normal biological conditions and show desired tumor eradication properties under ultrasound irradiation in mice carrying pancreatic tumors. These results indicate that the proposed ultrasound-triggered temporospatial catalytic cascades systems are promising for clinic anti-tumor applications.

Aggregate (IF 13.9) Published: 6 March 2024

Multifunctional inverse opal microcarriers-based cytokines delivery system with stem cell homing capability for osteoarthritis treatment.

Lingyu Sun, Jingjing Gan, Lijun Cai, Feika Bian, Wei Xu, Yuanjin Zhao

Osteoarthritis has been regarded as a complex and serious degenerative disease. Attempts in this area are focused on improving the curative effect of stem cell-based therapies. In this work, we present a novel inverse opal microcarriers-based cytokines delivery system to induce autologous stem cell homing for osteoarthritis treatment. Considering their important role in stem cell recruitment and chondrogenic differentiation respectively, platelet-derived growth factor BB (PDGF-BB) and transforming growth factor β3 (TGF-β3) are loaded into inverse opal microcarriers as model cytokines. Since cytokine release induces the corresponding variations in characteristic reflection spectra and structural colors, the inverse opal microcarriers possess the optical self-reporting capacity to monitor the release process. In vitro cell experiments reveal that inverse opal microcarriers could successfully recruit the gathering of mesenchymal stem cells through the release of loaded cytokines. Based on these features, we have demonstrated the enhanced therapeutic effect of PDGF-BB and TGF-β3 loaded inverse opal microcarriers in the treatment of rat osteoarthritis models. These results indicate that the multifunctional inverse opal microcarriers-based cytokines delivery system would find broad prospects in osteoarthritis treatment and other biomedical fields.

Advanced materials (IF 27.4) Published: 14 March 2024

Engineered Microorganisms for Advancing Tumor Therapy.

Jinxuan Jia, Xiaocheng Wang, Xiang Lin, Yuanjin Zhao

Engineered microorganisms have attracted significant interest as a unique therapeutic platform in tumor treatment. Compared with conventional cancer treatment strategies, engineering microorganism-based systems provide various distinct advantages, such as the intrinsic capability in targeting tumors, their inherent immunogenicity, in situ production of antitumor agents, and multiple synergistic functions to fight against tumors. Herein, the design, preparation, and application of the engineered microorganisms for advanced tumor therapy are thoroughly reviewed. This review presents a comprehensive survey of innovative tumor therapeutic strategies based on a series of representative engineered microorganisms, including bacteria, viruses, microalgae, and fungi. Specifically, it offers extensive analyses of the design principles, engineering strategies, and tumor therapeutic mechanisms, as well as the advantages and limitations of different engineered microorganism-based systems. Finally, the current challenges and future research prospects in this field, which can inspire new ideas for the design of creative tumor therapy paradigms utilizing engineered microorganisms and facilitate their clinical applications, are discussed.

Advanced materials (IF 27.4) Published: 15 March 2024

Electroacoustic Responsive Cochlea-on-a-Chip.

Yangnan Hu, Jiayue Xing, Hui Zhang, Xinyi Pang, Yabo Zhai, Hong Cheng, Dongyu Xu, Menghui Liao, Yanru Qi, Danqi Wu, Bin Zhang, Lin Cheng, Bo Chu, Chen Zhang, Yuanjin Zhao, Renjie Cha

Organ-on-chips can highly simulate the complex physiological functions of organs, exhibiting broad application prospects in developmental research, disease simulation, as well as new drug research and development. However, there is still less concern about effectively constructing cochlea-on-chips. Here, a novel cochlear organoids-integrated conductive hydrogel biohybrid system with cochlear implant electroacoustic stimulation (EAS) for cochlea-on-a-chip construction and high-throughput drug screening, is presented. Benefiting from the superior biocompatibility and electrical property of conductive hydrogel, together with cochlear implant EAS, the inner ear progenitor cells can proliferate and spontaneously shape into spheres, finally forming cochlear organoids with good cell viability and structurally mature hair cells. By incorporating these progenitor cells-encapsulated hydrogels into a microfluidic-based cochlea-on-a-chip with culture chambers and a concentration gradient generator, a dynamic and high-throughput evaluation of inner ear disease-related drugs is demonstrated. These results indicate that the proposed cochlea-on-a-chip platform has great application potential in organoid cultivation and deafness drug evaluation.

***ACS Nano* (IF 15.8)** Published: 18 March 2024

Biomimetic Tertiary Lymphoid Structures with Microporous Annealed Particle Scaffolds for Cancer Postoperative Therapy.

Gaizhen Kuang , Qingfei Zhang, Wenzhao Li, Yuanjin Zhao

Immunotherapy plays a vital role in cancer postoperative treatment. Strategies to increase the variety of immune cells and their sustainable supply are essential to improve the therapeutic effect of immune cell-based immunotherapy. Here, inspired by tertiary lymphoid structures (TLSs), we present a microfluidic-assisted microporous annealed particle (MAP) scaffold for the persistent recruitment of diverse immune cells for cancer postoperative therapy. Based on the thermochemical responsivity of gelatin methacryloyl (GelMA), the MAP scaffold was fabricated by physical cross-linking and sequential photo-cross-linking of GelMA droplets, which were prepared by microfluidic electrospraying. Due to the encapsulation of liquid nitrogen-inactivated tumor cells and immunostimulant, the generated MAP scaffold could recruit a large number of immune cells, involving T cells, macrophages, dendritic cells, B cells, and natural killer cells, thereby forming the biomimetic TLSs in vivo. In addition, by combination of immune checkpoint inhibitors, a synergistic anticancer immune response was provoked to inhibit tumor recurrence and metastasis. These properties make the proposed MAP scaffold-based artificial TLSs of great value for efficient cancer postoperative therapy.

***Materials Today* (IF 21.1)** Published: March 2024

Tailoring drug delivery systems by microfluidics for tumor therapy.

