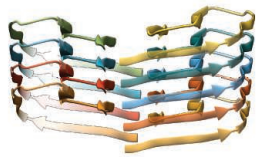
RESEARCH

A high-quality de novo atomic model of amyloid-β fibrils

Gremer et al., *p. 116*



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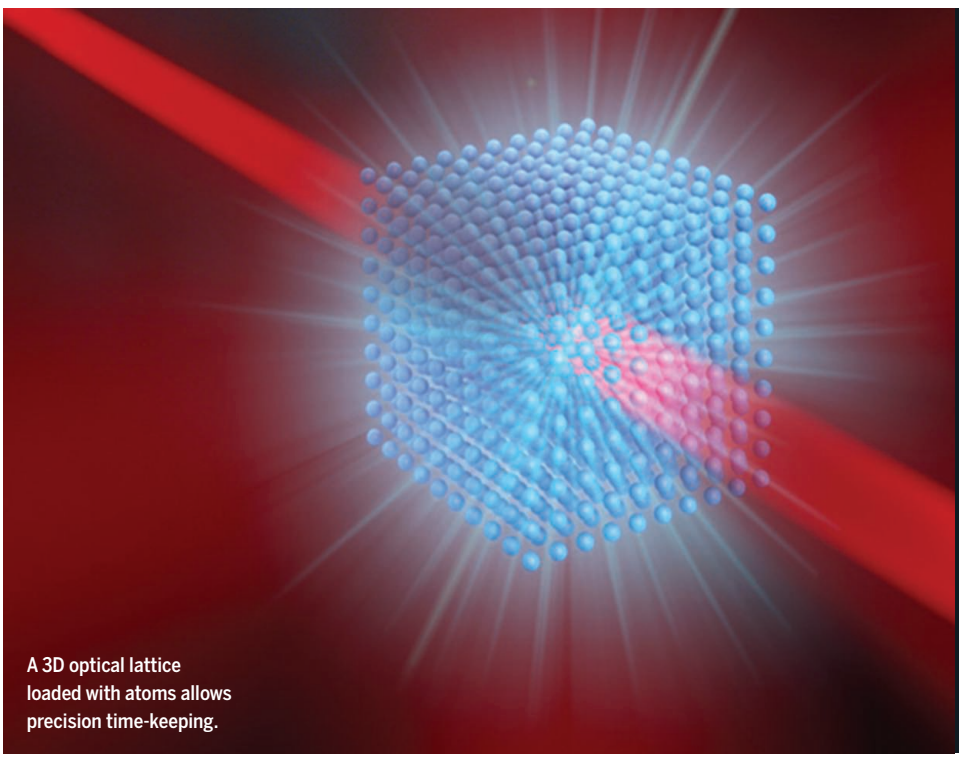


A 3D optical lattice loaded with atoms allows precision time-keeping.

OPTICAL CLOCKS

Making a denser optical lattice clock

Some of today's most advanced clocks are made up of large numbers of atoms lined up in a one-dimensional (1D) optical lattice. The numbers improve clock stability, but atomic interactions can limit accuracy. Campbell *et al.* loaded their fermionic strontium atoms into a 3D optical lattice. The low temperatures and strong interactions ensured that the atoms avoided one another, resulting in a neat pattern where each lattice site was occupied by exactly one atom. This ordering reduced the influence of interactions on the clock's accuracy, whereas the high density of atoms enabled by the 3D geometry improved the precision. —JS

Science, this issue p. 90

GLOBAL CARBON CYCLE

Climate and the carbon cycle

It is still not clear how global warming will affect the global carbon cycle, either in terms of the magnitude of the effect or even its sign. Help in answering that question will come from long-term field-based experiments designed to explore carbon cycle–climate feedbacks in an ecosystem context. Melillo *et al.* performed a 26-year soil-warming experiment in a mid-latitude hardwood forest (see the Perspective by Metcalfe). Warming has resulted in a complex pattern of net carbon loss from the soil. These results support projections of a long-term, positive carbon feedback from similar ecosystems as the world warms. —HJS

Science, this issue p. 101; see also p. 41

NEONICOTINOIDS

From bees to honey

Neonicotinoid pesticides are applied globally. Concern about their impacts has been increasing as evidence for negative effects on bee health and persistence has accumulated. Mitchell *et al.* looked at the prevalence of these pesticides in honey from across the world and found traces in the majority of samples tested (see the Perspective by Connolly). The neonicotinoid compounds occurred at levels considered safe for human consumption, but the contamination confirms the inundation of bees and their environments with these pesticides, despite some recent efforts to decrease their use. —SNV

Science, this issue p. 109; see also p. 38

VASCULAR BIOLOGY

Moving lymphatic endothelial cells about

Lymphatic vessels return fluid and immune cells from peripheral tissues back to the circulation. The growth of new lymphatic vessels and their remodeling are critical for clearing infection and, less helpfully, for metastasis of many cancer subtypes. Williams *et al.* identified genes that regulated lymphatic endothelial cell migration, a process that is essential for lymphatic vessel growth and remodeling. One of the top candidates, the glycan-binding protein galectin-1, promoted lymphatic vessel growth and was important for maintaining lymphatic endothelial cell identity. —WW

Sci. Signal. **10**, eaal2987 (2017).

