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An apoptotic cell (green) infected with SARS-COV-2 virus particles (yellow). Image credit: Flickr/NIAID, licensed under CC BY 2.0.

STATISTICS

Estimating the true prevalence of SARS-CoV-2

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a global pandemic, but the true extent of the pandemic remains unknown. Many cases are asymptomatic and may therefore go undetected, and the accuracy of various newly developed diagnostic tests is not well known. Constantin Yiannoutsos et al. analyzed SARS-CoV-2 testing data collected by the state of Indiana. More than 3,600 randomly selected Indiana residents were tested for SARS-CoV-2 between April 25–29, 2020. Even though participants were selected randomly, substantial nonresponse rates and potential diagnostic testing errors may bias estimates of disease prevalence based on the data. To address these concerns, the authors adjusted estimates of disease prevalence using Bayesian methods and data on test performance, daily and confirmed case and death counts, and census data. Census data suggested that non-White and Hispanic/Latino individuals were underrepresented in the sample. The adjusted statewide prevalence estimate was nearly 40% higher than the unadjusted estimate, largely as a result of false negative tests and of underrepresented demographic groups being disproportionately affected by the pandemic. Consequently, the authors estimated that there were 12 times as many total cases as confirmed cases statewide. — B.D.

PNAS e2013906118 (2021)

EVOLUTION

Genetic background and genomic evolution of antibiotic resistance

Understanding and predicting how bacterial resistance evolves could improve efforts to control antibiotic resistance, but such predictions are complicated by interactions between mutations that can affect the evolutionary paths taken by a particular bacterial lineage. Using strains from an *Escherichia coli* long-term evolution experiment, Kyle Card et al. previously found that differences between genetic backgrounds can lead to unpredictable responses in phenotypic resistance. To examine how a strain's genetic background can influence the genotypic evolution of resistance, the authors sequenced complete genomes of 61 antibiotic-resistant clones that evolved from several different founding strains during their earlier experiments. The authors demonstrated that mutations in particular genes were associated with each of the four antibiotic treatments. In addition, resistant clones that evolved independently from the same founding genotypes had on average more mutational targets in common than clones that evolved from different founding genotypes, although the effects were more subtle than those showing antibiotic specificity. The authors conclude that both antibiotic treatment and initial genotype can affect the genetic basis of evolved drug resistance and suggest that small differences in genetic

background—even those accumulated during prior evolution under identical conditions—can influence antibiotic-resistance evolution at both phenotypic and genotypic levels. — S.R.

PNAS e2016886118 (2021)

ENGINEERING

Wireless device enables fast, accurate measurements of skin hydration

Tools for evaluating skin hydration could shed light on skin structure and function and guide clinical decision-making. Conventional instruments that assess skin water content are expensive, bulky, rigid, and difficult to use repeatedly, while recently developed wireless alternatives that adhere to the skin have limited operating range and are sensitive to environmental conditions. To address these limitations, Kyeongha Kwon, Heling Wang, et al. developed a robust, miniaturized platform that flexibly adheres to the skin and allows long-range monitoring of thermal transport properties with high levels of repeatability. A Bluetooth Low Energy system on a chip controls the multisensor module and enables wireless data communication to a smartphone. The authors tested their electronics on three healthy individuals and two patients with atopic dermatitis—the most common inflammatory skin condition. The new platform and standard clinical devices yielded similar results before and after application of a moisturizer. According to the authors, the versatile system could be used to track the hydration level of healthy skin, diagnose and assess the severity of a wide range of skin diseases, and evaluate personal care products and medications. — J.W.