Qingfei Zhang, Gaizhen Kuang, Li Wang, Lu Fan, Yuanjin Zhao

Drug delivery systems (DDSs) for tumor treatment is a specialized method aimed at transporting therapeutic substances, especially anticancer drugs, to specific target areas in the body. The primary aim is to improve the therapeutic effect of anticancer substances while minimizing their impact on healthy tissues. Microfluidic technology can precisely control, manipulate, and analyze fluids at the microscopic level. In the field of tumor therapy, microfluidic technology has become an advanced tool for designing and manufacturing customized drug carriers to deliver drugs to cancer cells or tumor sites. Microfluidic DDSs hold significant promise for tumor therapy due to their unique features and capabilities such as precision, customization, versatility, scalability, etc. Thus, in this review, the advantages, design, and implementation of microfluidic drug delivery technology were introduced. It summarizes various DDSs from microfluidics, such as nanoparticles, microparticles, and scaffolds, and discusses their potential in a range of therapeutic modes. In addition, the challenges and prospects of microfluidic DDSs in tumor treatment were discussed. The main purpose of this review is to provide a comprehensive overview of the progress, potential impacts, and future directions of customizing DDSs for tumor treatment using microfluidic technology.

Advanced Functional Materials (IF 18.5) Published: 5 April 2024

Ion-Specific Hydrogel Microcarriers with Biomimetic Niches for Bioartifical Liver System.

Xiang Lin, Jinbo Li, Jinglin Wang, Anne M. Filppula, Hongbo Zhang, Yuanjin Zhao

Bioartificial livers have showcased significant value in the treatment of acute liver failure (ALF). Current efforts are directed toward overcoming challenges in the development of microcarriers, with a specific emphasis on integrating higher-density liver cells to enhance detoxification capabilities. Here, inspired by the radial filtration model in hepatic lobules, ion-specific silk fibroin microcarriers are proposed with biomimetic niches for cultivating functional liver cells at high density. These biomimetic microcarriers are generated by capillary microfluidic device with controllable adjustments of ion type or concentration within the aqueous phase. When cultivating human induced pluripotent stem cell -differentiated mature liver cells on these recrystallized microcarriers, notably enhanced cell proliferation activity, as well as increased metabolic and secretory functionality is observed. Based on these features, the microcarrier-integrated bioreactor can effectively reduce hepatic transaminase levels and significantly improve urea, albumin production, and survival rate in rabbit ALF models is demonstrated. Thus, it is believed that the biomimetic microcarriers and their derived bioreactor may hold potential for clinical applications in managing ALF and other liver diseases.

Smart medicine Published: 21 May 2024

Developing organs-on-chips for biomedical applications.

Lingyu Sun, Hanxu Chen, Dongyu Xu, Rui Liu, Yuanjin Zhao

In recent years, organs-on-chips have been arousing great interest for their bionic and stable construction of crucial human organs in vitro. Compared with traditional animal models and two-dimensional cell models, organs-on-chips could not only overcome the limitations of species difference and poor predict ability but also be capable of reappearing the complex cell-cell interaction, tissue interface, biofluid and other physiological conditions of humans. Therefore, organs-on-chips have been regarded as promising and powerful tools in diverse fields such as biology, chemistry, medicine and so on. In this perspective, we present a review of organs-on-chips for biomedical applications. After introducing the key elements and manufacturing craft of organs-on-chips, we intend to review their cut-edging applications in biomedical fields, incorporating biological analysis, drug development, robotics and so on. Finally, the emphasis is focused on the perspectives of organs-on-chips.

Science Bulletin (IF 18.8) Published: 30 May 2024

Biomimetic hepatic lobules from three-dimensional imprinted cell sheets.

Jinglin Wang, Danqing Huang, Hanxu Chen, Yuanjin Zhao

Liver-tissue engineering has proven valuable in treating liver diseases, but the construction of liver tissues with high fidelity remains challenging. Here, we present a novel three-dimensional (3D)-imprinted cell-sheet strategy for the synchronous construction of biomimetic hepatic microtissues with high accuracy in terms of cell type, density, and distribution. To achieve this, the specific composition of hepatic cells in a normal human liver was determined using a spatial proteogenomics dataset. The data and biomimetic hepatic micro-tissues with hexagonal hollow cross-sections indicate that cell information was successfully generated using a homemade 3D-imprinted device for layer-by-layer imprinting and assembling the hepatic cell sheets. By infiltrating vascular endothelial cells into the hollow section of the assembly, biomimetic hepatic microtissues with vascularized channels for nutrient diffusion and drug perfusion can be obtained. We demonstrate that the resultant vascularized biomimetic hepatic micro-tissues can not only be integrated into a microfluidic drug-screening liver-on-a-chip but also assembled into an enlarged physiological structure to promote liver regeneration. We believe that our 3D-imprinted cell sheets strategy will open new avenues for biomimetic microtissue construction.

Engineering (IF 10.1) Published: 1 June 2024

Bio-Inspired Screwed Conduits from the Microfluidic Rope-Coiling Effect for Microvessels and Bronchioles.

Rui Liu, Jiahui Guo, Bin Kong, Yunru Yu, Yuanjin Zhao, Yuanjin Zhao

Tubular microfibers have recently attracted extensive interest for applications in tissue engineering. However, the fabrication of tubular fibers with intricate hierarchical structures remains a major challenge. Here, we present a novel one-step microfluidic spinning method to generate bio-inspired screwed conduits (BSCs). Based on the microfluidic rope-coiling effect, a viscous hydrogel precursor is first curved into a helix stream in the channel, and then consecutively packed as a hollow structured stream and gelated into an SC via ionic and covalent crosslinking. By taking advantage of the excellent fluid-controlling ability of microfluidics, various tubes with diverse structures are fabricated via simple control over fluid velocities and multiple microfluidic device designs. The perfusability and permeability results, as well as the encapsulation and culture of human umbilical vein endothelial cells (HUVECs), human pulmonary alveolar epithelial cells (HPAs), and myogenic cells (C2C12), demonstrate that these SCs have good perfusability and permeability and the ability to induce the formation of functional biostructures. These features support the uniqueness and potential applications of these BSCs as biomimetic blood vessels and bronchiole tissues in combination with tissue microstructures, with likely application possibilities in biomedical engineering.

Nano-Micro Letters (IF 31.6) Published: 2 July 2024

Self-Healing Dynamic Hydrogel Microparticles with Structural Color for Wound Management.

