



Cover image: As the 21st president of the US National Academy of Sciences, Ralph J. Cicerone served as a steadfast champion of science. During his tenure from July 1, 2005, to June 30, 2016, Cicerone conducted informed and balanced discussions with politicians and policymakers concerning many complex and controversial scientific issues facing the nation. At the same time, he remained a strong advocate for providing independent scientific advice to the government and the public—a goal central to the Academy's mission since its founding in 1863. See the Retrospective on Cicerone's life and legacy by Veerabhadran Ramanathan on pages 4273–4274. Photograph by Mark Finkenstaedt and image courtesy of the National Academy of Sciences.

From the Cover

- 4273 **Ralph J. Cicerone, 1943–2016**
 E3444 **Mountain uplift and biodiversity**
 4365 **Spread and retreat of languages**
 4424 **Regulatory proteins, environmental stressors, and entropy**
 4549 **Interaction between bacteria and plant roots**

Contents

THIS WEEK IN PNAS

- 4267 **In This Issue**

LETTERS (ONLINE ONLY)

- E3368 **Controversy in statistical analysis of functional magnetic resonance imaging data**
Emery N. Brown and Marlene Behrmann
- E3370 **fMRI clustering and false-positive rates**
Robert W. Cox, Gang Chen, Daniel R. Glen, Richard C. Reynolds, and Paul A. Taylor
- E3372 **Reevaluating “cluster failure” in fMRI using nonparametric control of the false discovery rate**
Daniel Kessler, Mike Angstadt, and Chandra S. Sripada
- E3374 **Reply to Brown and Behrmann, Cox, et al., and Kessler et al.: Data and code sharing is the way forward for fMRI**
Anders Eklund, Thomas E. Nichols, and Hans Knutsson

NEWS FEATURE—An in-depth look at trending science issues

- 4268 **Is video game addiction really an addiction?**
Mark Zastrow

RETROSPECTIVE

- 4273 **Ralph J. Cicerone: His scientific legacy and a long friendship**
Veerabhadran Ramanathan

COMMENTARIES

- 4275 **Are there many different routes to becoming a global biodiversity hotspot?**
Colin E. Hughes
 → See companion article on page E3444
- 4278 **Bringing disorder and dynamics in protein allostery into focus**
A. Joshua Wand
 → See companion article on page 4424
- 4281 **Shining a light on the dark world of plant root–microbe interactions**
Philip Poole
 → See companion article on page 4549

PNAS PLUS**4284 Significance Statements**

Brief statements written by the authors about the significance of their papers.

PERSPECTIVE**4288 A close-up look at the spliceosome, at last**

John Abelson

PHYSICAL SCIENCES**APPLIED PHYSICAL SCIENCES****E3376 Achiral symmetry breaking and positive Gaussian modulus lead to scalloped colloidal membranes**

Thomas Gibaud, C. Nadir Kaplan, Prerna Sharma, Mark J. Zakhary, Andrew Ward, Rudolf Oldenbourg, Robert B. Meyer, Randall D. Kamien, Thomas R. Powers, and Zvonimir Dogic

4294 Enhanced hyperuniformity from random reorganization

Daniel Hexner, Paul M. Chaikin, and Dov Levine

CHEMISTRY**E3385 Automated glycan assembly using the Glycoconer 2.1 synthesizer**

Heung Sik Hahm, Mark K. Schlegel, Mattan Hurevich, Steffen Eller, Frank Schuhmacher, Johanna Hofmann, Kevin Pagel, and Peter H. Seeberger

4300 Oncogene KRAS activates fatty acid synthase, resulting in specific ERK and lipid signatures associated with lung adenocarcinoma

Arvin M. Gouw, Livia S. Eberlin, Katherine Margulis, Delaney K. Sullivan, Georgia G. Toal, Ling Tong, Richard N. Zare, and Dean W. Felsner

4306 Formation of nucleobases in a Miller–Urey reducing atmosphere

Martin Ferus, Fabio Pietrucci, Antonino Marco Saitta, Antonín Knížek, Petr Kubelík, Ondřej Ivanek, Violetta Shestivska, and Svatopluk Civiš

