
《自然》（20261008出版）一周论文导读

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编译李言

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化学Chemistry

Organic two-dimensional van der Waals heterostructures

有机二维范德华异质结构

▲ 作者：Anupam Prasoon, Nguyen Ngan Nguyen et al.

▲ 链接：

<https://www.nature.com/articles/s41586-026-11074-6>

▲ 摘要：

研究者提出一种自下而上的策略，用于二维聚合物有机范德华异质结构中的可编程晶格工程。

通过顺序水表面组装技术能够逐层堆叠化学上不同的二维聚合物，并精确控制晶格配准、堆叠顺序和厚度，从而获得晶格匹配和可控晶格失配的异质结构。

结构表征显示，在晶格匹配和小失配体系中存在共格外延，而大失配界面则表现出莫尔特征和应变释放畸变。超快光谱证明存在高效的界面电荷分离，第一性原理计算揭示了由界面偶极排列产生的内建电场和界面电势阶跃。

器件表现出超过 10^3 的二极管整流比，且该比值随晶格失配增加而系统性降低，确立了有机二维

聚合物范德华异质结构作为（光）电子和量子现象中晶格工程化平台的地位。

▲ Abstract :

Here we introduce a bottom-up strategy for programmable lattice engineering in organic van der Waals heterostructures of 2D polymers. Sequential on-water-surface assembly enables layer-by-layer stacking of chemically distinct 2D polymers with defined lattice registry, stacking sequence and thickness, yielding both lattice-matched and controlled lattice-mismatched heterostructures. Structural characterization reveals commensurate epitaxy in lattice-matched and small-mismatched systems, whereas large-mismatch interfaces exhibit moiré features and strain-relief distortions. Ultrafast spectroscopy demonstrates efficient interfacial charge separation and first-principles calculations reveal built-in electric fields and interfacial potential steps arising from interfacial dipole alignment. Devices exhibit diode-like rectification ratios exceeding 10^7 that systematically decrease with increasing lattice mismatch, establishing organic 2D polymer van der Waals heterostructures as a lattice-engineered platform for (opto)electronic and quantum phenomena.

机器人学Robotics

A quadruped robot designed to complete a marathon on a single battery charge

一款为单次充电可完成马拉松而设计的四足机器人

▲ 作者：Choongin Lee, Donghoon Youm et al.

▲ 链接：

<https://www.nature.com/articles/s41586-026-11102-5>

▲摘要：

研究者展示了RAIBO2，一款通过对其整体能量损失模型进行全面分析而开发的高能效四足机器人。其效率通过力透明轻量化机械硬件、低电阻电机驱动电路和低能量耗散运动控制策略得以提升。

RAIBO2在单次充电下以4小时19分52秒完成全程马拉松，实现了0.25的总运输成本，超越了人类0.37的基准。

与现有四足机器人相比，RAIBO2每次充电的行驶里程是其三倍以上。这一能效突破为电池寿命至关重要的长时间户外应用铺平了道路。

▲ Abstract：

Here we show RAIBO2, an energy-efficient quadruped developed through a comprehensive analysis of its overall energy-loss model. Efficiency is enhanced through a force-transparent, lightweight mechanical hardware, a low-resistance motor driving circuit and a low-energy-dissipation locomotion policy. RAIBO2 completed a full marathon in 4?hours, 19?minutes and 52?seconds on a single battery charge⁷, achieving a total cost of transport of 0.25: surpassing the human benchmark of 0.37. Compared with existing quadrupeds, RAIBO2 offers more than three times the travel range per battery charge. This breakthrough in energy efficiency paves the way for extended outdoor applications in which prolonged battery life is critical.

生物学Biology

Gasdermin D-mediated delivery of caspase inhibitors to suppress pyroptosis

Gasdermin D介导的caspase抑制剂递送抑制细胞焦亡

▲ 作者：Katarzyna M. Grobocz, Melissa E. Truong et al.

▲ 链接：

<https://www.nature.com/articles/s41586-026-10957-y>

▲ 摘要：

研究者在此介绍了共价caspase抑制剂，它们能够选择性阻断细胞焦亡和IL-1 β 分泌，尽管被健康细胞排除在外。

这些抑制剂不阻止caspase驱动细胞凋亡，表明GSDMD孔道促进了它们的摄取。膜不可渗透性染料进入了从焦亡中获救的细胞，这与GSDMD孔道引起的瞬时膜通透化一致。

Caspase抑制阻止而非延迟了细胞死亡，这与膜修复机制中和初始GSDMD孔道的作用一致。

在内毒素休克小鼠模型中，抑制caspase-1和caspase-11抑制了IL-1 β 和IL-18的产生，凸显了利用GSDMD孔道进行靶向caspase抑制在炎症性疾病中的治疗潜力。

▲ Abstract：

Here we describe covalent caspase inhibitors that selectively block pyroptosis and IL-1 β secretion despite being excluded from healthy cells. These inhibitors did not prevent caspase-driven apoptosis, implying that GSDMD pores facilitated their uptake. Membrane-impermeable dyes entered the cells rescued from pyroptosis, consistent with transient membrane permeabilization by GSDMD pores. Caspase inhibition prevented rather than delayed cell death, consistent with membrane repair mechanisms neutralizing the initial GSDMD pores. Inhibiting caspase-1 and caspase-11 suppressed IL-1 β and IL-18 production in a mouse model of endotoxic shock, underscoring the therapeutic potential of exploiting GSDMD pores for

targeted caspase inhibition in inflammatory diseases.