Li Wang, Xiaoya Ding, Lu Fan, Anne M Filppula, Qinyu Li, Hongbo Zhang, Yuanjin Zhao, Luoran Shang

Chronic diabetic wounds confront a significant medical challenge because of increasing prevalence and difficult-healing circumstances. It is vital to develop multifunctional hydrogel dressings, with well-designed morphology and structure to enhance flexibility and effectiveness in wound management. To achieve these, we propose a self-healing hydrogel dressing based on structural color microspheres for wound management. The microsphere comprised a photothermal-responsive inverse opal framework, which was constructed by hyaluronic acid methacryloyl, silk fibroin methacryloyl and black phosphorus quantum dots (BPQDs), and was further re-filled with a dynamic hydrogel. The dynamic hydrogel filler was formed by Knoevenagel condensation reaction between cyanoacetate and benzaldehyde-functionalized dextran (DEX-CA and DEX-BA). Notably, the composite microspheres can be applied arbitrarily, and they can adhere together upon near-infrared irradiation by leveraging the BPQDs-mediated photothermal effect and the thermoreversible stiffness change of dynamic hydrogel. Additionally, eumenitin and vascular endothelial growth factor were co-loaded in the microspheres and their release behavior can be regulated by the same mechanism. Moreover, effective monitoring of the drug release process can be achieved through visual color variations. The microsphere system has demonstrated desired capabilities of controllable drug release and efficient wound management. These characteristics suggest broad prospects for the proposed composite microspheres in clinical applications.

PNAS (IF 9.4) Published: 3 July 2024

Flexible liquid-diode microtubes from multimodal microfluidics.

Chaoyu Yang, Wenzhao Li, Yuanjin Zhao, Luoran Shang

Directional transport of liquids is of great importance in energy saving, chemical/biomedical engineering, and microfluidics applications. Despite considerable progress in engineering different open surfaces to achieve liquid manipulation, the realization of diode-like liquid transport in enclosed spaces is still challenging. Here, a flexible diode microtube is presented for directional liquid transport within confined spaces using pulsed microfluidics. The microtubes exhibit sophisticated microstructures on the inner wall, replicated from a precisely controlled flow configuration in the microfluidic channel.

Under the effect of asymmetric pinning and unbalanced Laplace pressure, such microtubes enable directional liquid transport in closed channels. More importantly, by integrating in situ flow lithography with the microfluidic system, segmented liquid diodes are fabricated as assembly units for the construction of fluidic–electronic circuits that perform logic operations. These results demonstrate the capacity of the present liquid-diode microtubes for flexible, directional, and programmable liquid transport. We believe that it can open an avenue for designing advanced fluidic circuit-based devices toward versatile practical applications.

Chemical Engineering Journal **(IF 13.3)** Published: 10 July 2024

Dental pulp stem cells-loaded kartogenin-modified hydrogel microspheres with chondrocyte differentiation property for cartilage repair.

Chuanhui Song, Xiangyi Wu, Zheng Wei, Ye Xu, Yongxiang Wang, Yuanjin Zhao

Stem cell-based regimens have evolved as a promising approach to cartilage reparations. Research efforts in this realm aim to enhance the therapeutic capabilities of stem cells and develop more effective cell delivery strategies. Herein, we present novel dental pulp stem cells (DPSCs)-loaded kartogenin-modified hydrogel microspheres with chondrocyte differentiation property for temporomandibular joint (TMJ) osteoarthritis treatment. Leveraging microfluidic technology, DPSCs were successfully encapsulated in hydrogel microspheres, serving as the pivotal contributors to cartilage repair. By modifying the hydrogel with kartogenin, these microspheres facilitated sustained stimulation of DPSCs' chondrogenic differentiation. In vitro experimental results revealed that the DPSCs exhibited advanced cartilage-forming differentiation, as evidenced by the up-regulation of relative gene expressions and protein markers. Additionally, the DPSCs-loaded microspheres system displayed a capacity to regenerate and repair tissue at the cartilage defects in a TMJ osteoarthritis animal model. Thus, the DPSCs-loaded kartogenin-modified hydrogel microspheres exhibit significant promise for cartilage repair, showcasing the substantial potential for future clinical applications.

Science China Materials **(IF 6.8)** Published: 12 July 2024

Biomimetic cell encapsulations by microfluidics.

Jinglin Wang,Danqing Huang,Yile Fang,Haozhen Ren,Yuanjin Zhao

Cell encapsulated in biomaterials for organ repair or disease treatment is indeed an emerging field. Currently, microfluidics is being utilized to precisely control the quantity, size, and scaffold structure of encapsulated cells. Specifically, microfluidics offers the ability to design biomimetic morphologies that enhance the activity and function of encapsulated cells, thereby improving the effectiveness of disease treatment. In this review, we report the latest advancements in microfluidic-based biomimetic cell encapsulation. To begin with, we provide a brief overview of various naturally derived biomimetic structures that promote cellular functionality, such as those inspired by cells, plants, animals, and natural responses. Moving forward, we discuss recent cell encapsulation methods based on microtechnology and provide detailed descriptions of the relevant processes. Finally, we address the challenges and future directions of biomimetic cell encapsulation in disease treatment and clinical applications.

Materials Futures **(IF 12.0)** Published: 17 July 2024

Tailoring esophageal tumor spheroids on a chip with inverse opal scaffolds for drug screening.

Ruolin Shi, Xiangyi Wu, Yuanjin Zhao, Shegan Gao and Gaofeng Liang

Esophageal cancer (EC) is characterized by high morbidity and mortality, and chemotherapy has become an indispensable means for comprehensive treatment. However, due to the limitation of the effective in vitro disease model, the development of chemotherapeutic agents still faces great challenges. In this paper, we present a novel tumor spheroid on a chip platform based on inverse opal hydrogel scaffolds to screen chemotherapeutic agents for EC treatment. With the microfluidic

emulsion approach, the inverse opal hydrogel scaffolds were generated with tunable and organized pores, which could provide spatial confinement for cell growth. Thus, the suspended KYSE-70 cells could successfully form uniform cell spheroids on the inverse opal hydrogel scaffolds. It was demonstrated that the tumor cell spheroids could recapitulate 3D growth patterns in vivo and exhibited higher sensitivity to the chemotherapy agents compared with monolayer cells. Besides, by employing the scaffolds into a microfluidics to construct esophageal tumor on a chip, the device could realize high-throughput tumor cell spheroids generation and drug screening, indicating its promising role in chemotherapy drug development.

***Chemical Engineering Journal* (IF 13.3)** Published: 1 August 2024

Biomimetic cascade-released hydrogel scaffolds from microfluidics for efficient T cell recruitment and expansion.