PNAS e2020398118 (2021)

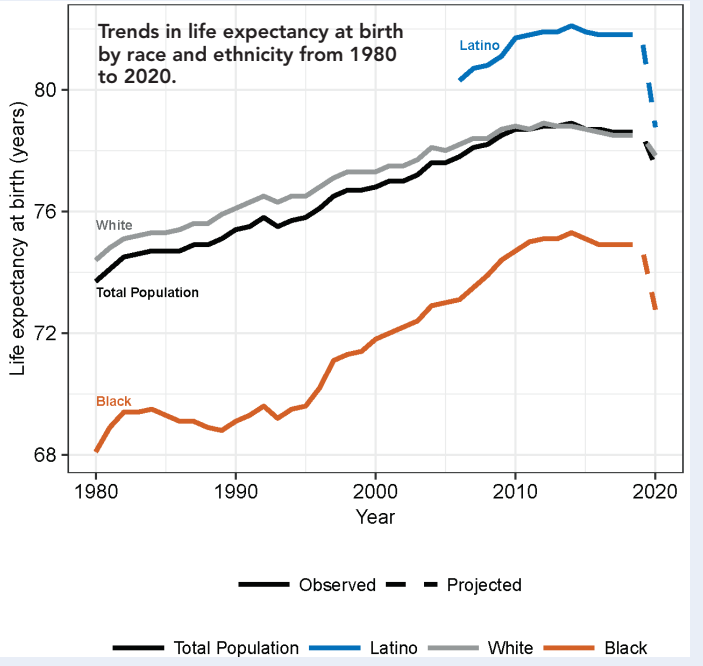
SYSTEMS BIOLOGY

Capturing ultrafast insect movement

When click beetles bend their bodies along a thoracic hinge, quick release of the hinge propels the beetles forward in a spring-like fashion and emits a clicking sound. This extreme motion is too powerful to be generated by muscles alone. Ophelia Bolmin et al. report that high-speed X-ray analysis reveals how click beetles can perform ultrafast movements and avoid significant damage from the massive accelerations generated. The authors captured the bending motion of four *Elater abruptus* specimens with high-speed synchrotron X-ray imaging that allowed the visualization of internal structures. Analysis revealed three distinct phases of the bending maneuver: latching, loading, and energy release. Energy is released much faster

SOCIAL SCIENCES

Racial and ethnic disparities in COVID-19's impact on life expectancy



A disproportionate number of US COVID-19 deaths have occurred among Black and Latino populations. To better quantify the racial and ethnic disparities in COVID-19 mortality, Theresa Andrasfay and Noreen Goldman estimated the effects of COVID-19 on life expectancies at birth in the United States based on projections of total COVID-19 deaths through December 31, 2020. The authors estimated life expectancy in 2020 to be approximately 1.1 years lower than expected in the absence of COVID-19. Black and Latino life expectancies were projected to decline by approximately 2.1 and 3.1 years, respectively, whereas the projected decline in White life expectancy was 0.7 years. Consequently, the Black–White gap in life expectancy would increase from 3.6 years to more than 5 years, the largest value since 2006. Since Latinos began to be separately identified in the National Vital Statistics system in 2006, Latino life expectancy has been higher than White life expectancy. The projected impact of COVID-19 would reduce this Latino advantage from 3.3 years to less than one year, the lowest value ever recorded. According to the authors, some reduction in life expectancy will likely persist after 2020 due to the continued presence of the SARS-CoV-2 virus and the long-term health, social, and economic impacts of the pandemic. — B.D.

PNAS e2014746118 (2021)

than it is stored, supporting the idea that click beetles can amplify mechanical power during the bend. The images revealed large displacements of the hinge's soft cuticle during loading and energy release, indicating that it is likely part of the distributed spring mechanism. The authors used nonlinear system identification to characterize forces associated with the hinge's release. Oscillations at the hinge are governed by snap-through buckling, an instability also used by Venus flytraps to capture prey. According to the authors, understanding the dynamics of extreme maneuvers could inform the development of insect-inspired robots. — T.H.D.