4312 Pressure dependence of viscosity in supercooled water and a unified approach for thermodynamic and dynamic anomalies of water

Lokendra P. Singh, Bruno Issenmann, and Frédéric Caupin

4406 Aggregation landscapes of Huntingtin exon 1 protein fragments and the critical repeat length for the onset of Huntington's disease

Mingchen Chen and Peter G. Wolynes

COMPUTER SCIENCES**4365 Quantifying the driving factors for language shift in a bilingual region**

Katharina Prochazka and Gero Vogl

EARTH, ATMOSPHERIC, AND PLANETARY SCIENCES**4318 Tectonic controls on the long-term carbon isotope mass balance**

Graham A. Shields and Benjamin J. W. Mills

4324 Subduction zone forearc serpentinites as incubators for deep microbial life

Oliver Plümper, Helen E. King, Thorsten Geisler, Yang Liu, Sonja Pabst, Ivan P. Savov, Detlef Rost, and Thomas Zack

ENVIRONMENTAL SCIENCES**4330 Role of surface and subsurface processes in scaling N₂O emissions along riverine networks**

Alessandra Marzadri, Martha M. Dee, Daniele Tonina, Alberto Bellin, and Jennifer L. Tank

PHYSICS**E3390 Pseudomagnetic fields for sound at the nanoscale**

Christian Brendel, Vittorio Peano, Oskar J. Painter, and Florian Marquardt

4336 Universal modal radiation laws for all thermal emitters

David A. B. Miller, Linxiao Zhu, and Shanhui Fan

4342 Spontaneous emergence of catalytic cycles with colloidal spheres

Zorana Zeravcic and Michael P. Brenner

STATISTICS**4436 El Niño and the shifting geography of cholera in Africa**

Sean M. Moore, Andrew S. Azman, Benjamin F. Zaitchik, Eric D. Mintz, Joan Brunkard, Dominique Legros, Alexandra Hill, Heather McKay, Francisco J. Luquero, David Olson, and Justin Lessler

SOCIAL SCIENCES**PSYCHOLOGICAL AND COGNITIVE SCIENCES****4348 Eight-minute self-regulation intervention raises educational attainment at scale in individualist but not collectivist cultures**

René F. Kizilcec and Geoffrey L. Cohen

4354 Life skills, wealth, health, and wellbeing in later life

Andrew Steptoe and Jane Wardle

4360 Increasing honesty in humans with noninvasive brain stimulation

Michel André Maréchal, Alain Cohn, Giuseppe Ugazio, and Christian C. Ruff

4555 Adaptation aftereffects reveal that tactile distance is a basic somatosensory feature

Elena Calzolari, Elena Azañón, Matthew Danvers, Giuseppe Vallar, and Matthew R. Longo

SOCIAL SCIENCES**4365 Quantifying the driving factors for language shift in a bilingual region**

Katharina Prochazka and Gero Vogl

SUSTAINABILITY SCIENCE**4442 Floodplains as an Achilles' heel of Amazonian forest resilience**

Bernardo M. Flores, Milena Holmgren, Chi Xu (徐驰), Egbert H. van Nes, Catarina C. Jakovac, Rita C. G. Mesquita, and Marten Scheffer

BIOLOGICAL SCIENCES**BIOCHEMISTRY****E3396 The cryo-EM structure of YjeQ bound to the 30S subunit suggests a fidelity checkpoint function for this protein in ribosome assembly**