Xin Shou, Dan Wu, Changjiang Chen, Liyun Shi, Luoran Shang, Yuanjin Zhao, Xian Shen

Adoptive T-cell immunotherapy has shown powerful therapeutic effects in cancer treatment. Attempts to implement T cell therapy have tended to focus on providing T cells with specific targeting and sufficient activation to enhance their tumor killing ability. Although biomaterial-based scaffolds can provide necessary molecular cues for T cell activation, efficient stimulation necessitates more attention on the reconstruction of natural T cell activation processes. Here, we present a novel biomimetic scaffold with cascade-released capacity for T-cell recruitment and activation. Core-shell structured hydrogel scaffolds are fabricated by single-step microfluidic electrospray, and chemokines and stimulatory antibodies are compartmentalized in the shell and core, respectively. Benefiting from the heterogeneity in the microstructure and swelling degree of the core and shell hydrogels, chemokine peptides are robustly released to recruit tumor-reactive T cells, and stimulatory antibodies are continuously released to support T cell proliferation. Such biomimetic recruitment and activation processes contribute to the formation of T cell clusters, which enhances their proliferation and infiltration in tumor tissues. Owing to the high expression of cytotoxic receptor and chemokine receptor, the activated T cells exhibit potent antitumor activity in vitro and in vivo. These features demonstrate that the cascade-released hydrogel scaffolds are promising for the local recruitment and activation of tumor-reactive T cells.

***Journal of Nanobiotechnology* (IF 10.6)** Published: 20 August 2024

Bio-inspired biorthogonal compartmental microparticles for tumor chemotherapy and photothermal therapy.

Qingfei Zhang, Gaizhen Kuang, Li Wang, Lu Fan, Yechao Zhou, Luoran Shang, Yuanjin Zhao, Weijian Sun

Microcarrier is a promising drug delivery system demonstrating significant value in treating cancers. One of the main goals is to devise microcarriers with ingenious structures and functions to achieve better therapeutic efficacy in tumors. Here, inspired by the nucleus-cytoplasm structure of cells and the material exchange reaction between them, we develop a type of biorthogonal compartmental microparticles (BCMs) from microfluidics that can separately load and sequentially release cyclooctene-modified doxorubicin prodrug (TCO-DOX) and tetrazine-modified indocyanine green (Tz-ICG) for tumor therapy. The Tz-ICG works not only as an activator for TCO-DOX but also as a photothermal agent, allowing for the combination of bioorthogonal chemotherapy and photothermal therapy (PTT). Besides, the modification of DOX with cyclooctene significantly decreases the systemic toxicity of DOX. As a result, the developed BCMs demonstrate efficient in vitro tumor cell eradication and exhibit notable tumor growth inhibition with favorable safety. These findings illustrate that the formulated BCMs establish a platform for bioorthogonal prodrug activation and localized delivery, holding significant potential for cancer therapy and related applications.

Journal of Nanobiotechnology (IF 10.2) Published: 27 August 2024

Stem cell recruitment polypeptide hydrogel microcarriers with exosome delivery for osteoarthritis treatment.

Lei Yang, Wenzhao Li, Yuanjin Zhao, Yongxiang Wang, Luoran Shang

With the accelerated aging tendency, osteoarthritis (OA) has become an intractable global public health challenge. Stem cells and their derivative exosome (Exo) have shown great potential in OA treatment. Research in this area tends to develop functional microcarriers for stem cell and Exo delivery to improve the therapeutic effect. Herein, we develop a novel system of Exo-encapsulated stem cell-recruitment hydrogel microcarriers from liquid nitrogen-assisted microfluidic electrospray for OA treatment. Benefited from the advanced droplet generation capability of microfluidics and mild cryogelation procedure, the resultant particles show uniform size dispersion and excellent biocompatibility. Moreover, acryloylated stem cell recruitment peptides SKPPGTSS are directly crosslinked within the particles by ultraviolet irradiation, thus simplifying the peptide coupling process and preventing its premature release. The SKPPGTSS-modified particles can recruit endogenous stem cells to promote cartilage repair and the released Exo from the particles further enhances the cartilage repair performance through synergistic effects. These features suggest that the proposed hydrogel microcarrier delivery system is a promising candidate for OA treatment.

Chemical Engineering Journal (IF 13.3) Published: 28 August 2024

Bioinspired micro-nano hierarchical delivery system for sequential targeted therapy of inflammatory bowel disease.

Peipei Xi , Xiangyu Wei , Yongxin Xu , Nengjie Yang , Yunan Wang , Yuting Huang , Minjie Chen , Ya Wen , Yujuan Zhu , Yuanjin Zhao , Zhifeng Gu

Inflammatory bowel disease (IBD) constitutes an immense health and economic burden worldwide, highlighting the need for improved therapy. Up to now, various delivery systems have been proposed to enhance IBD treatment. Herein, inspired by cellular communication in nature, we present a novel micro-nano hierarchical microsphere system with the enhanced targeting capability for IBD treatment. The hierarchical microspheres are designed for oral delivery, with astaxanthin nanoparticles in the core and Zein protein shell. Similar to a stepwise process of cellular communication, microscale spheres can escape from the gastric acid due to Zein coating. Once reach into the intestine, mucoadhesive Zein coating and the core could be enzymatically digested, following the targeted release of astaxanthin nanoparticles. Particularly, these astaxanthin nanoparticles are endowed with the mitochondria targeting capability, thereby greatly attenuating pro-inflammatory response of macrophages. Based on these features, practical performances of the hierarchical delivery system have been investigated in both acute and chronic colitis model. Animal experiments have revealed the desired therapeutic effects of the hierarchical microspheres by inhibiting inflammatory responses and modulating gut microbiota. These results suggested the present hierarchical delivery system offers a stepwise strategy for nanodrug delivery to the intestine as well as the effective treatment of IBD.

Engineering (IF 10.1) Published: September 2024

Biomimetic Erythrocyte-Like Particles from Microfluidic Electrospray for Tissue Engineering.

