MEDICINE NOBEL FOR DUO WHO DISCOVERED BIOLOGY OF SENSES

David Julius and Ardem Patapoutian share award for uncovering how cells sense temperature and touch.

By Heidi Ledford & Ewen Callaway

Two researchers who discovered the molecular basis for our ability to sense temperature and touch have won this year's Nobel Prize in Physiology or Medicine.

Physiologist David Julius at the University of California, San Francisco, used capsaicin – the compound that gives chilli peppers their gustatory kick – to track down a protein called TRPV1 that responds to painful heat. Molecular neurobiologist Ardem Patapoutian at Scripps Research in La Jolla, California, identified receptors in skin and other organs that respond to mechanical forces, such as those generated by touch and pressure.

In addition to explaining the basic biology of such senses, the findings have potential medical applications: to combat chronic pain, researchers are looking for compounds that target some of the proteins Julius and Patapoutian discovered.

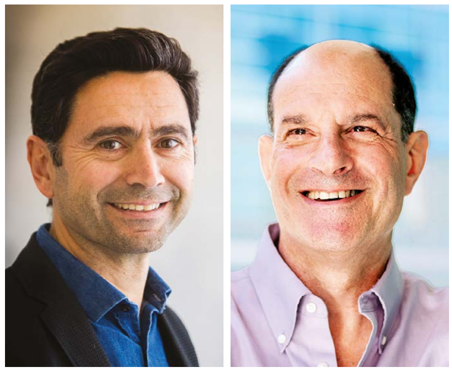
Making sense of senses

The pair's work provided crucial links between external stimuli – such as temperature or touch – and the electrical signals that drive nervous-system responses.

Capsaicin, for example, was known to trigger pain responses, but it was unclear how. In the 1990s, Julius and his colleagues searched through the genes that are switched on in response to pain, heat and touch to find one that would react to capsaicin. Their search led them to a gene that codes for TRPV1, a protein that forms a channel in cell membranes that, when activated, allows ions to pass through[1].

Patapoutian and his collaborators, meanwhile, were looking for molecules that became activated by mechanical forces. The team identified cells that emitted an electrical signal when prodded, and then hunted for genes that might control this response. This led to the discovery of two more ion channels, named Piezo1 and Piezo2, which are activated by pressure[2].

Julius and Patapoutian also independently used menthol – a compound that creates a cooling sensation – to study how cells respond to cold. This led to the discovery of another ion channel, called TRPM8, that is activated by cold[3].



Ardem Patapoutian (L) and David Julius (R), recipients of the 2021 medicine Nobel prize.

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"Both David and Ardem have really changed our understanding of sensory biology. I think it's a fantastic decision to have awarded this," says Michael Caterina, a neuroscientist at the Johns Hopkins University School of Medicine in Baltimore, Maryland, who was part of the team that identified the capsaicin-sensing TRPV1 channel in Julius's laboratory.

The identification of TRPV1 and other related pain-sensing proteins has helped researchers to understand the molecular basis of pain – and seek out new treatments. "We knew it had a chance of being medically important if it could explain some aspects of pain," says Caterina.

"It's a well-deserved award for Ardem and David, and very exciting to me," says Bailong Xiao, a biochemist at Tsinghua University in Beijing and a former postdoctoral researcher in Patapoutian's lab. Patapoutian's discovery of Piezo1 and Piezo2 was especially significant, Xiao says, because the molecules had little in common with other known ion channels, opening up fresh avenues of research for labs worldwide.

"There are a lot of medical problems involving pain and [these] receptors will, for sure, be targets for drug development in the future," medicine Nobel committee chair Nils-Göran Larsson said at the announcement ceremony.

Additional reporting by Tosin Thompson.

1. Caterina, M. *et al. Nature* **389**, 816–824 (1997).
2. Coste, B. *et al. Science* **330**, 55–60 (2010).
3. McKemy, D. D., Neuhausser, W. M. & Julius, D. *Nature* **416**, 52–58 (2002).

CLIMATE MODELLERS AND SYSTEMS THEORIST SHARE PHYSICS NOBEL

Syukuro Manabe, Klaus Hasselmann and Giorgio Parisi split the award for work on complex systems.

By Davide Castelvecchi & Nisha Gaind

Three researchers have won the 2021 Nobel Prize in Physics for their work on describing complex physical systems – including foundational research that created a pioneering mathematical model of Earth's climate and predicted that increasing levels of carbon dioxide in Earth's atmosphere would raise global temperatures.

Syukuro Manabe and Klaus Hasselmann share half of the prize for this modelling. Theoretical physicist Giorgio Parisi at the Sapienza University of Rome receives the other half for his contributions to the theory of complex systems. His work has affected many areas, from neuroscience to how granular materials pack, the Nobel committee said.

"These are two different prizes, but there is the common theme that has to do with this order, these fluctuations together that can give rise to something that we can understand and predict," said Thors Hans Hansson, chair of the physics Nobel committee. "We can predict what is happening with the climate in the future if we know how to code the chaotic weather."

Climate models

Manabe, now at Princeton University in New Jersey, showed in the 1960s how increased levels of carbon dioxide in Earth's atmosphere lead to increased temperatures at the surface, and developed early mathematical models of the planet's climate. Around a decade later, Hasselmann, at the Max Planck Institute for

Meteorology in Hamburg, Germany, built on this work to create a model linking weather and climate.

Gabriele Hegerl, a climate modeller at the University of Edinburgh, UK, who worked with Hasselmann as a postdoctoral researcher, says he was a "fantastic" mentor and supervisor, who was "full of ideas and enthusiasm".