Aida Razi, Alba Guarné, and Joaquin Ortega

- E3404 Ubiquitinated proteins promote the association of proteasomes with the deubiquitinating enzyme Usp14 and the ubiquitin ligase Ube3c**
Chueh-Ling Kuo and Alfred Lewis Goldberg
- 4370 Cyclooxygenase-derived proangiogenic metabolites of epoxyeicosatrienoic acids**
Amy A. Rand, Bogdan Barnych, Christophe Morisseau, Tomas Cajka, Kin Sing Stephen Lee, Dipak Panigrahy, and Bruce D. Hammock
- 4376 Structural basis of Tie2 activation and Tie2/Tie1 heterodimerization**
 *Veli-Matti Leppänen, Pipsa Saharinen, and Kari Alitalo*
- 4382 Dimerization of Tie2 mediated by its membrane-proximal FNIII domains**
 *Jason O. Moore, Mark A. Lemmon, and Kathryn M. Ferguson*
- 4388 Proteolytic control of the mitochondrial calcium uniporter complex**
Chen-Wei Tsai, Yujiao Wu, Ping-Chieh Pao, Charles B. Phillips, Carole Williams, Christopher Miller, Matthew Ranaghan, and Ming-Feng Tsai
- 4394 Molecular basis for the interaction between Integrator subunits IntS9 and IntS11 and its functional importance**
Yixuan Wu, Todd R. Albrecht, David Baillat, Eric J. Wagner, and Liang Tong
- 4400 Structure of a DNA glycosylase that unhooks interstrand cross-links**
Elwood A. Mullins, Garrett M. Warren, Noah P. Bradley, and Brandt F. Eichman
- BIOPHYSICS AND COMPUTATIONAL BIOLOGY**
- E3414 Altering the allosteric pathway in IGPS suppresses millisecond motions and catalytic activity**
George P. Lisi, Kyle W. East, Victor S. Batista, and J. Patrick Loria
- 4406 Aggregation landscapes of Huntingtin exon 1 protein fragments and the critical repeat length for the onset of Huntington's disease**
Mingchen Chen and Peter G. Wolynes
- 4412 In situ structural studies of tripeptidyl peptidase II (TPPII) reveal spatial association with proteasomes**
 *Yoshiyuki Fukuda, Florian Beck, Jürgen M. Plitzko, and Wolfgang Baumeister*
- 4418 Balance of microtubule stiffness and cortical tension determines the size of blood cells with marginal band across species**
Serge Dmitrieff, Adolfo Alsina, Aastha Mathur, and François J. Nédélec
- 4424 Entropy redistribution controls allostery in a metalloregulatory protein**
Daiana A. Capdevila, Joseph J. Braymer, Katherine A. Edmonds, Hongwei Wu, and David P. Giedroc
→ See Commentary on page 4278
- 4430 CryoEM structure of a prokaryotic cyclic nucleotide-gated ion channel**
Zachary M. James, Andrew J. Borst, Yoni Haitin, Brandon Frenz, Frank DiMaio, William N. Zagotta, and David Veasley
- CELL BIOLOGY**
- E3424 SHPRH regulates rRNA transcription by recognizing the histone code in an mTOR-dependent manner**
Deokjae Lee, Jungeun An, Young-Un Park, Hungjiun Liaw, Roger Woodgate, Jun Hong Park, and Kyungjae Myung
- E3434 PIK3CA mutant tumors depend on oxoglutarate dehydrogenase**
Nina Ilic, Kvanç Birsoy, Andrew J. Aguirre, Nora Kory, Michael E. Pacold, Shambhavi Singh, Susan E. Moody, Joseph D. DeAngelo, Nicole A. Spardy, Elizaveta Freinkman, Barbara A. Weir, Aviad Tshemiak, Glenn S. Cowley, David E. Root, John M. Asara, Francisca Vazquez, Hans R. Widlund, David M. Sabatini, and William C. Hahn
- 4300 Oncogene KRAS activates fatty acid synthase, resulting in specific ERK and lipid signatures associated with lung adenocarcinoma**
Arvin M. Gouw, Livia S. Eberlin, Katherine Margulis, Delaney K. Sullivan, Georgia G. Toal, Ling Tong, Richard N. Zare, and Dean W. Felsher
- ECOLOGY**
- 4436 El Niño and the shifting geography of cholera in Africa**
 *Sean M. Moore, Andrew S. Azman, Benjamin F. Zaitchik, Eric D. Mintz, Joan Brunkard, Dominique Legros, Alexandra Hill, Heather McKay, Francisco J. Luquero, David Olson, and Justin Lessler*
- 4442 Floodplains as an Achilles' heel of Amazonian forest resilience**
 *Bernardo M. Flores, Milena Holmgren, Chi Xu (徐驰), Egbert H. van Nes, Catarina C. Jakovac, Rita C. G. Mesquita, and Marten Scheffer*
- 4447 Experimental dispersal reveals characteristic scales of biodiversity in a natural landscape**
Rachel M. Germain, Sharon Y. Strauss, and Benjamin Gilbert
- ENVIRONMENTAL SCIENCES**
- 4330 Role of surface and subsurface processes in scaling N₂O emissions along riverine networks**
Alessandra Marzadri, Martha M. Dee, Daniele Tonina, Alberto Bellin, and Jennifer L. Tank
- 4453 Salting our freshwater lakes**
 *Hilary A. Dugan, Sarah L. Bartlett, Samantha M. Burke, Jonathan P. Dubeck, Flora E. Krivak-Tetley, Nicholas K. Skaff, Jamie C. Summers, Kaitlin J. Farrell, Ian M. McCullough, Ana M. Morales-Williams, Derek C. Roberts, Zutao Ouyang, Facundo Scordo, Paul C. Hanson, and Kathleen C. Weathers*
- EVOLUTION**
- E3444 Uplift-driven diversification in the Hengduan Mountains, a temperate biodiversity hotspot**
 *Yaowu Xing and Richard H. Ree*
→ See Commentary on page 4275
- 4459 Mechanosensation is evolutionarily tuned to locomotor mechanics**
Brett R. Aiello, Mark W. Westneat, and Melina E. Hale
- 4465 Determining the factors driving selective effects of new nonsynonymous mutations**
 *Christian D. Huber, Bernard Y. Kim, Clare D. Marsden, and Kirk E. Lohmueller*
- GENETICS**
- E3452 Parallel adaptive evolution of geographically distant herring populations on both sides of the North Atlantic Ocean**
 *Sangeet Lamichhaney, Angela P. Fuentes-Pardo, Nima Rafati, Nils Ryman, Gregory R. McCracken, Christina Bourne, Rabindra Singh, Daniel E. Ruzzante, and Leif Andersson*

