

RESEARCH

IN SCIENCE JOURNALS

Edited by Michael Funk

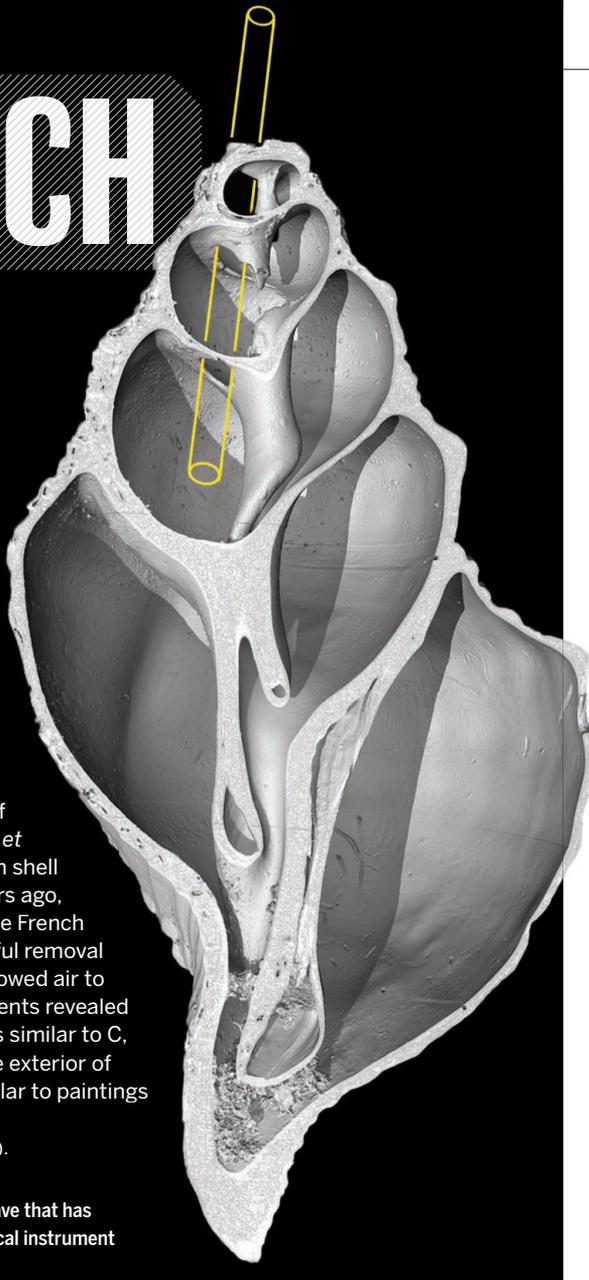
ARCHAEOLOGY

Sounds from a Paleolithic seashell horn

Although flutes and whistles made of bone have been found at Upper Paleolithic archaeological sites in Europe, musical instruments made of other materials are uncommon. Fritz *et al.* have identified the earliest known conch shell in the world, dating from about 17,000 years ago, which was used as a wind instrument at the French Magdalenian site of Marsoulas Cave. Careful removal of the apex of the shell in ancient times allowed air to flow through it to produce sound. Experiments revealed that playing the shell produces three notes similar to C, C-sharp, and D. Image enhancement of the exterior of the shell revealed dots of red pigment similar to paintings found on the cave walls.

—MSA *Sci. Adv.* 10.1126/sciadv.abe9510 (2021).

Cross section of the conch shell from Marsoulas Cave that has been modified with drilled holes to serve as a musical instrument



GEOLOGY

A boring billion for mountains

Earth's crust has changed over time as supercontinents formed and broke apart. Tied into this cycle are the building and erosion of high mountains, which are tied to collisions between tectonic plates. Tang *et al.* use europium anomalies in zircons to estimate the mean thickness of crust over Earth's history. This proxy shows that mountain building has not always been as active as it is today or as it was very early in Earth's history. Mountain building, and the subsequent erosion, was less

intense for about a billion years, roughly correlated with a so-called "boring billion" period of biological evolution. —BG