Ultrafast and reference-free sequence discovery in single-cell data

单细胞数据中的超快和无参考序列发现

▲ 作者：Daniel León-Peri¹, Nikos Karaïskos, Nikolaus Rajewsky

▲ 链接：

<https://www.nature.com/articles/s41586-026-10975-w>

▲ 摘要：

研究者介绍计算平台Malva，它能够对原始序列空间进行超快速、物种无关且无需参考的探查，从而支持搜索任意序列、突变、剪接位点或病原体，或任意转录本的空间位置。

持续扩展的Malva索引目前包含来自数千项健康与疾病实验的约7400万个细胞。Malva实现了无需参考的发现——例如，研究人员可以直接从序列组成中识别细胞类型并预测细胞间相似性。

基于Malva的速度和准确性，研究者展示了如何将Malva灵活连接至最先进的神经网络，以及如何执行复杂搜索并实现自动化分析。

Malva将单细胞图谱从静态基因计数表转变为动态的、序列解析的资源，有望帮助弥合人类与机器在生物学推理上的差距。

▲ Abstract :

Here we present Malva, a computational platform that enables ultrafast, species-agnostic and reference-free interrogation of the raw sequence space, enabling searching for any sequence, mutation, splice junction or pathogen, or spatial location of arbitrary transcripts. The continuously expanding Malva Index currently comprises around 74 million cells from thousands of experiments in health and disease. Malva enables reference-free discovery—researchers can, for example, identify cell types and predict cell – cell similarity directly from sequence composition. Building on Malva ’ s speed and accuracy, we demonstrate how Malva can be flexibly connected to state-of-the-art neural networks and how to execute complex searches and enable automated analyses. Malva transforms single-cell atlases from static gene count tables into dynamic, sequence-resolved resources that may help to bridge human – machine reasoning about biology.

医学Medicine

Structure and operating principles of a monkeypox virus replisome

猴痘病毒复制体的结构与激活机制

▲ 作者 : Zishuo Yu, Pradeep Sathyanarayana et al.

▲ 链接 :

<https://www.nature.com/articles/s41586-026-10937-2>

▲ 摘要 :

研究者利用冷冻电镜解析了结合DNA的猴痘病毒复制体结构, 该复制体包含聚合酶全酶 (F8、A22和E4) 以及E5解旋酶六聚体。

研究表明，在复制体组装过程中，E5发生大规模构象变化，使其两个引物酶结构域能够与聚合酶F8的拇指结构域及A22亚基相互作用。

生化实验和单分子实验揭示，E5的这一构象变化与解旋酶激活相耦合，并增强引物酶活性。综上所述，这些发现鉴定了一类重要病毒病原体在DNA复制过程中协调解旋酶与聚合酶活性的基本机制。

▲ Abstract :

Here we used cryo-electron microscopy to determine the structures of DNA-bound MPXV replisomes comprising the polymerase holoenzyme (F8, A22 and E4) and the E5 helicase hexamer. We show that, during replisome assembly, E5 undergoes large-scale conformational changes that allow two of its primase domains to interact with the polymerase F8 thumb and A22 subunit. Biochemical assays and single-molecule experiments reveal that this E5 conformational change is coupled to helicase activation and enhances primase activity. Taken together, these findings identify fundamental mechanisms governing coordinated helicase and polymerase activities during DNA replication for an important class of viral pathogens.

An Icelandic pangenome reference

冰岛人泛基因组参考

▲ 作者：Guillaume Holley, Hannes P. Eggertsson et al.

▲ 链接：

<https://www.nature.com/articles/s41586-026-10924-7>

▲摘要：

研究者在此介绍两种解决参考偏差的新方法：用于泛基因组构建的Emblask和用于大规模泛基因组比对的Weaver。Emblask是一种针对亲本—子代三联体数据的混合长读长与短读长单倍型解析双组装流程。

利用Emblask，研究者组装了698个冰岛人单倍型，并将其加入人类泛基因组参考联盟泛基因组，构建了包含5141万个小型变异的冰岛泛基因组参考。研究者利用Weaver将57630名冰岛人的短读长序列比对至HPRC-ICE，并检测到9896万个变异，相比比对至线性参考增加了6.17%。

研究者在低比对区域发现了新变异，包括一个与早发性帕金森病相关的GBA1致病性单核苷酸多态性，以及一个导致高胱氨酸尿症的CBS错义单核苷酸多态性。

通过对429193名英国和爱尔兰参与者进行靶向重比对，在英国生物银行中重复验证了GBA1的关联。

▲ Abstract：

Here we introduce two new methods to address reference bias: Emblask for pangenome construction and Weaver for mapping to pangenomes at scale. Emblask is a hybrid long- and short-read haplotype-resolved dual assembly pipeline for parent – offspring trio data. Using Emblask, we assembled 698 Icelandic haplotypes and added them to the Human Pangenome Reference Consortium (HPRC) pangenome4 to construct an Icelandic pangenome reference (HPRC-ICE) including 51.41 million small variants. We mapped the short reads of 57,630 Icelanders to HPRC-ICE with Weaver and called 98.96 million variants, representing a 6.17% increase over mapping to a linear reference. We uncovered new variants in low-mappability regions, including a pathogenic single nucleotide polymorphism (SNP) in GBA1 that associates with early onset Parkinson ’ s disease and a missense SNP in CBS that is pathogenic for homocystinuria. We replicated the GBA1 association in the UK Biobank6 with a targeted remapping of 429,193 British and Irish participants.

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