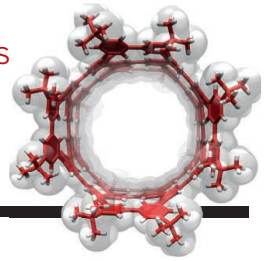
RESEARCH

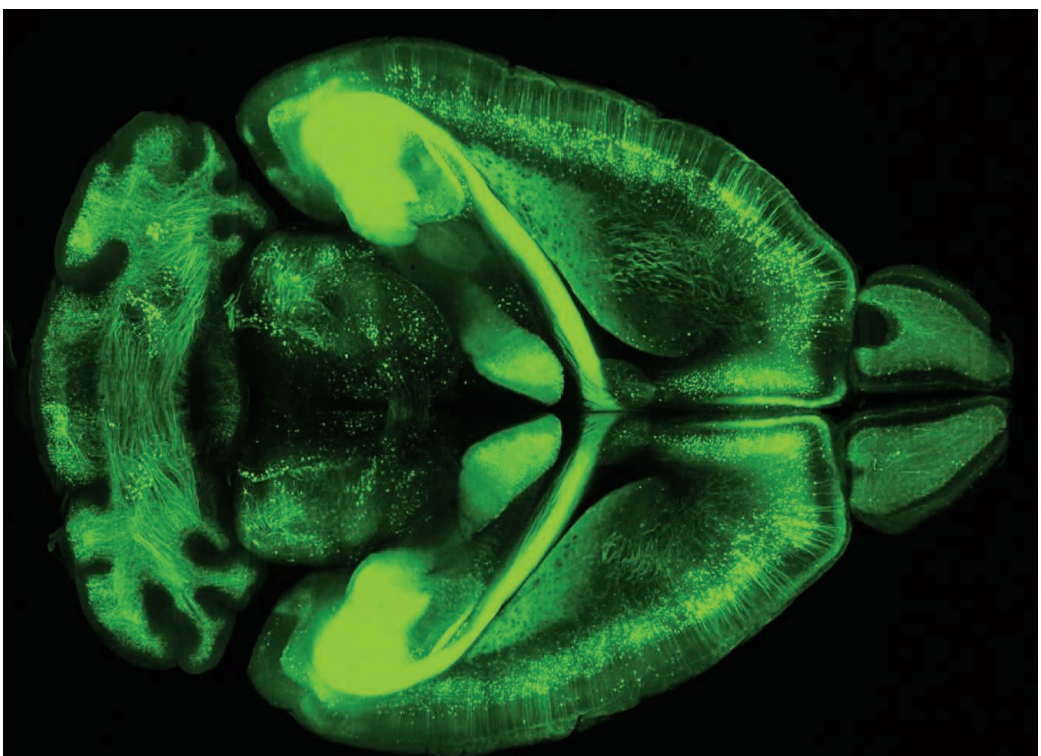
A step toward nanotubes with holes in the walls

Sun et al., *p. 151*



IN *SCIENCE* JOURNALS

Edited by **Stella Hurtley**



RESEARCH METHODS

Advancing 3D imaging of organs

Viewing intact tissue structures is crucial to biological research. The current methods for obtaining three-dimensional (3D) images of tissues and even whole organs, characterized by the clearing of the tissue with an organic solvent, are still limited by the level of clarity, transparency, and efficiency at which they can produce samples. Qi *et al.* developed an advanced optical clearing method, FDISCO, that overcomes some of these limitations. The authors used this method to gather high-resolution images of neuronal and vascular structures in the brain, kidney, and muscles. —PJB

Sci. Adv. 10.1126/sciadv.aau8355 (2018).

Light-sheet fluorescent image of whole mouse brain cleared by FDISCO.

IMAGE: QI *ET AL.*

MEMBRANES

Only the water may pass

Removing objects by size to keep only the smallest ones is simple in theory, but it requires a sieve, membrane, or filter with holes small enough to allow only the smallest objects to pass. Gopinadhan *et al*. engineered two-dimensional water channels by removing an atomic plane of atoms from a sandwich made from bulk crystal with a graphene spacer. Water flowed through the channels without resistance, but the channels excluded all ions except for protons because the ion hydration shells could not squeeze through the channels. —MSL