Science, this issue p. 728

SUPERCONDUCTIVITY

A superconducting interface

Interfaces between materials can harbor quantum states that belong to neither of the materials. A classic example is the superconducting interface between two insulating oxides, LaAlO_3 and SrTiO_3 , with a critical temperature of around 200 millikelvin. Liu *et al.*

observed superconductivity at a different interface—formed between KTaO_3 as a substrate and an overlayer of either EuO or LaAlO_3 —at a considerably higher temperature of about 2 kelvin. Transport measurements displayed anisotropy, which may indicate an unusual superconducting state. —JS

Science, this issue p. 716

CORONAVIRUS

Fighting zoonotic coronaviruses

In the past 20 years, three betacoronaviruses thought to have originated in bats have

caused devastating disease in humans. The global pandemic caused by the latest such virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), highlights the need to protect against other strains that could present a threat to humans. Cohen *et al.* constructed nanoparticles displaying the protein domain that binds the host cell receptor (receptor-binding domain or RBD), either a homotypic SARS-CoV-2 particle or mosaic particles displaying RBDs from four or eight different betacoronaviruses. In mice, antibodies to the SARS-CoV-2 RBD were elicited just as well by mosaic particles as by homotypic nanoparticles. The mosaic nanoparticles elicited antibodies that, beyond recognizing the strains displayed, also recognized mismatched strains. —VV

Science, this issue p. 735

NUCLEOTIDE SYNTHESIS

A P catalyst for stereogenic P(III)

Phosphodiester, the key linkage in DNA, RNA, and bioactive oligonucleotide and cyclic nucleotides, are typically synthesized from phosphoramidite precursors. Phosphorothioate linkages, which are more stable, can also be produced this way but have the complication of chirality at the P center, which is synthetically problematic, especially for multiple linkages. Featherston *et al.* found that two different chiral phosphoric acid catalysts provide stereodivergent synthesis of a stereogenic phosphite intermediate that can be oxidatively modified to the desired stereopure nucleotide derivative. They used this approach in the synthesis of a phosphorothioate derivative of the cyclic dinucleotide 2',3'-cyclic guanosine monophosphate adenosine monophosphate, which is an important human immune signaling molecule. —MAF

Science, this issue p. 702

CANCER**An “Ama”-zing antibody-drug conjugate**

Antibody-drug conjugates (ADCs) targeting HER2 are an attractive candidate for treating patients with HER2⁺ breast cancer. Li *et al.* developed an ADC that is especially effective at killing breast cancer cells that express HER2 at low levels. HER2-low breast cancer cells often have loss of chromosome 17p, which the authors showed sensitizes tumor cells to the drug α -amantin. The authors treated mice bearing HER2-low tumors with an ADC of trastuzumab and α -amantin (T-Ama), and found that this combination induced immunogenic cell death of tumor cells, which enhanced the response to immune check-point blockade. —CSM

Sci. Transl. Med. **13**, eabc6894 (2021).

OCEANOGRAPHY**Structure from a whale song**

Probing the structure of the ocean crust requires a wave source. The most common source is an air gun, which is effective but potentially harmful for ocean life and not easy to use everywhere. Kuna and Nábělek found that fin whale

songs can also be used as a seismic source for determining crustal structure. Fin whale vocalizations can be as loud as large ships and occur at frequencies useful for traveling through the ocean floor. These properties allow fin whale songs to be used for mapping out the density of ocean crust, a vital part of exploring the seafloor. —BG

Science, this issue p. 731

CRIMINAL JUSTICE**Diversity in policing**

In the wake of high-profile police shootings of Black Americans, it is important to know whether the race and gender of officers and civilians affect their interactions. Ba *et al.* overcame previous data constraints and found that Hispanic and Black officers make far fewer stops and arrests and use force less than white officers, especially against Black civilians. These differences are largest in majority-Black neighborhoods in the city of Chicago (see the Perspective by Goff). Female officers also use less force than male officers. These effects are supportive of the efficacy of increasing diversity in police forces. —TSR

Science, this issue p. 696;

