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计算机科学Computer Science

A thermodynamically favoured molecular computer

一种热力学有利的分子计算机

▲作者：Tristan St é rin, Abeer Eshra et al.

▲链接：

https://www.nature.com/articles/s41586-026-10996-5

▲摘要：

研究者展示了一种热力学有利的支架DNA计算机，其在10个程序上得到验证，包括乘以3、除以2、8位奇偶检测以及25位数相加——即100位计算。该支架DNA计算机的算法具有简单的实验方案，可重复使用数十次，且小规模实例可在不到一分钟内运行。

数学、物理和计算机科学原理共同解释了为何该支架DNA计算机是热力学有利的，为何它不需要纠错或精确的动力学控制，以及它如何实现可编程性和可扩展性。这项工作为思考各类合成系统中的平衡计算开辟了新途径。

▲Abstract：

Here we demonstrate a thermodynamically favoured Scaffolded DNA Computer (SDC) on 10 programs, including Multiplication-by-3, Division-by-2, 8-bit Parity-detection and Addition of 25-bit numbers—a 100-bit computation. SDC algorithms have simple experimental protocols, can be reused dozens of times and small instances run in under a minute. Mathematical, physical and computer science principles explain why the SDC is thermodynamically favoured, why it does not require error-correction or precise kinetic control, and how it is programmable and scalable. This work creates a new way to think about equilibrium computation in all manner of synthetic systems..

生物学Biology

Human brain organoids record the passage of time over multiple years

人脑类器官记录多年时间流逝

▲作者：Irene Faravelli, Noelia Ant ó n-Bolaos et al.

▲链接：

https://www.nature.com/articles/s41586-026-10877-x

▲摘要：

研究者将人脑类器官在培养中维持了5年，优化生长条件使兴奋性神经元的存活时间超越了此前的极限。利用源自内源性人脑的成熟相关模块，他们表明脑类器官在多年培养中随培养时间发生具有细胞类型特异性的转录组衰老。全基因组甲基化分析揭示，类器官的预测表观基因组年龄与体外培养时间精确相关，并与体内表观基因组衰老相平行。

值得注意的是，研究者表明在由不同年龄神经祖细胞混合产生的嵌合类器官中，年老祖细胞迅速产生晚期神经元命运，跳过了早期神经元后代的产生，因此表明在类器官中衰老的祖细胞保留了体外培养时间的记忆。这些数据表明，人脑类器官可以在培养中持续成熟并记录多年时间的流逝。

▲Abstract：

Here we develop human brain organoids for 5 years in culture, optimizing growth conditions to extend excitatory neuron viability beyond previous limits. Using maturation-associated modules derived from endogenous human brain, we show that brain organoids transcriptionally age with cell type specificity over years in culture. Whole-genome methylation profiling reveals that the predicted epigenomic age of organoids correlates precisely with time spent in vitro, and parallels epigenomic ageing in vivo. Notably, we show that in chimeric organoids generated by mixing neural progenitors of different ages, old progenitors rapidly produce late neuronal fates, skipping the production of earlier neuronal progeny, therefore showing that progenitors that age in organoids retain a memory of the time spent in vitro. The data indicate that human brain organoids can continue to mature and record the passage of time over many years in culture.

Stimulation modulates gene-linked cell assemblies in the human brain

刺激调节人脑中基因相关的细胞组合

▲作者：Haley Moore, Mantre Dehnad et al.

▲链接：

https://www.nature.com/articles/s41586-026-10879-9

▲摘要：

为直接研究人类脑刺激引发的神经调控机制，研究者开发了一个离体平台，将微电极阵列刺激与同步记录及单核基因组学相结合，研究对象为接受神经外科手术患者切除的颞叶皮层组织。研究者发现刺激增强了细胞组装，并将这一效应与细胞类型特异性的基因调控网络相关联。

进一步通过识别体内刺激后人类皮层中常见的细胞类型特异性基因表达特征，证明了这些发现的普适性。总之，研究结果为识别与生理功能相关的可靶向遗传特征奠定了基础，这些特征或可通过神经调控策略用于治疗获益。

▲Abstract：

Here, to directly investigate the mechanisms of neuromodulation elicited by human brain stimulation, we developed an ex vivo platform that integrates microelectrode array stimulation with simultaneous recording and single-nucleus genomics from resected temporal cortex obtained from patients undergoing neurosurgery. We found that stimulation strengthens cell assemblies and then linked this effect to cell-type-specific gene regulatory networks. We further demonstrated the generalizability of these findings by identifying common cell-type-specific gene expression signatures in the human cortex following in vivo stimulation. Together, our results establish a foundation for identifying targetable genetic signatures linked with physiology that may be harnessed for therapeutic benefit via neuromodulation strategies.