Science, this issue p. 145

TOPOLOGICAL OPTICS

A photonic Weyl system by design

Theoretically proposed exotic physics is now being explored and realized in condensed matter and photonic systems. Weyl physics arises when the valence band and conduction bands meet at discrete points in the band structure. Jia *et al*. designed and fabricated a photonic metamaterial in which the position of the Weyl points in momentum space could be tuned using a huge artificial magnetic field. Because these points are stable, the ability to design and control such a Weyl system with a robust chiral optical mode could be exploited in future optical information processing applications. —ISO

Science, this issue p. 148

SURFACE CHEMISTRY

Broken on impact

Two competing models have been proposed for the adsorption of molecular hydrogen on platinum surfaces. Both invoke dissociation at surface defects but differ on whether hydrogen molecules diffuse along the surface before encountering a defect or adsorb only if they initially impact a defect site. Van Lent *et al*. studied the sticking of hydrogen molecules from a molecular beam scanned across a curved platinum single-crystal surface that varied in the density and type of defects exposed. Modeling of the results was consistent only with the second model invoking direct impact. —PDS

Science, this issue p. 155

CHEMISTRY

Mating disks and rods into an ordered phase

Disk-shaped molecules tend to stack in columns, whereas rod-shaped ones tend to align parallel to each other. When the two types of molecules are mixed, they tend to phase separate. Yano *et al*. found the right recipe that allowed enough affinity between the disks and rods so that they formed a blended twisted columnar phase. The phase could be stabilized by polymerizing the disks. The orientation of the twisted columns could be altered using electric fields, whereas optical stimuli could lead to a second ordering transition. —MSL

Science, this issue p. 161

TROPICAL ECOLOGY

Forest termites mitigate the effects of drought

In many tropical regions, where drought is predicted to become more frequent in the coming years, termites are key components of ecosystem function. Ashton *et al*. experimentally manipulated termite communities to quantify their role during the 2015–2016 "super El Niño" drought in a Malaysian tropical rainforest. Termite relative abundance more than doubled in control plots during drought, maintaining three major ecosystem processes: decomposition, nutrient heterogeneity, and moisture retention. Seedling mortality increased where termites were suppressed. —AMS

Science, this issue p. 174

SEXUAL SELECTION

Who's a clever boy then?

There is considerable value in choosing a smart mate. The suggestion that mate choice has thus shaped the evolution of cognition has been around since Darwin's time, but testing this hypothesis is difficult. Chen *et al*. found that female budgerigars shifted their preference to previously nonpreferred males after these males demonstrated the ability to solve a problem that stumped the originally preferred males (see the Perspective by Striedter). This preference shift was specific to problem-solving and to choosing males. —SNV

Science, this issue p. 166; see also p. 120

CIRCADIAN RHYTHMS

Astrocytes can drive the master clock in the brain

The neurons of the suprachiasmatic nucleus (SCN) of the hypothalamus function as a central circadian clock, coordinating mammalian physiology with the 24-hour light-dark cycle. Brancaccio *et al*. found that these neurons have help from neighboring astrocytes (see the Perspective by Green). In mice lacking the *Cry* gene, which encodes a critical clock component, restoration of *Cry* expression and molecular clock function in the astrocytes, but not the neighboring neurons, restored rhythmic transcriptional oscillations in the SCN and reestablished circadian behaviors in the mice. —LBR

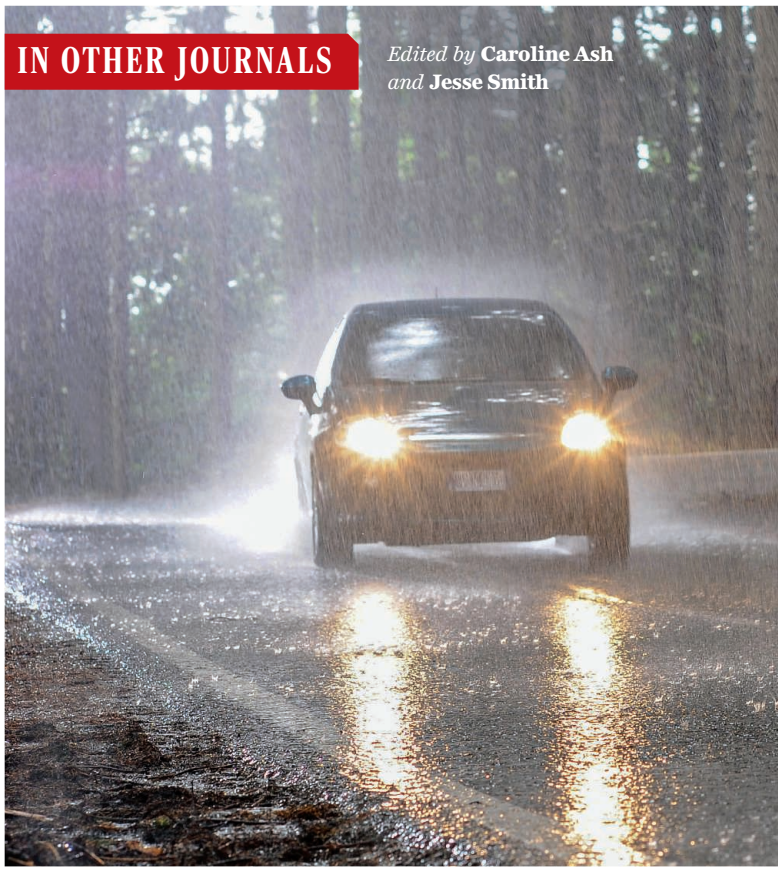
Science, this issue p. 187; see also p. 124