NEUROSCIENCE

Price modulates early pain processing

Patients in randomized clinical trials frequently stop taking their drug, complaining of side effects. However, it turns out that some of these subjects are part of the placebo group and thus never received any active medication.

ILLUSTRATION: CAMPBELL *ET AL.*

Published by AAAS

This is a case of the nocebo effect seriously interfering with medical treatment. Tinnermann *et al*. investigated whether value information such as the price of a medication can further modulate behavioral nocebo effects and the underlying neural network dynamics (see the Perspective by Colloca). They used brain imaging to characterize the circuits involved in nocebo hyperalgesia within the descending pain pathway from the prefrontal cortex to the spinal cord. Their findings revealed how value information increased the nocebo effect. —PRS

Science, this issue p. 105; see also p. 44

TRANSCRIPTION

Gene expression during mitosis

During mitosis, long-range interactions within chromosomes are lost, and many enhancers become inactive. It is generally thought that gene expression is silent at this time. However, transcription must be reactivated when cells reenter the cell cycle in order to maintain cell identity. Palozola *et al.* used a sensitive nascent RNA labeling and sequencing method to reveal low-level transcription of many genes in mitosis. Upon mitotic exit, the amplitude of gene expression was reestablished with basic cell functions prioritized over cell-specific genes. Thus, transcription itself may retain gene expression patterns through mitosis. —BAP

Science, this issue p. 119

ANTIBIOTIC RESISTANCE

Rapidly recognizing resistance

Reducing the time required to determine whether a bacterial sample is resistant to an antibiotic could hasten proper treatment of infections. Schlappi *et al.* developed an antibiotic susceptibility test that could be performed within 30 min using clinical urine samples. The test uses digital loop–mediated isothermal amplification to measure the amount of nucleic acid markers of antibiotic susceptibility produced by bacteria present within a clinical sample after a brief incubation with an antibiotic. Performing the test on a microfluidic platform enabled single-molecule amplification and quantification in real time, determining *Escherichia coli* susceptibility comparably to gold-standard methods, but more quickly. —CC

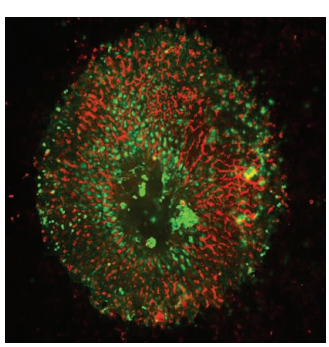
Sci. Transl. Med. **9**, eaal3693 (2017).

IMMUNOLOGY

Imaging the unforeseen fate of neutrophils

Inflammation that results from insults such as ischemia and reperfusion or trauma in the absence of microorganisms is known as "sterile inflammation." Neutrophils are recruited in vast numbers during sterile inflammation and have been thought to play a detrimental role. Wang *et al.* used intravital microscopy to show that neutrophils actually perform helpful tasks such as removing and regenerating thermally damaged blood vessels in the liver (see the Perspective by Garner and de Visser). Moreover, neutrophils neither die nor are phagocytosed. Instead, they return to the circulation in a process called "reverse transmigration," making a pit stop in the lungs, before ending their lives where they began—in the bone marrow. Thus, a reconsideration of the use of anti-neutrophil therapies after injury may be warranted. —STS

Science, this issue p. 111; see also p. 42



Neutrophils (red) inside a focal lesion at 12 hours post-injury

Cigarette smoke–induced epigenetic changes sensitize cells for mutation.

CANCER

Initiating lung cancer

Cigarette smoke contributes to epigenetic and genetic changes in lung cancer. But whether and how these alterations interact in lung cancer initiation has remained unclear. Vaz *et al.* showed that in immortalized lung epithelial cells, exposure to cigarette smoke condensate progressively altered the binding of chromatin-modifying enzymes to DNA and induced changes in DNA methylation in the absence of DNA mutations. Such epigenetically altered cells exhibited a stem cell–like chromatin state that sensitized them to later acquire oncogenic mutations and become lung cancer cells. Modeling cancer initiation is extremely difficult, but this is an important process to understand if we hope to find effective strategies to prevent cancer initiation and/or progression. —GKA

Cancer Cell **32**, 360 (2017).