Zhiqiang Luo,Lijun Cai,Hanxu Chen,Guopu Chen,Yuanjin Zhao

Microparticles have demonstrated value for regenerative medicine. Attempts in this field tend to focus on the development of intelligent multifunctional microparticles for tissue regeneration. Here, inspired by erythrocytes-associated self-repairing process in damaged tissue, we present novel biomimetic erythrocyte-like microparticles (ELMPs). These ELMPs, which are composed of extracellular matrix-like hybrid hydrogels and the functional additives of black phosphorus, hemoglobin, and growth factors (GFs), are generated by using a microfluidic electrospray. As the resultant ELMPs have the capacity for

oxygen delivery and near-infrared-responsive release of both GFs and oxygen, they would have excellent biocompatibility and multifunctional performance when serving as microscaffolds for cell adhesion, stimulating angiogenesis, and adjusting the release profile of cargoes. Based on these features, we demonstrate that the ELMPs can stably overlap to fill a wound and realize controllable cargo release to achieve the desired curative effect of tissue regeneration. Thus, we consider our biomimetic ELMPs with discoid morphology and cargo-delivery capacity to be ideal for tissue engineering.

Research **(IF 8.5)** Published: 12 September 2024

A Biomimetic Optical Cardiac Fibrosis-on-a-Chip for High-Throughput Anti-Fibrotic Drug Screening.

Yixuan Shang, Dongyu Xu , Lingyu Sun, Yuanjin Zhao, Lingyun Sun

Cardiac fibrosis has emerged as the primary cause of morbidity, disability, and even mortality in numerous nations. In light of the advancements in precision medicine strategies, substantial attention has been directed toward the development of a practical and precise drug screening platform customized for individual patients. In this study, we introduce a biomimetic cardiac fibrosis-on-a-chip incorporating structural color hydrogels (SCHs) to enable optical high-throughput drug screening. By cocultivating a substantial proportion of cardiac fibroblasts (CFBs) with cardiomyocytes on the SCH, this biomimetic fibrotic microtissue successfully replicates the structural components and biomechanical properties associated with cardiac fibrosis. More importantly, the structural color shift observed in the SCH can be indicative of cardiac contraction and relaxation, making it a valuable tool for evaluating fibrosis progression. By incorporating such fibrotic microtissue into a microfluidic gradient chip, we develop a biomimetic optical cardiac fibrosis-on-a-chip platform that accurately and efficiently screens potential anti-fibrotic drugs. These characteristics suggest that this microphysiological platform possesses the capability to establish a preclinical framework for screening cardiac drugs, and may even contribute to the advancement of precision medicine.

Advanced Materials **(IF 27.4)** Published: 13 September 2024

Biomimetic Multichannel Silk Nerve Conduits with Multicellular Spatiotemporal Distributions for Spinal Cord Injury Repair.

Tao Yuan, Wenzhao Li, Minyu Zhou, Xiaocheng Wang, Bing Wang, Yuanjin Zhao

Bioengineered nerve conduits have shown great promise for spinal cord injury (SCI) repair, while their practical values are limited by poor regenerative efficacy and lack of multi-level structural design. Here, inspired by the ingenious anatomy of natural spinal cords, a biomimetic multichannel silk nerve conduit (namely BNC@MSCs/SCs) with multicellular spatiotemporal distributions for effective SCI repair is presented. The biomimetic silk nerve conduit (BNC) with hierarchical channels and aligned pore structures is prepared via a modified directional freeze-casting strategy. Such hierarchical structures provide appropriate space for the mesenchymal stem cells (MSCs) and Schwann cells (SCs) settled in specific channels, which contributes to the generation of BNC@MSCs/SCs resembling the cellular spatiotemporal distributions of natural spinal cords. The in vitro results reveal the facilitated SC migration and MSC differentiation in such BNC@MSCs/SCs multicellular system, which further promotes the tube formation and cell migration of endothelial cells as well as M2 polarization of macrophages. Moreover, BNC@MSCs/SCs can effectively promote the tissue repair and function recovery in SCI rats by attenuating glial scar formation while promoting neuron regeneration and myelin sheath reconstruction. Thus, it is believed that the biomimetic multichannel silk nerve conduits with multicellular spatiotemporal distributions are valuable for SCI repair and other neural tissue regeneration.

Advanced Science **(IF 14.3)** Published: 19 September 2024

Biomimetic Liver Lobules from Multi-Compartmental Microfluidics.

Danqing Huang, Zhuhao Wu, Ji Wang, Jinglin Wang, Yuanjin Zhao

Engineered liver lobule is highly practical in hepatic disease treatment, while constructing a 3D biomimetic lobule with a heterogeneous architecture on a large scale is challenging. Here, inspired by the natural architectural construction of hepatic lobules, biomimetic hepatic lobules are proposed with coaxially through-pores for nutrient exchange via microfluidic technology. This multi-channel microfluidic chip is made by parallelly installing capillaries. Sodium alginate (Alg) is pumped through its central channel, while Ca2+-loaded gelatin methacrylate (GelMA) solutions encapsulating hepatocytes, mesenchymal stem cells, and endothelia cells are pumped through surrounding channels, respectively. The rapid gelation of Alg and Ca2+ brings about an in situ formation of Alg fiber, with heterogeneous multi-cell-laden GelMA microcarriers forming around it. The peeled-off microcarriers each featured with a coaxially through pore, simulating the cord-like structure of hepatic lobule and facilitating nutrients exchange. Meanwhile, the spatially anisotropic arrangement of cells highly simulates the hepatic architecture. It is demonstrated that by transplanting these biomimetic microparticles into liver in situ, the failed liver in rat shows increased regeneration and decreased necrosis. These results indicated that the microfluidic multi-compartmental microcarriers provide a new strategy to engineer 3D artificial livers for clinical translation.

Nature Chemical Engineering Published: 26 September 2024

Biomimetic air purification with liquid-gating topological gradient microfluidics.

Hanxu Chen, Lingyu Sun, Yu Wang, Lijun Cai, Yuanjin Zhao, Luoran Shang

Particle capture is vital for air purification in environmental protection, regional climate regulation and public health. In particular, filters operating with gas–liquid interfaces can provide efficient particle absorption and removal while serving in a maintenance-free manner. Here a liquid-gating topological gradient microfluidics (LGTGM) device is developed for air purification inspired by the liquid-assisted filtration mechanism of the human respiratory system. The LGTGM device is based on the continuous generation of microbubbles from a supplied gas flow. Due to the large specific interfacial surface area, together with tailored wettability in the device, particulate pollutants in the microbubbles preferentially transfer across the gas–liquid interface and enter a collection liquid. Benefiting from the fine regulation of bubble generation dynamics, multiple LGTGM devices can be combined in series or parallel to achieve efficient air purification as well as high-throughput processing. Moreover, the application potential of LGTGM is demonstrated for smoke filtration, disease prevention and visual detection.