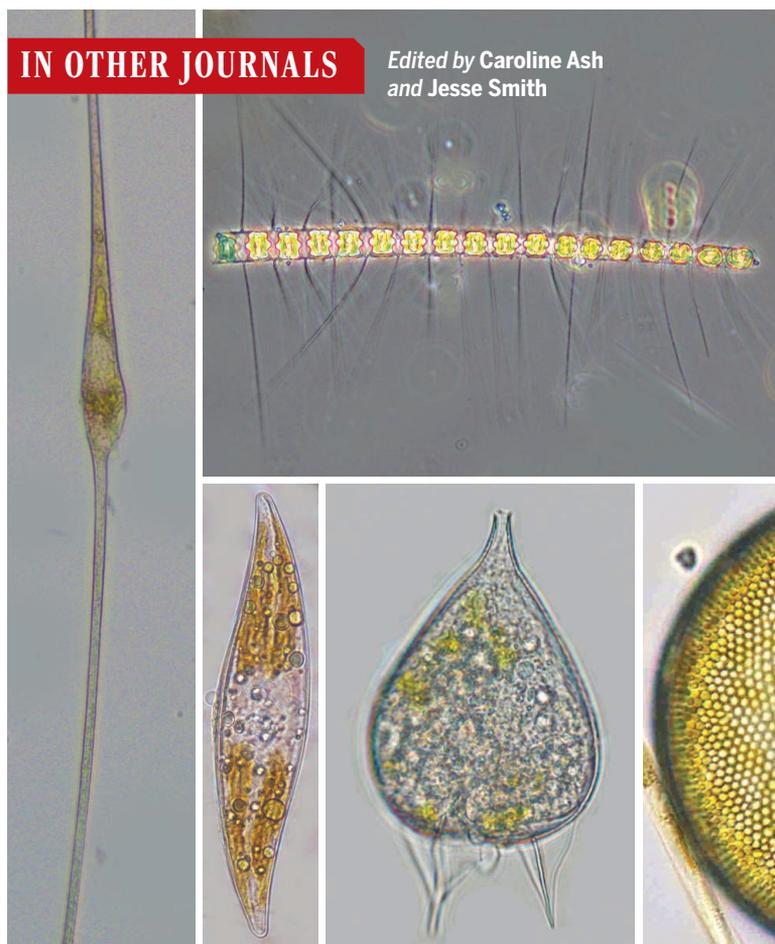
see also p. 677



Fin whales produce vocalizations that can be used to study the structure of the Earth's subocean crust.

IN OTHER JOURNALS

Edited by Caroline Ash and Jesse Smith

**CANCER****Painting portraits of tumors**

Detailed assessment of tumor genomics, epigenomics, and transcriptomics is becoming increasingly common. As these methods generate ever-increasing collections of data, it can be difficult to analyze all of this information and determine how it applies to individual patients or rare cancer subtypes. To help interpret the accumulating data, Zhou *et al.* designed a web-based tool called GenomePaint, which can visualize a variety of omics data in cohorts of patients and in individual samples. The authors also used GenomePaint to identify previously unreported and likely pathogenic alterations in several tumor types, demonstrating the potential power of this method. —YN

Cancer Cell **39**, 83 (2021).

NEUROSCIENCE**Brain disease and network reorganization**

Parkinson's disease (PD) offers an opportunity to study the interplay between compensatory functional and molecular mechanisms. Although postsynaptic dopamine D2 receptors are up-regulated in PD, their importance in neural activity has never been identified. To investigate the relationship between reorganization of dopaminergic networks and functional reorganization of brain activity patterns, Rebelo *et al.* combined PET and fMRI scans of the brain areas involved in the execution of saccades. They found a tight link between functional activation and synaptic changes at the molecular level, reflecting network reorganization in PD. The association between D2 receptor binding and reorganization of the saccadic cortical network

TOXICOLOGY**Health effects of microplastics**

Microplastics—organic polymer particles smaller than 5 millimeters—have been found throughout the global biosphere. In addition to their effects on wildlife and ecosystems, there is growing concern about whether ingestion of microplastics through drinking water, inhalation, or food can affect human health. In a Perspective, Vethaak and Legler discuss the many unknowns, including exposure levels, whether microplastics can enter cells, and, if they do, what damage might be caused. It is also unclear whether microplastics are contaminated with possible pathogens. Much more research is needed to understand the impact of microplastics on human health. —GKA