GENE REGULATION

Regulation through clustering

Transcription factors convey information from the environment to influence gene regulation. These proteins bind promoter sequences for gene repression or activation, but the mechanism by which they find their target sequence is unclear. Wollman *et al.* examined gene regulation by the Mig1 repressor and the Msn2 activator. The Mig1 repressor is a zinc-finger DNA-binding protein that localizes to the nucleus when the yeast *Saccharomyces cerevisiae* is exposed to glucose. Using single-molecule fluorescent microscopy to track localization, the authors found that six to nine transcription factor molecules form clusters that move from the cytoplasm to the nucleus. The clusters may be stabilized in live cells by the properties of the cytoplasmic colloid. Clustered transcription factors seem to reduce promoter search time and

PHOTO: CORSICASMART/ISTOCK

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HIV THERAPY

A triple threat for HIV

The HIV virus continually evolves tricks to evade elimination by the host. Prevention and a cure will likely rely on broadly neutralizing antibodies that can recognize and conquer multiple viral strains or subtypes. Xu *et al*. engineered a single antibody molecule to recognize three highly conserved proteins needed for HIV infection (see the Perspective by Cohen and Corey). This "trispecific" antibody uses two sites (V1V2 and MPER) to bind HIV-infected cells, while the third site (CD4bs) recruits killer T lymphocytes that can eliminate the virus. When tested against >200 different HIV strains, trispecific antibodies were highly potent and broadly neutralized ~99% of HIV viruses. This approach could potentially simplify HIV treatment regimens and improve therapy response. —PNK

Science, this issue p. 85; see also p. 46

ATOMIC PHYSICS

How big is the proton?

The discrepancy between the size of the proton extracted from the spectroscopy of muonic hydrogen and the value obtained by averaging previous results for "regular" hydrogen has puzzled physicists for the past 7 years. Now, Beyer *et al.* shed light on this puzzle (see the Perspective by Vassen). The authors obtained the size of the proton using very accurate spectroscopic measurements of regular hydrogen. Unexpectedly, this value was inconsistent with the average value of previous measurements of the same type. Also unexpectedly, it was consistent with the size extracted from the muonic hydrogen experiments. Resolving the puzzle must now include trying to understand how the old results relate to the new, as well as reexamining the sources of systematic errors in all experiments. —JS

Science, this issue p. 79; see also p. 39

LASER PHYSICS

Harnessing complexity in laser light

The development of lasers and the quality of the output light has been crucially dependent on understanding and being able to control the process occurring within the laser-generating cavity. In a real laser cavity, there are both longitudinal and transverse modes; for the highest-quality lasers, reducing the effects of the latter has been standard practice. However, using a graded index fiber cavity, Wright *et al.* demonstrate that the longitudinal and transverse modes can be locked to provide an output of complex coherent light. Harnessing, rather than filtering out, the transverse modes could produce a valuable and flexible light source applicable across a broad range of disciplines. —ISO

Science, this issue p. 94

METALLURGY

Giving grain boundaries more structure

The properties of metals change depending on the composition and structure of grain boundaries in polycrystalline materials. Yu *et al.* discovered a surprising grain boundary superstructure in a nickel-bismuth alloy. Previously, the structure was only known to exist in a specific type of uncommon grain boundary, and experiments had focused on bicrystals. Unexpectedly, this alloy has grain boundary superstructures across a wide range of boundaries in polycrystalline samples. This likely also occurs in other alloys, which opens an avenue for grain boundary engineering to tune the physical properties of metals and ceramics. —BG

Science, this issue p. 97

STRUCTURAL BIOLOGY

Elucidating pathological fibril structure

Amyloid-β (Aβ) is a key pathological contributor to Alzheimer's disease. Gremer *et al.* used cryoelectron microscopy data to build a high-quality de novo atomic model of Aβ fibrils (see the Perspective by Pospich and Raunser). The complete structure reveals all 42 amino acids (including the entire N terminus) and provides a structural basis for understanding the effect of several disease-causing and disease-preventing mutations. The fibril consists of two intertwined protofilaments with an unexpected dimer interface that is different from those proposed previously. The structure has implications for the mechanism of fibril growth and will be an important stepping stone to rational drug design. —SMH

Science, this issue p. 116; see also p. 45

AUTOIMMUNITY

A revealing repertoire for systemic sclerosis

Systemic sclerosis (SSc) is an autoimmune disease associated with fibrosis and serious complications including pulmonary arterial hypertension (PAH). Abnormal B cell responses have been associated with SSc pathogenesis. De Bourcy *et al.* analyzed immunoglobulin heavy chain transcripts of SSc-PAH patients enrolled in a clinical study of B cell depletion. SSc-PAH was associated with several B cell development anomalies, particularly underuse of the IGHV2-5 segment and B cell homeostasis abnormalities. Depletion temporarily reversed these anomalous SSc-PAH disease signatures, and the rate of naïve B cell replenishment could be estimated from baseline measurements. These results define antibody signatures associated with SSc-PAH and reveal how B cell depletion shapes the antibody repertoire during reconstitution. —CNF

Sci. Immunol. **2**, eaan8289 (2017).