4471 **Mutation in sorghum *LOW GERMINATION STIMULANT 1* alters strigolactones and causes *Striga* resistance**



Daniel Gobena, Mahdere Shimels, Patrick J. Rich, Carolien Ruyter-Spira, Harro Bouwmeester, Satish Kanuganti, Tesfaye Mengiste, and Gebisa Ejeta

IMMUNOLOGY AND INFLAMMATION

E3462 **Hepatitis C virus triggers Golgi fragmentation and autophagy through the immunity-related GTPase M**



Marianne D. Hansen, Ingvild B. Johnsen, Kim A. Stiberg, Tatyana Sherstova, Takaji Wakita, Gabriel Mary Richard, Richard K. Kandasamy, Eliane F. Meurs, and Marit W. Anthonsen

E3472 ***Flicr*, a long noncoding RNA, modulates *Foxp3* expression and autoimmunity**

David Zemmour, Alvin Pratama, Scott M. Loughhead, Diane Mathis, and Christophe Benoist

E3481 **Roles of the *TRAF6* and *Pellino E3* ligases in *MyD88* and *RANKL* signaling**



Sam Strickson, Christoph H. Emmerich, Eddy T. H. Goh, Jiazhen Zhang, Ian R. Kelsall, Thomas Macartney, C. James Hastie, Axel Knebel, Mark Peggie, Francesco Marchesi, J. Simon C. Arthur, and Philip Cohen

4477 **Antigenicity-defined conformations of an extremely neutralization-resistant HIV-1 envelope spike**



Yongfei Cai, Selen Karaca-Griffin, Jia Chen, Sai Tian, Nicholas Fredette, Christine E. Linton, Sophia Rits-Volloch, Jianming Lu, Kshitij Wagh, James Theiler, Bette Korber, Michael S. Seaman, Stephen C. Harrison, Andrea Carfi, and Bing Chen

4483 **Endotoxin-induced autocrine ATP signaling inhibits neutrophil chemotaxis through enhancing myosin light chain phosphorylation**