"I am really pleased that Suki and Klaus were chosen together, as they both contributed hugely in different ways and are two giants of climate science," she adds.

Manabe was "gobsmacked" when he heard he had won the prize, said John Wettlaufer, an Earth and planetary scientist at Yale University in New Haven, Connecticut, and a member of the physics Nobel committee. "He said, 'But I'm just a climatologist.'"

Hidden order

Parisi started his career in particle physics, but his research has since touched many other subfields. In the late 1970s, he switched his attention to the theory of complex systems, where he discovered a hidden and counter-intuitive type of order in the interactions of many objects (G. J. Parisi *Phys. A. Math. Gen.* **13**, 1101; 1980). In some systems — such as magnetic materials, for example — atoms tend to align parallel to their neighbours, but complex systems are less predictable. Still, Parisi discovered that they satisfy a kind of symmetry that is noticeable only when comparing how the individual atoms arrange over different scales, says physicist Federico Ricci-Tersenghi at Sapienza.

"He opened up a way to see and interpret complex phenomena that until then had been missed," says Ricci-Tersenghi, who is a former student and long-time collaborator of Parisi's. The theory turned out to be useful even for systems that at first sight seem to be completely random, such as the structure of glass, he adds.

Parisi's research looks at underlying disorder and fluctuations and predicts emerging behaviour, said Wettlaufer. The link between his work and that of Manabe and Hasselmann is that fluctuations are key for predictability, he said. "We're recognizing that emerging phenomena sometimes require you to look at all the individual complicated physical mechanisms and knit them together to make a prediction."

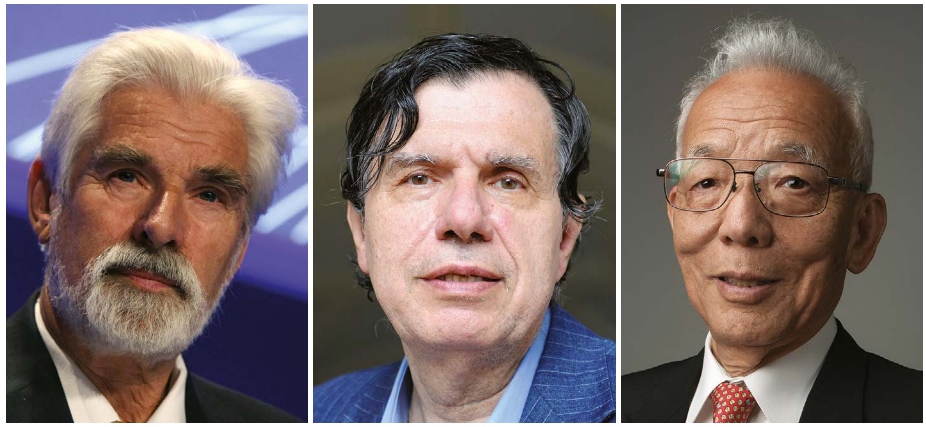
Parisi fosters a "happy environment" in his research group, Ricci-Tersenghi says, and has always encouraged those he mentors to follow their curiosity and intellectual interests.

Reacting to news of his Nobel win, Parisi told reporters during the announcement: "I was very happy and I was not really expecting it." He continued: "But I knew I had some chance — so I kept the telephone near me."

The award comes before a pivotal climate meeting — the 26th United Nations Climate Change Conference, due to take place in Glasgow, UK, in November.

Asked if the Nobel committee was sending a message to world leaders with the award, Göran Hansson, secretary-general of the Royal Swedish Academy of Sciences in Stockholm, said: "What we are saying is that the modelling climate is solidly based in physical theory and solid physics." He added: "Global warming is resting on solid science. That is the message."

Additional reporting by Quirin Schiermeier, Tosin Thompson and Emma Stoye.



2021 Physics Nobel laureates Klaus Hasselmann, Giorgio Parisi and Syukuro Manabe.

J. J. GUILLEN/EPA/SHUTTERSTOCK; TANIA/CONTRASTO/EYEVINE; MARKUS MARCETIC/THE ROYAL SWEDISH ACADEMY OF SCIENCES

'TRULY ELEGANT' CATALYSTS SCOOP CHEMISTRY NOBEL

Benjamin List and David MacMillan share the award for developing cheap, sustainable catalysts.

By Davide Castelvecchi & Emma Stoye

Two researchers who developed techniques to speed up and control chemical reactions have won the 2021 Nobel Prize in Chemistry.

Benjamin List and David MacMillan separately developed a new type of catalysis in the 1990s. The technique — called asymmetric organocatalysis — is widely used today for the production of drugs and other chemicals. Crucially, the catalysts that the pair developed can distinguish left from right, synthesizing molecules that are different from their mirror image.

The pair developed "a truly elegant tool for making molecules — simpler than one could ever imagine", said chemistry Nobel committee member Pernilla Wittung-Stafshede at the prize announcement. "Until the year 2000, we only knew about two forms of catalysts. But then everything changed. Benjamin List and David MacMillan independently reported that you can use small organic molecules to do the same job as big enzymes and metal catalysts in reactions that are precise, cheap, fast and environmentally friendly."

Catalysts, substances that accelerate reactions without being used up, are fundamental tools for chemists. List, who is based at the Max Planck Institute for Coal Research in Mülheim an der Ruhr, Germany, and MacMillan, at Princeton University in New Jersey, developed catalysts that can drive asymmetric catalysis, in which a reaction produces more of the left-handed version of a molecule than the right-handed one, or vice versa.

David MacMillan (L) and Benjamin List (R), recipients of the 2021 chemistry Nobel prize.

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