Chemical Engineering Journal **(IF 13.3)** Published: 9 October 2024

Spatiotemporal piezoelectric microcapsules for programmable sonodynamic sterilization and wound healing.

Danqing Huang, Min Nie, Jinglin Wang, Yuanjin Zhao, Lingyun Sun

Hydrogel particles have certain practicability in facilitating wound healing, nowadays endeavors have been devoted to developing particles with architectural construction and controllable cargo release property for infected wound management. Here, inspired by the cocktail treatment, we propose a spatiotemporal piezoelectric microcapsule with potassium sodium niobate (KNN)-encapsulated shell and vascular endothelial growth factor (VEGF)-loaded core (KV-MPs) via microfluidic technology for ultrasound (US)-assisted infected wound treatment. As a biocompatible piezoelectric material, KNN exert piezocatalytic redox and reactive oxygen species (ROS)-generating property under US excitation, contributing to bacterial elimination. With the degradation of the shell, the core exposes and sustainedly releases VEGF for angiogenesis and promoting tissue regeneration. In mice with infected wound, we have demonstrated that the US-excited KV-MPs can effectively fight bacteria and subsequent accelerate wound repair. These results indicated our spatiotemporal piezoelectric microcapsules provide an effective strategy for sonodynamic sterilization meanwhile realize tissue regeneration.

Research (IF 8.5) Published: 14 October 2024

Glycyrrhizic Acid Hydrogel Microparticles Encapsulated with Mesenchymal Stem Cell Exosomes for Wound Healing.

Luting Zhang, Zhiqiang Luo, Hanxu Chen, Xiangyi Wu, Yuanjin Zhao

Hydrogel microparticles have been proved to be curative to diabetic wounds. Current trends focus on the integration of bioactive matrix and their smart stimulus-responsive release to meet the complex demand of regeneration in diabetic wound. In this paper, we present novel stem cell exosome-encapsulated Chinese herb glycyrrhizic acid (GA) hydrogel microparticles for wound healing. The integrated GA endows the hydrogel microparticles with antibacterial properties, while the encapsulated exosomes impart them with pro-angiogenesis ability. In addition, as the black phosphorus is incorporated into these hybrid hydrogel microparticles, the release profile of GA and exosomes could be controllable under near-infrared irradiation due to the excellent photothermal effect of black phosphorus and the reversible phase transformation properties of GA. Based on these features, we have demonstrated that these microparticles can effectively kill bacteria, scavenge free radical, and promote angiogenesis from in vitro experiments. Besides, they could also markedly accelerate the wound healing process by down-regulating inflammation and promoting collagen deposition and angiogenesis in bacteria-infected in vivo diabetic wound. These results indicate that the proposed exosome-integrated GA hydrogel microparticles present great potential for clinical diabetic wound treatment.

Advanced Functional Materials (IF 18.5) Published: 22 October 2024

Biomimetic Mineralized Organic–Inorganic Hybrid Scaffolds From Microfluidic 3D Printing for Bone Repair.

Lei Yang, Wenzhao Li, Xiaoya Ding, Yuanjin Zhao, Xiaoyun Qian, Luoran Shang

Bone defect is a common clinical orthopedic disease. The trend in this field is to develop tissue engineering scaffolds with appropriately designed components and structures for bone repair. Herein, inspired by the organic and inorganic components of bone matrix and the natural biomineralization mechanism, a MgSiO3@Fe3O4 nanoparticle composite polycaprolactone (PCL) hybrid mineralized scaffold for bone repair is developed by microfluidic 3D printing. The incorporation of MgSiO3@Fe3O4 within the PCL scaffold can effectively improve the bioactivity. In addition, a biomimetic mineralized layer is prepared on the surface of the scaffold, which endowed it with unique microstructural characteristics, enhanced cell adhesion and osteogenic activity, and thus improved the bone repair performance. Owing to these advantages, both in vivo and in vitro experiments have demonstrated that the designed scaffold has outstanding biocompatibility and bone repair performance. These features indicate that the organic–inorganic biomineralized hybrid scaffold can be a potential bone graft substitute for clinical bone repair.

Chemical Engineering Journal (IF 13.3) Published: 28 October 2024

Mesenchymal stem cells-laden self-healing hydrogel microfiber fragments from microfluidic bubbles interrupted spinning for wound healing.

Yingbo Shen, Rui Liu, Xiangyi Wu, Ying Lu, Bin Kong, Yuanjin Zhao

Mesenchymal stem cells (MSCs) loaded hydrogels have shown positive therapeutic effects in skin wound treatment, while their application is still impractical on the wound bed. Here, we propose novel MSCs-loaded self-healing hydrogel microfiber fragments from microfluidic bubbles interrupted spinning for wound healing. The hydrogel microfibers are composed of sodium alginate, gelatin, polyvinyl alcohol, and borax, vesting them with good biocompatibility and self-healing ability. Their fragments with adjustable length are generated by introducing bubbles into microfluidic channels. We have demonstrated that the self-healing microfibers can promote the proliferation of MSCs, which are seeded alongside fragments' surfaces to further facilitate the wound healing process. In addition, these MSCs laden self-healing hydrogel

microfibers (MSG-fibers) showed obvious healing effect in rat wound model, which significantly promoted granulation tissue formation, collagen deposition and vascular construction at the wound site. Thus, we believe that our proposed MSC-laden microfiber fragments are valuable in promoting wound healing and have promising prospect in becoming new options for wound management.

Advanced Healthcare Materials **(IF 10.0)** Published: 29 October 2024

Multifunctional Analgesic Sutures from Microfluidic Spinning Technology.

Yunan Peng, Yixuan Shang, Junyi Che, Yunru Yu, Yuanjin Zhao, Xiaoping Gu

Sutures are the most commonly used wound repair method after surgery. However, addressing delayed recovery and pain management remains a significant challenge. Here, microfibers are developed from microfluidic spinning with long-lasting analgesia capabilities for sutures. By using a solvent extraction manner, the polycaprolactone (PCL) microfibers encapsulated with ropivacaine (ROP), a well-known analgesic, can be continuously obtained from microfluidics. The intrinsic property of PCL and the advantage of microfluidic spinning technique impart the microfiber with highly controlled morphologies, mechanical strengths, as well as drug release. After exploring their biocompatibility both at in vitro and in vivo levels, the microfibers are directly applied to wound suture. The results demonstrate the lasting analgesic effect of the microfiber on mice with incision pain, highlighting its potential as promising suture for post-surgery treatments. It is anticipated that the multifunctional analgesic sutures produced through microfluidic spinning will pave the way for utilizing fibers as effective sutures in clinical incision wound treatment.