OPIOID OVERDOSE

A step toward preventing overdose

Opioid addiction and overdose remain serious health concerns in the United States. Naloxone can reverse opioid overdose but must be administered in a timely manner. Toward this goal, Nandakumar *et al.* configured a smartphone to detect changes in respiration that precede opioid overdose. Using sonar, the smartphone detected respiratory depression and apnea (temporary lack of breathing) after self-injected drug use in a supervised injection facility. Respiratory changes while under general anesthesia, which simulates opioid-induced overdose, were also detected in a clinical setting. —CC

Sci. Transl. Med. **11**, eaau8914 (2019).



IN OTHER JOURNALS

Edited by **Caroline Ash** *and* **Jesse Smith**

NEUROSCIENCE

Chronic short sleep and neurodegeneration

The locus ceruleus is a brain region that is critical for optimal cognitive performance and brain health. Its neurons degenerate during mild cognitive impairment and the early stages of Alzheimer's disease (AD). Zhu *et al.* investigated the role of chronic sleep deprivation on the protein tau, which is found abundantly in the brain and is associated with AD. In mice, a shortage of sleep in early life advanced the temporal progression of toxic tau accumulation, worsened neurobehavioral impairment, and increased the abundance of soluble tau oligomers within the locus ceruleus and other regions. Lack of sleep promoted neurodegeneration in the locus ceruleus and other tau-affected areas, and the effects persisted for months. Chronic sleep disruption may thus contribute to the progression of AD and related diseases. —PRS

J. Neurosci. **38**, 10255 (2018).

INFLUENZA

More tricks up its sleeve

Influenza viruses are famous for generating variants that evade immune surveillance—and our vaccines. Vahey and Fletcher describe another way these viruses elude control. The authors made a strain of influenza A virus that expressed fluorescently labeled components and used them to infect cells. Live-cell imaging was then used to monitor the composition and morphology of virus particles as they were released from infected cells. Influenza A was found to produce very variable virus particles, unlike many other human viruses whose morphology and composition are consistent. This variability appears to be stochastic and allows progeny viruses to escape the effects of neuraminidase drugs, which would normally prevent successful infections. —SMH

Cell 10.1016/j.cell.2018.10.056 (2019).

PHOTOS: (TOP) PIRTUSS/SHUTTERSTOCK; (FACING PAGE) FOTOTRIPS/SHUTTERSTOCK

ALSO IN *SCIENCE* JOURNALS

Edited by **Stella Hurtley**

IMMUNOMETABOLISM

Metabolism as a driver of immune response

All living organisms need energy and metabolic building blocks to sustain biological processes. Wang *et al*. review immunometabolism, applying the principles of life history theory. They highlight recent advances showing the reciprocal interactions between systemic metabolism and immunity, as well as how inflammation can alter the functional state of metabolic organs and their central control by the hypothalamus. Such coordinated cross-talk between whole-body and immune cell metabolism is involved in a variety of health and disease states. —PNK