Xu Wang, Weiting Qin, Xiaohan Xu, Yuyun Xiong, Yisen Zhang, Huafeng Zhang, and Bingwei Sun

MEDICAL SCIENCES

4489 **Formation of neurodegenerative aggregates and death-inducing signaling complex in maternal diabetes-induced neural tube defects**

Zhiyong Zhao, Lixue Cao, and E. Albert Reece

MICROBIOLOGY

E3490 **Plasma fibronectin stabilizes *Borrelia burgdorferi*-endothelial interactions under vascular shear stress by a catch-bond mechanism**



Alexandra F. Niddam, Rhodaba Ebady, Anil Bansal, Anne Koehler, Boris Hinz, and Tara J. Moriarty

E3499 **SAGA complex mediates the transcriptional up-regulation of antiviral RNA silencing**

Ida Bagus Andika, Atif Jamal, Hideki Kondo, and Nobuhiro Suzuki

4495 **Enhanced respiration prevents drug tolerance and drug resistance in *Mycobacterium tuberculosis***

Catherine Vilch ze, Travis Hartman, Brian Weinrick, Paras Jain, Torin R. Weisbrod, Lawrence W. Leung, Joel S. Freundlich, and William R. Jacobs Jr.

4501 **Convergence of DNA methylation and phosphorothioation epigenetics in bacterial genomes**



Chao Chen, Lianrong Wang, Si Chen, Xiaolin Wu, Meijia Gu, Xi Chen, Susu Jiang, Yunfu Wang, Zixin Deng, Peter C. Dedon, and Shi Chen

4507 ***Enterococcus faecalis* bacteriocin EntV inhibits hyphal morphogenesis, biofilm formation, and virulence of *Candida albicans***

Carrie E. Graham, Melissa R. Cruz, Danielle A. Garsin, and Michael C. Lorenz

NEUROSCIENCE

E3507 **Identification of a cono-RFamide from the venom of *Conus textile* that targets ASIC3 and enhances muscle pain**

Catharina Reimers, Cheng-Han Lee, Hubert Kalbacher, Yueming Tian, Chih-Hsien Hung, Axel Schmidt, Lea Prokop, Silke Kaufenstein, Dietrich Mebs, Chih-Cheng Chen, and Stefan Gr nder

E3516 **Context-dependent spatially periodic activity in the human entorhinal cortex**



Zoltan Nadasdy, T. Peter Nguyen,  goston T r k, Jason Y. Shen, Deborah E. Briggs, Pradeep N. Modur, and Robert J. Buchanan

E3526 **Serotonin neurons in the dorsal raphe mediate the anticataleptic action of orexin neurons by reducing amygdala activity**

Emi Hasegawa, Takashi Maejima, Takayuki Yoshida, Olivia A. Maseck, Stefan Herlitze, Mitsuhiro Yoshioka, Takeshi Sakurai, and Michihiro Mieda

E3536 **Intranasal MSC-derived A1-exosomes ease inflammation, and prevent abnormal neurogenesis and memory dysfunction after status epilepticus**



Qianfa Long, Dinesh Upadhyay, Bharathi Hattiangady, Dong-Ki Kim, Su Yeon An, Bing Shuai, Darwin J. Prockop, and Ashok K. Shetty

4513 **APC/*C^{dhl}*-Rock2 pathway controls dendritic integrity and memory**



Ver nica Bobo-Jim nez, Mar a Delgado-Esteban, Julie Angibaud, Irene S nchez-Mor n, Antonio de la Fuente, Javier Yajeya, U. Valentin N gerl, Jos  Castillo, Juan P. Bola os, and Angeles Almeida

4519 **Selective entrainment of gamma subbands by different slow network oscillations**

Weiwei Zhong, Mareva Ciatipis, Th r se Wolfenstetter, Jakob Jessberger, Carola M ller, Simon Ponsel, Yevgenij Yanovsky, Jurij Brankack, Adriano B. L. Tort, and Andreas Draguhn

4525 **Orexin-driven GAD65 network of the lateral hypothalamus sets physical activity in mice**