医学Medicine

The Virtual Tissues foundation model resolves spatial proteomics across scales

虚拟组织基础模型实现跨尺度空间蛋白质组学解析

▲作者：Johann Wenckstern, Eeshaan Jain et al.

▲链接：

https://www.nature.com/articles/s41586-026-10884-y

▲摘要：

在此，研究提出虚拟组织（VirTues），一个用于空间蛋白质组学的通用基础模型，能够直接从多重成像数据中学习标记感知的、多尺度的蛋白质、细胞、生态位和组织表征。基于单一预训练骨干网络，VirTues支持标记物重建、细胞分割与分型、生态位注释、空间生物标志物发现和患者分层，包括跨异质性panel和数据集进行零样本注释。

在三阴性乳腺癌中，VirTues衍生的生物标志物可预测抗PD-L1化疗—免疫治疗反应，并在独立队列中分层无病生存期，其表现优于源自相同数据集的最先进生物标志物以及当前临床分层方案。

▲ Abstract：

Here we present Virtual Tissues (VirTues), a general-purpose foundation model for spatial proteomics that learns marker-aware, multi-scale representations of proteins, cells, niches and tissues directly from multiplex imaging data. From a single pretrained backbone, VirTues supports marker reconstruction, cell segmentation and typing, niche annotation, spatial biomarker discovery and patient stratification, including zero-shot annotation across heterogeneous panels and datasets. In triple-negative breast cancer, VirTues-derived biomarkers predict anti-PD-L1 chemo-immunotherapy response2 and stratify disease-free survival in an independent cohort3, outperforming state-of-the-art biomarkers derived from the same datasets and current clinical stratification schemes.

A dependency map enhanced with next-generation 3D cancer models

结合下一代3D癌症模型的依赖性图谱

▲作者：James V. Neiswender, Samuel Maffa et al.

▲链接：

https://www.nature.com/articles/s41586-026-10843-7

▲摘要：

研究者在此对10种癌症类型的下一代癌症模型（类器官和球状体）进行了147次全基因组CRISPR筛选和多组学表征。该策略使DepMap得以扩展，覆盖新的基因组和分子亚型，并识别新的生物标志物相关脆弱性。这些新模型还保留了在传统细胞系中被沉默的转录程序，并有助于发现与这些程序相关的特定基因依赖性。

传统与下一代癌症模型的比较进一步揭示了生长形式和培养基对基因必需性的不同影响。该整合数据集结合了两种模型类型的数据，为探索癌症脆弱性提供了一个宝贵且广泛的资源，可通过DepMap门户网站访问。

▲Abstract：

Here we perform 147 genome-scale CRISPR screens and multi-omic characterizations of next-generation (NextGen) cancer models (organoids and spheroids) across 10 cancer types. This strategy enables the expansion of DepMap to cover new genomic and molecular subtypes and to identify new biomarker-associated vulnerabilities. These new models also preserve transcriptional programs that are silenced in traditional cell lines and facilitate the discovery of specific gene dependencies associated with these programs. Comparisons of traditional and NextGen cancer models enable further identification of distinct effects of growth format and culture medium on gene essentiality. The integrated dataset combines data from both model types to offer a valuable, expansive resource for exploring cancer vulnerabilities and is accessible via the DepMap portal.

教育Education

Mobile education builds resilience during shocks in five countries

移动教育在国家震荡期间构建教育韧性

▲作者：Noam Angrist, Micheal Ainomugisha et al.

▲链接：

https://www.nature.com/articles/s41586-026-10990-x

▲摘要：

研究者展现了来自印度、肯尼亚、尼泊尔、菲律宾和乌干达五国随机试验的结果，旨在评估紧急情况下的教育提供。他们测试了多种可扩展的远程定向辅导教学模式，比较了政府和非政府组织的实施效果。短信的效果参差不齐，而通过电话进行的辅导在不同环境中均显示出有效性。研究者发现了对学习的大幅且稳健的效应量。

这些效应极具成本效益，每花费100美元即可提供约4年的高质量教学。由政府的教师或非政府组织的辅导员实施时，效果同样显著。综合来看，结果表明增强教育系统的韧性、在中断期间提供教育，并在不同情境下与政府合作实现具有成本效益的学习收益是可行的。

▲Abstract：

Here we present results from five randomized trials in India, Kenya, Nepal, the Philippines and Uganda to evaluate the provision of education in emergency settings. We test multiple scalable models of remote targeted tutoring instruction, comparing delivery by governments and non-governmental organizations (NGOs). Whereas text messages have mixed results, tutorials conducted via phone call show effectiveness across diverse settings. We find large and robust effect sizes on learning. These effects are highly cost-effective, and deliver approximately 4 years of high-quality instruction per US$100 spent. Results show large effects when delivered by government teachers or NGO instructors. Together, our results reveal that it is possible to strengthen the resilience of education systems, enabling education provision amid disruptions, and to deliver cost-effective learning gains across contexts and with governments.

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