Science, this issue p. 140

MOLECULAR BIOLOGY

A cap-specific m^{6}A writer

N^6,2′-*O*-dimethyladenosine (m^{6}Am) is present at the transcription start nucleotide of capped mRNAs in vertebrates. Akichika *et al*. quantified the abundance of this modification in the transcriptome and identified the writer protein, cap-specific adenosine methyltransferase (CAPAM), needed for this modification. CAPAM contains a unique structure that recognizes cap-specific *N*^{6}-methyladenosine (m^{6}A) as the substrate. The protein interacts with RNA polymerase II, suggesting that the modification occurs cotranscriptionally. The m^{6}Am promotes the translation of capped mRNAs in a eIF4E-independent fashion. —SYM

Science, this issue p. 141

IMMUNOLOGY

Unmasking an agent of inflammatory anemia

Infectious and autoimmune diseases are associated with anemia and thrombocytopenia. A severe form of inflammatory cytopenia called macrophage activation syndrome (MAS) may occur during rheumatological disorders and viral infections. Akilesh *et al*. show that monocyte recognition of self- or pathogen-derived nucleic acids via Toll-like receptors 7 and 9 (TLR7 and TLR9) drives MAS-like disease in mice. TLR7 or TLR9 signaling in monocytes causes these cells to differentiate into inflammatory hematophagocytes (iHPCs), which are similar to but distinct from red pulp macrophages. Preventing iHPC differentiation by depleting monocytes relieves MAS-like symptoms. When mice were subjected to a model of malarial anemia, MyD88- and endosomal TLR-dependent iHPC differentiation also occurred. Thus, iHPCs may play a role in both MAS-driven and malarial anemia, as well as thrombocytopenia. —STS

Science, this issue p. 142

NEUROSCIENCE

A physiological function for sAPP?

Although the pathological role of the amyloid-β precursor protein (APP) in Alzheimer's disease is well studied, the physiological role of this protein has remained elusive. Rice *et al*. found that the secreted ectodomain of APP (sAPP) binds to $GABA_BR1a$, the metabotropic receptor for the inhibitory neurotransmitter γ-aminobutyric acid (GABA) (see the Perspective by Korte). Binding suppressed synaptic vesicle release and modulated synaptic transmission and plasticity in mice. A short, 17–amino acid peptide in APP bound to $GABA_BR1a$'s sushi 1 domain, conferring structure to this unstructured domain. Therapeutics targeting this interaction could potentially benefit a range of neurological disorders in which GABA signaling is implicated. —SMH

Science, this issue p. 143; see also p. 123

CHEMISTRY

Clear directions for a robotic platform

The chemistry literature contains more than a century's worth of instructions for making molecules, all written by and for humans. Steiner *et al*. developed an autonomous compiler and robotic laboratory platform to synthesize organic compounds on the basis of standardized methods descriptions (see the Perspective by Milo). The platform comprises conventional equipment such as round-bottom flasks, separatory funnels, and a rotary evaporator to maximize its compatibility with extant literature. The authors showcase the system with short syntheses of three common pharmaceuticals that proceeded comparably to manual synthesis. —JSY

Science, this issue p. 144; see also p. 122

ORGANIC CHEMISTRY

Toward nanotubes with periodic gaps

Carbon nanotubes consist of a continuous array of benzene rings fused along their edges. It is not straightforward to excise regular fragments in a top-down fashion to produce periodic gaps. Sun *et al*. showcase the beginnings of a bottom-up strategy toward this end. They used borylations and catalytic cross-coupling chemistry to prepare a discrete cylindrical carbon compound composed of 40 benzene rings bonded to one another at the 1, 3, and 5 positions to leave regular void spaces in the walls. Catenation of multiple similar segments could ultimately lead to an extended nanotube with periodic wall defects. —JSY

Science, this issue p. 151

CHEMICAL PHYSICS

Climbing vibrational levels

Vibrational excitation of molecules adsorbed on a surface is usually limited because the vibrational energy is rapidly transferred into phonons, the vibrational modes of the substrate. Chen *et al*. found that this is not the case for CO molecules adsorbed on a surface of NaCl. The CO molecules efficiently transferred vibrational energy within groups of molecules from one high excitation state to another until they reached the dissociation limit. This process was possible because of the close proximity of the molecules and the limited transfer of energy to just one phonon mode in the salt surface. —PDS