PNAS e2014569118 (2021)

BIOPHYSICS AND COMPUTATIONAL BIOLOGY

Explaining the formation of termite nests

The nest of the African termite, with its structural complexity, is excavated underground by the colony. Alexander Heyde et al. report a newly developed mathematical model that helps explain the intricate architecture. The authors explored how the feedback loop between individual termite behavior and the changing structure of the nest during the construction period lead to a self-organized architecture. The authors visualized the interior structures of two nests using computerized tomography scans, quantifying the spacing and arrangement of floors and the linear and spiral ramps between floors. Then, incorporating the experimentally observed fact that pheromones secreted by the termites serve as indicators of previous activity in the environment and provide a cue for building action, the authors developed a mathematical model of nest construction that is dependent on the spatiotemporal evolution of the density of termite workers, density of nest material, and concentration of pheromones. Simulations of the model showed that nests spontaneously reproduced the consistent vertical spacing of floors and the horizontal spacing of ramps and reflected the process of nest building. According to the authors, the study highlights how these natural architectures are collectively built via multiscale processes linking physics and behavior, with potential relevance to fields such as swarm robotics. — T.H.D.

PNAS e2006985118 (2021)

POPULATION BIOLOGY

Improving rabies vaccination rates with data

Vaccinating dogs can help eliminate human rabies infection in regions like sub-Saharan Africa, where the disease causes thousands of deaths annually. Stella Mazeri et al. report that a recent redesign of an urban dog vaccination campaign in Malawi based on real-time data collection increased the efficiency of rabies prevention. From 2015 to 2017 the authors vaccinated more than 70% of the local dog population in Blantyre city, Malawi, with a combination of fixed locations and door-to-door vaccinations. The latter was necessary to account for suboptimal turnout, but was expensive and time consuming. In 2018, the authors increased the number of fixed service points, setting up additional locations within 812 m of 77% of dog owners, a distance previous research showed was the average that people were willing or able to travel. The authors also set up additional, auxiliary locations in areas with low coverage. Even with door-to-door vaccination removed, approximately the same number of dogs were vaccinated as in previous years but in 11 days versus 20 days and with 904 staff versus 1,719 staff. According to the authors, the strategy of real-time data feedback could be applied to vaccination campaigns to prevent other human diseases transmitted by dogs. — T.H.D.

PNAS e2003722118 (2021)

NEUROSCIENCE

Readying neurotransmitters for launch

Within milliseconds of sensing a calcium ion signal, neuronal cells release neurotransmitters into the synaptic junction via primed vesicles docked on the cells' membranes. The process is essential for information processing in the brain. Abhijith Radhakrishnan, Xia Li, et al. report that a symmetrical arrangement of six proteins appears to enable the coordinated and rapid release of neurotransmitters from their holding pens along the cell membrane. The authors analyzed images of 7,527 synaptic vesicles at various stages of docking with the membranes of cultured neurons using cryoelectron tomography, which provides 3D visualization at the protein level. The analysis revealed vesicles are initially tethered 8–18 nm away from the membrane via proteins that do not appear to be arranged in a discernible pattern. Primed vesicles, however, appear to be held within 4 nm of the membrane by a symmetrically arranged complex of six protein masses. Each protein mass connects the synaptic vesicle to the membrane. While resolution prevents identification of the proteins contained within, the authors hypothesize that each mass likely includes a SNAREpin. According to the authors, these SNAREpins are prearranged into a cooperative fusion machinery structure that forms a critical element of calcium ion signaling. — T.H.D.

PNAS e2024029118 (2021)

JOURNAL CLUB

Highlighting recent, timely papers selected by Academy member labs

February 2, 2021

NEUROSCIENCE

Friends appear to share patterns of brain activity

Posted on January 15, 2021

Amber Dance

Great minds think alike, so goes the saying. Greatness notwithstanding, a study in PNAS finds that the minds of friends do appear to share patterns of activity. "A lot of us have the intuition that our friends are kind of similar to us," says senior author Carolyn Parkinson, a social neuroscientist at the University of California, Los Angeles. The new work suggests that there's some neurological basis behind that suspicion. Continue Reading➲

Researchers asked whether MRI scans from Korean villagers correlated with social ties. Image credit: Shutterstock/Yeongsik Im.