Small **(IF 13.0)** Published: 30 October 2024

Melanin Hydrogel Inverse Opal Microneedle Patches for Wound Healing.

Minhui Lu, Xinyue Cao, Zhiqiang Luo, Feika Bian, Yu Wang, Yuanjin Zhao

Bacterial infected wounds bring an economic burden to the worldwide medical care field. A variety of bioactives-integrated hydrogel patches are developed in response to this challenge. Here, the melanin hydrogel inverse opal microneedle patches (MNs) with antioxidant and visual color sensing abilities for the management of bacterial infected wounds are proposed. The MNs are fabricated by applying melanin-loaded polyethylene glycol diacrylate (PEGDA) as the inverse opal hydrogel and using bacitracin-carried gelatin to fill those nanopores of hydrogel scaffold. Benefitting from the antioxidant capacity of melanin nanoparticles and the local antimicrobial ability of bacitracin, the resulting MNs possess the integrated functions of reactive oxygen species scavenging and antibacterial. Besides, the inverse opal structure endows the MNs with vivid structure color and detectable reflected wavelength, which can gradually shift with the release of the drug, thus allowing MNs to assess the drug delivery. Based on these characteristics, MNs perform excellent in in vitro drug delivery and monitoring, as well as the promotion of bacterial infected wound recovery in vivo, indicating the potential of MNs in the future wound management field.

Aggregate **(IF 13.9)** Published: 31 October 2024

Biomimetic Triplet Messenger RNA Formulation in MXene Hydrogel Microneedles for Wound Healing.

Ji Wang, Yu Wang, Minhui Lu, Xinyue Cao, Ming Xia, Miaoqing Zhao, Yuanjin Zhao

Messenger RNA (mRNA) has demonstrated immense potential in disease therapeutic applications. The current direction is focused on imparting mRNA with competitive synthetic functions and delicate carrier systems. Here, inspired by the collaborative regulation of growth factors by the cellular microenvironment, we present novel transition metal carbide/nitride (MXene) hydrogel microneedles loaded with a biomimetic triplet mRNA formulation (TM) for diabetic wound treatment. Such microneedles were composed of TM, MXene, and hyaluronic acid hydrogel. The presence of

MXene imparted the microneedles with great photo-thermal responsiveness properties, thus realizing controlled active release by the shrinkage/swelling of hydrogel. With the effective release of TM, the microneedles were proven to enhance endothelial cell migration, growth, and angiogenesis. Through in vivo animal experiments, we have confirmed that TM-microneedles (TM-MNs) can promote tissue regeneration and collagen deposition more effectively than intravenous and intradermal administration. Thus, we believe that the proposed TM-MN platform with precise delivery and controllable release of TM will show great potential for promoting the healing of clinic diabetic wounds.

Engineering **(IF 10.1)** Published: 1 November 2024

Controllable Histotomy Based on Hierarchical Magnetic Microneedle Array Robots.

Xiaoxuan Zhang, Hanxu Chen,Taiyu Song, Jinglin Wang, Yuanjin Zhao

Investigation of patient-derived primary tissues is of great importance in the biomedical field, but recent tissue slicing and cultivation techniques still have difficulties in satisfying clinical requirements. Here, we propose a controllable histotomy strategy that utilizes hierarchical magnetic microneedle array robots to tailor primary tissues and establish the desired high-throughput tissue-on-a-chip. This histotomy is performed using a three-dimensional printed, mortise-tenon-structured slicing device coupled with a magnetic-particle-loaded and pagoda-shaped microneedle array scaffold. Due to the multilayered structure of these microneedles, tissue specimens can be fixed onto the microneedle scaffold via mechanical interlocking, thereby effectively avoiding tissue slipping during the slicing process. Owing to the encapsulation of magnetic microneedle fragments, these tissue pieces can act as magnetically responsive biohybrid microrobots and can be easily manipulated by magnetic fields, facilitating their separation, transportation, and dynamic culture. Using this strategy, we demonstrate that primary pancreatic cancer tissues can be tailored into tiny pieces and cultured in multilayered microfluidic chips for efficient high-throughput drug screening, indicating the promising future of this technique’s application in clinical settings.

Advanced Science **(IF 14.3)** Published: 6 November 2024

Black Phosphorus Tagged Responsive Strontium Hydrogel Particles for Bone Defect Repair.

Zhengwei Liu, Hui Zhang, Jingjing Gan, Yuanjin Zhao, Yongxiang Wang

Hydrogel-derived implants have proven value in bone tissue regeneration, and current efforts have concentrated on devising strategies for producing functional implants with desired structures and functions to improve therapeutic outcomes. Herein, a novel black phosphorus (BP) tagged responsive strontium (Sr) hydrogel particles are presented for bone defect repair. By applying microfluidic technology, Sr and carboxymethyl chitosan, and BP are integrated into poly(N-isopropyl acrylamide) (pNIPAM) hydrogel matrix to generate such microparticles called pNBCSMs. Upon exposure to near-infrared irradiation, the pNBCSMs experience volume shrinkage and provoke the extrusion of the incorporated Sr, ascribed to the photothermal conversion ability of BP and the thermosensitivity of pNIPAM. In vitro and in vivo experimental results reveal that pNBCSMs subjected to near-infrared light display superior anti-inflammatory, anti-apoptotic, bacterial inhibitory, as well as osteogenesis-promoting effects, thereby effectively improving defective cranial bone repair. These features suggest that the proposed pNBCSMs can be promising candidates for bone repair.

Materials Today Bio **(IF 8.7)** Published: 23 November 2024

Mussel-inspired multi-bioactive microsphere scaffolds for bone defect photothermal therapy.