Science, this issue p. 158

NEUROSCIENCE

Memory capabilities develop with age

During memory formation, time-compressed neuronal sequences underlie consolidation as well as encoding of novel information. Such memory traces are largely contributed by a selection of preconfigured neuronal patterns. However, when and how these preconfigured patterns first emerge in the hippocampus is unknown. Farooq and Dragoi identified an age-dependent development of network preconfiguration into trajectory-like sequences. This preconfiguration was expressed spontaneously during sleep and emerged from the assembly of persistent, location-depicting ensembles, largely controlled by intrinsic developmental programs. Thus, the compressed binding of adjacent locations into spatial trajectories during navigation and their experience-dependent replay emerge in coordination from spontaneous preconfigured sequences. —PRS

Science, this issue p. 168

PALEOECOLOGY

Ancient changes in the African tropics

Long-term records of past vegetation change are key to understanding how climate change affects ecosystems, but data are scarce—especially in highly biodiverse regions in the tropics. Lezine *et al*. present a detailed 90,000-year pollen core from an upland crater-lake site in the west African tropical montane forest, which is important from conservation and biogeographic standpoints. The upper treeline moved in response to climate change during the Pleistocene glacial and interglacial periods, whereas the lower limit of the Afromontane forest was stable. The constituent species of the forest also changed. This record resolves debates concerning the biogeographic history of Afromontane vegetation. —AMS

Science, this issue p. 177

ANTIBIOTIC RESISTANCE

Switching ON resistance

Clonal bacterial colonies will often grow dissimilar patches, similar to a tortoiseshell pattern. These differing phenotypes arise by reversible mechanisms called phase variation. Jiang *et al*. developed an algorithm to survey bacterial genomes for invertible promoters that cause phase variation. Inverted repeats signal the presence of these promoters, which can flip between ON and OFF states catalyzed by phage integrase analogs called invertases. Invertible promoters linked to antibiotic resistance genes were widespread among vertebrate gut–associated organisms, including Bacteroidetes, Spirochaetes, and Verrucomicrobia. These bacteria are thus equipped and prepared for sudden environmental stress, including antibiotic exposure. —CA

Science, this issue p. 181

CLIMATE CHANGE

Getting warmer, faster

Rising greenhouse gas concentrations are warming Earth's atmosphere and oceans. However, it has been difficult to reconcile model results and observational time series. In a Perspective, Cheng *et al.* highlight recent studies that have improved the methods used to account for systematic errors and for gaps in the observational record; one study reports an independent measure of ocean heat content changes. The results from these studies are close to those seen in models, suggesting that the models reliably capture the overall change in ocean heat content. Accelerating ocean warming since 1991 underscores the urgency of both mitigating and adapting to climate change. —JFU

Science, this issue p. 128

NEUROSCIENCE

Combining organoids to assemble brain regions

Organoids are three-dimensional cultures of cells, which form complex morphological structures. Recently, numerous advances in organoid culture of cells from human brain regions have helped us understand how the cells behave in a more native, three-dimensional environment. In a Perspective, Paşca discusses how brain organoids derived from cells in different regions of the human brain can be combined, and how multiple cell types can be combined in one organoid, to produce complex brain assembloids. These could be used to understand how brain regions interconnect and develop, as well as how neurodegeneration and neuropsychiatric disorders might arise. —GKA

Science, this issue p. 126

T CELLS

T cells need nuclear F-actin

T cell activation is regulated by numerous mechanisms upon T cell antigen receptor (TCR) engagement, including induction of specific cytokines by transcription factors such as NF-κB and NFAT. Tsopoulidis *et al*. found that TCR engagement caused rapid nuclear actin polymerization to create a dynamic actin filament network critical for $CD4^+$ T cell effector functions. Nuclear actin filament polymerization involved the nuclear Arp2/3 complex induced by nuclear Ca^{2+} and regulated by N-Wasp and NIK. Specific inhibition of nuclear actin filament formation impaired T cell effector responses, including cytokine expression and $CD4^+$ T cell help for antibody production. —CNF

Sci. Immunol. **4**, eaav1987 (2019).

INFLAMMATION

Manganese mobilizes microglial exosomes

Chronic occupational exposure to manganese is associated with the development of Parkinson's disease. Sarkar *et al.* found that exposure of primed microglia or mice to manganese increased the levels and activation of the NLRP3 inflammasome, an inflammation-promoting protein complex. Manganese treatment of microglia caused mitochondrial dysfunction and the release of exosomes containing the inflammasome adaptor protein ASC. Serum exosomes from welders contained more ASC and were more inflammatory than those from normal donors. —ERW

Sci. Signal. **12**, eaat9900 (2019).