Science, this issue p. 672

PHYSIOLOGY**Regulating multiple body clocks**

Circadian rhythms that affect multiple tissues and organ systems are aligned with the dark-light cycle and other external inputs such as feeding. But how is such time keeping modulated throughout complex systems and anatomical regions? Koronowski and Sassone-Corsi reviewed how central regulators in the brain and peripheral regulators throughout organs can behave cooperatively or independently to modulate circadian rhythms. This systemic view of circadian rhythm modulation is important to understand behavior and disease, because dysregulated clocks are associated with metabolic syndrome and cancer. —GKA

Science, this issue p. 690

CORONAVIRUS**A double punch against SARS-CoV-2**

Monoclonal antibodies are an important weapon in the battle against COVID-19. However, these large proteins are difficult to produce in the needed quantities and at low cost. Attention has turned to nanobodies, which are aptly named, single-domain antibodies that are easier to produce and have the potential to be administered by inhalation. Koenig *et al.* describe four nanobodies that bind to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein and prevent infection of cells (see the Perspective by Saelens and Schepens). Structures show that the nanobodies target two distinct epitopes on the SARS-CoV-2 spike protein. Multivalent nanobodies neutralize virus much more potently than single nanobodies, and multivalent nanobodies that bind two epitopes prevent the emergence of viral escape mutants. —VV

Science, this issue p. 691;

see also p. 681

MOLECULAR MOTOR**Kinesin takes substeps**

Simultaneously measuring the nanoscale motion and forces that molecular machines generate provides insights into how they work mechanically to fulfill their cellular function. To study these machines, Sudhakar *et al.* developed germanium semiconductor nanospheres as probes for so-called optical tweezers. With these high-refractive index nanospheres, they improved the resolution of optical tweezers and discovered that the motor kinesin takes 4-nanometer substeps. Further, instead of detaching from their microtubule track under load, motors slid back on it, enabling rapid reengagement in transport. The new technology will allow

investigation of a range of other proteins and their behaviors at nanometer scales. —DJ

Science, this issue p. 692

HEART VALVE DISEASE**Machine learning for medicine**

Small-molecule screens aimed at identifying therapeutic candidates traditionally search for molecules that affect one to several outputs at most, limiting discovery of true disease-modifying drugs. Theodoris *et al.* developed a machine-learning approach to identify small molecules that broadly correct gene networks dysregulated in a human induced pluripotent stem cell disease model of a common form of heart disease involving the aortic valve. Gene network correction by the most efficacious therapeutic candidate generalized to primary aortic valve cells derived from more than 20 patients with sporadic aortic valve disease and prevented aortic valve disease *in vivo* in a mouse model. —BAP

Science, this issue p. 693

HUMAN EVOLUTION**Brain organoids with Neanderthal genes**

The genomes of Neanderthals and modern humans are overall very similar. To understand the impact of genetic variants that are specific to modern humans, Trujillo *et al.* performed a genome-wide analysis to identify 61 coding variants in protein-coding genes. Identifying the gene encoding the RNA-binding protein *NOVA1* as a top candidate for functional analyses, they introduced the archaic gene variant into human pluripotent stem cells and generated brain organoids. These organoids showed alterations in gene expression and splicing as well as morphology and synaptogenesis, suggesting that this method could be used

to explore other genetic changes that underlie the phenotypic traits separating our species from extinct relatives. —LMZ

Science, this issue p. 694

NEUROSCIENCE**The cells of songbird motor circuits**

Birds have complex motor and cognitive abilities that rival or exceed the performance of many mammals, but their brains are organized in a notably different way. Parts of the bird brain have been functionally compared to the mammalian neocortex. However, it is still controversial to what extent these regions are truly homologous with the neocortex or if instead they are examples of evolutionary convergence. Colquitt *et al.* used single-cell sequencing to identify and characterize the major classes of neurons that comprise the song-control system in birds (see the Perspective by Tosches). They found multiple previously unknown neural classes in the bird telencephalon and shed new light on the long-standing controversy regarding the nature of homology between avian and mammalian brains. —PRS