Christin Kosse, Cornelia Sch ne, Edward Bracey, and Denis Burdakov

PHARMACOLOGY

4531 **Size-selective opening of the blood-brain barrier by targeting endothelial sphingosine 1-phosphate receptor 1**



Keisuke Yanagida, Catherine H. Liu, Giuseppe Faraco, Sylvain Galvani, Helen K. Smith, Nathalie Burg, Josef Anrather, Teresa Sanchez, Costantino Iadecola, and Timothy Hla

PHYSIOLOGY

E3546 **Dual optical control and mechanistic insights into photoswitchable group II and III metabotropic glutamate receptors**

Joshua Levitz, Johannes Broichhagen, Philipp Leippe, David Konrad, Dirk Trauner, and Ehud Y. Isacoff

PLANT BIOLOGY

E3555 **PIF4-controlled auxin pathway contributes to hybrid vigor in *Arabidopsis thaliana***




Li Wang, Li Min Wu, Ian K. Greaves, Anyu Zhu, Elizabeth S. Dennis, and W. James Peacock

E3563 **Malate-dependent Fe accumulation is a critical checkpoint in the root developmental response to low phosphate**




Javier Mora-Mac as, Jonathan Odil n Ojeda-Rivera, Dolores Guti rrez-Alan s, Lenin Yong-Villalobos, Araceli Oropeza-Aburto, Javier Raya-Gonz lez, Gabriel Jim nez-Dom nguez, Gabriela Ch vez-Calvillo, Rub n Rell n- lvarez, and Luis Herrera-Estrella

4537  **The carbonic anhydrase CAH1 is an essential component of the carbon-concentrating mechanism in *Nannochloropsis oceanica***
Christopher W. Gee and Krishna K. Niyogi

4543 **Ploidy-dependent changes in the epigenome of symbiotic cells correlate with specific patterns of gene expression**
Marianna Nagymihály, Alaguraj Veluchamy, Zoltán Györgypál, Federico Ariel, Teddy Jégu, Moussa Benhamed, Attila Szűcs, Attila Kereszt, Peter Mergaert, and Éva Kondorosi

4549 **Live imaging of root–bacteria interactions in a microfluidics setup**
Hassan Massalha, Elisa Korenblum, Sergey Malitsky, Orr H. Shapiro, and Asaph Aharoni
→ See Commentary on page 4281

PSYCHOLOGICAL AND COGNITIVE SCIENCES

E3573  **Variations in crowding, saccadic precision, and spatial localization reveal the shared topology of spatial vision**
John A. Greenwood, Martin Szinte, Bilge Sayim, and Patrick Cavanagh

4555 **Adaptation aftereffects reveal that tactile distance is a basic somatosensory feature**
Elena Calzolari, Elena Azañón, Matthew Danvers, Giuseppe Vallar, and Matthew R. Longo

CORRECTIONS (ONLINE ONLY)

IMMUNOLOGY AND INFLAMMATION

E3583 **Engineered erythrocytes covalently linked to antigenic peptides can protect against autoimmune disease**
Novalia Pishesha, Angelina M. Bilate, Marsha C. Wibowo, Nai-Jia Huang, Zeyang Li, Rhogerry Dhesycka, Djenet Bousbaine, Hojun Li, Heide C. Patterson, Stephanie K. Dougan, Takeshi Maruyama, Harvey F. Lodish, and Hidde L. Ploegh

PHYSIOLOGY

E3584 **AgRP to Kiss1 neuron signaling links nutritional state and fertility**
Stephanie L. Padilla, Jian Qiu, Casey C Nestor, Chunguang Zhang, Arik W. Smith, Benjamin B. Whiddon, Oline K. Rønnekleiv, Martin J. Kelly, and Richard D. Palmiter

SI CORRECTION (ONLINE ONLY)

CELL BIOLOGY, APPLIED PHYSICAL SCIENCES

E3585 **Independent active and thermodynamic processes govern the nucleolus assembly in vivo**
Hanieh Falahati and Eric Wieschaus

ix **Subscription Form**