Kaixuan Ma, Lei Yang, Wenzhao Li, Kai Chen, Luoran Shang, Yushu Bai, Yuanjin Zhao

Hydrogel microspheres hold great promise as scaffolds for bone repair. Their hydrated matrix, biocompatibility, and functional properties make them an attractive choice in regenerative medicine. However, the irregularity of defect requires shape adaptability of the microspheres. Additionally, there is still room for improvement regarding the component of the

microspheres to achieve sufficient bioactivity. Here, we prepare multi-bioactive microspheres composed of methacrylated silk fibroin (SFMA) via microfluidic electrospray. Magnesium ascorbyl phosphate (MAP) is encapsulated within the microspheres, whose sustained release facilitates angiogenesis and osteogenic differentiation. The microspheres are further coated with a polydopamine (PDA) layer, allowing them to assemble insitu into a scaffold that conforms to the non-uniform contours of bone defects. The photothermal conversion capability of PDA also provides mild photothermal stimulation to further promote bone regeneration. Based on the synergistic effects, our in vivo experiments demonstrated that the microsphere scaffold effectively promotes bone defect healing. Thus, this multi-bioactive scaffold offers a versatile strategy for bone repair with promising clinical potential.

Science Bulletin **(IF 18.8)** Published: 27 November 2024

Frog tongue-inspired wettable microfibers for particles capture.

Jiahui Guo, Lingyu Sun, Han Zhang, Yuanjin Zhao

Fibers have been of great significance in our daily lives, especially in the industrial production of masks. Research in this area has been focused on developing microfibers with superior functions to enhance the filtration performances of the masks. Herein, inspired by the frog's predation mechanism using its tongues to swiftly grab flying insects, we propose novel porous wettable microfibers from microfluidics to efficiently capture particles in the air for filtration. Upon pre-dispersing LP emulsions into polyurethane (PU), porous microfibers dispersed with oil droplets could be continuously spun from a co-flow microfluidic device based on the quick phase inversion of PU. To design an optimal system with frog-tongue-like interfacial adhesion properties, the wettability performances of the porous microfibers are investigated under full, partial, and no oil coverage conditions. When implemented in a mask, the 3D patterned networks based on the frog-tongue-inspired microfibers have been proven with remarkable particle capture performances while maintaining good air permeability. Based on these features, we believe that frog-tongue-inspired microfibers and their derived masks are of practical significance in multiple applications.

Chemical Engineering Journal **(IF 13.3)** Published: 3 December 2024

Structural color heart-on-a-chip for evaluating the myocardial protection effects of traditional Chinese medicine.

Xuhong Guo, Lingyu Sun, Dongyu Xu, Yuanjin Zhao

Many Chinese medicines have shown protective effects on the heart, while their specific effects and modes of action are still lacking of intuitive studies. In this paper, we propose a structural color heart-on-a-chip from layer assembly for evaluating the myocardial protection effects of traditional Chinese medicine. The structural color scaffolds are imparted with a striped microstructure on one side for inducing the alignment of cardiomyocytes, and an inverse opal nanostructure on the other side for optical sensing. Because the scaffold could generate obvious color changes upon cardiomyocyte contraction, its integration into a microfluidic chip provides a simple screening platform to study the pre-protective effects of Chinese medicine against cardiac injury. We have demonstrated that with the induction of doxorubicin, the injured cardiomyocytes presented abnormal morphology, disappeared sarcomere and depressed beating behaviors that could be reflected by reduced structural color changes. On the contrary, traditional Chinese medicine pre-protection can increase the vitality of cardiomyocytes, reduce reactive oxygen species production, and improve the contractile function of cardiomyocytes, which is highly consistent with the known conclusion. These results indicated that our structural color heart-on-a-chip with real-time visualization characteristics could provide an ideal platform for traditional Chinese medicine development and drug screening.

Advanced Science (IF 14.3) Published: 24 December 2024

Biomimetic Vascularized iPSC-Hepatocyte Spheroids for Liver Regeneration.

Jinglin Wang, Danqing Huang, Haozhen Ren, Yuanjin Zhao

Human induced pluripotent stem cell derived hepatocytes (hiPSC-heps) hold promising value for acute liver failure (ALF) treatment, while their therapeutic efficacy is usually limited by low cell bioactivity and untargeted in vivo accumulation. Here, inspired by vascularity supporting cellular architectures in the tissues and organs, a novel vascularized hiPSC-heps spheroid based on microfluidic microcapsules is presented for liver repair via orthotopic transplantation. The microcapsules are comprised of aqueous cores that facilitate hiPSC-hep aggregating into spheroids, and hybrid hydrogel shells of sodium alginate and hyaluronic acid methacryloyl (HAMA). By selectively degrading the alginate, the microcapsules are imparted with porous HAMA shells, which not only allowed human umbilical vein endothelial cells (HUVECs) to attach and form vascularized networks, but also facilitated communication between HUVECs and hiPSC-heps. The specific spatial distributions of these cells in the vascularized hiPSC-hep spheroids can provide nutrition support, promote the hepatic functions, and avoid immune cell attacks. Based on these features, it is illustrated that the vascularized hiPSC-hep spheroids can repair the acute failing liver more effectively, indicating their practical values in clinical liver repair.

Chemical Engineering Journal (IF 13.3) Published: 28 December 2024

Vitamin C Encapsulated Biomimetic Nanogels with Macrophage Membrane Decoration for Chronic Wound Healing.

Xin Yang, Xiang Lin, Jinbo Li, Tapani Viitala, Yuanjin Zhao, Hongbo Zhang, Luoran Shang

Diabetic wound healing is usually accompanied by uncontrolled inflammation. Drug delivery systems containing antioxidants are expected to resolve inflammation in local wounds and beneficially accelerate the repairing efficiency of wound healing. In this paper, we designed a biomimetic nanogel to deliver magnesium ascorbate phosphate (MAP, a vitamin C derivative) for relieving local inflammation in the wound. We applied the microfluidic technology to prepare nanogels composed of gelatin methacrylate (GelMA) and alginate, loaded with MAP. The macrophage membrane is further wrapped on the surface of the nanogel, endowing it with the inflammation targeting ability. During wound treatment, MAP was continuously released from the nanogel, which then cleared reactive oxygen species and promoted the polarization of M2 macrophages, thereby regulating the inflammatory wound microenvironment. This biomimetic nanogel efficiently solved the multifaceted challenges of chronic wound healing and showed beneficial repair effects in diabetic rat wounds. The in vitro and in vivo results all demonstrate the superb potentiality of biomimetic nanogels in bioactive drug delivery, chronic wound treatment, and related applications.