Science, this issue p. 695;

see also p. 676

CORONAVIRUS**Lineage dynamics**

The scale of genome-sequencing efforts for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unprecedented. The United Kingdom has contributed more than 26,000 sequences to this effort. This volume of data allowed du Plessis *et al.* to develop a detailed picture of the influxes of virus reaching U.K. shores as the pandemic developed during the first months of 2020 (see the Perspective by Nelson). Before lockdown, high travel volumes

and few restrictions on international travel allowed more than 1000 lineages to become established. This accelerated local epidemic growth and exceeded contact tracing capacity. The authors were able to quantify the abundance, size distribution, and spatial range of the lineages that were transmitted. Transmission was highly heterogeneous, favoring some lineages that became widespread and subsequently harder to eliminate. This dire history indicates that rapid or even preemptive responses should have been used as they were elsewhere where containment was successful. —CA

Science, this issue p. 708;
see also p. 680

GALAXIES

Early assembly of a galaxy disk and bulge

Galaxy formation in the early Universe is thought to have been a chaotic process, producing disturbed and asymmetric galaxy morphologies. Over billions of years, galaxies dynamically relaxed to form stable morphological features. Lelli *et al.* observed a distant galaxy at a redshift when the Universe was 1.2 billion years old (see the Perspective by Wardlow). They used gas and dust emission to measure its kinematics, and then modeled the mass distribution within the galaxy. The authors found that the galaxy contains a massive stellar bulge and a regularly rotating disk, features that models predict take billions of years to form. These results indicate that galaxy evolution is a more rapid process than previously thought. —KTS

Science, this issue p. 713;
see also p. 674

THERMOELECTRICS

Ordering up better conductivity

Improving a thermoelectric material's ability to convert heat to electricity involves optimizing one property without changing another in a detrimental way. Roychowdhury *et al.* found that

cadmium doping of silver antimony telluride enhances cationic ordering, which simultaneously improves electric properties and helpfully decreases thermal conductivity (see the Perspective by Liu and Ibáñez). This strategy markedly improves thermoelectric properties and could be used for other materials. —BG

Science, this issue p. 722;
see also p. 678

CORONAVIRUS

Taming a pandemic

One year after its emergence, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become so widespread that there is little hope of elimination. There are, however, several other human coronaviruses that are endemic and cause multiple reinfections that engender sufficient immunity to protect against severe adult disease. By making assumptions about acquired immunity from its already endemic relatives, Lavine *et al.* developed a model with which to analyze the trajectory of SARS-CoV-2 into endemicity. The model accounts for SARS-CoV-2's age-structured disease profile and assesses the impact of vaccination. The transition from epidemic to endemic dynamics is associated with a shift in the age distribution of primary infections to younger age groups, which in turn depends on how fast the virus spreads. Longer-lasting sterilizing immunity will slow the transition to endemicity. Depending on the type of immune response it engenders, a vaccine could accelerate establishment of a state of mild disease endemicity. —CA

Science, this issue p. 741

MYELOID CELLS

Basophil lineage commitment

Basophils and mast cells are innate myeloid cells involved in immunoglobulin E (IgE)-mediated immediate hypersensitivity reactions, but identification of

committed progenitors for these cell types has been challenging. Wanet *et al.* used gene expression data from hematopoietic progenitors in mice to identify E-cadherin as a candidate marker that is associated with early basophil and mast cell progenitors and is present on some cells on which the high-affinity IgE receptor is not yet detected. Combining E-cadherin and a mature basophil marker offers an alternative technique for selecting mature basophils for functional studies, and this work provides insights into how hematopoietic progenitors commit to differentiating into basophils or mast cells. —IRW

Sci. Immunol. **6**, eaba0178 (2021).

BONE BIOLOGY

Extraskelatal bones in the closet

Heterotopic ossification (HO) is the formation of ectopic bone in soft tissues at sites of injury-induced inflammation. Working in mice, Mundy *et al.* found that inflammatory cells and skeletal progenitor cells initially recruited to sites of HO formation expressed the gene *Inhba*, which encodes the TGF- β superfamily member activin A. Treating mice with an activin A-neutralizing antibody inhibited HO formation. These results suggest that interfering with activin A signaling may be effective in patients with HO. —AMV

Sci. Signal. **14**, eabd0536 (2021).