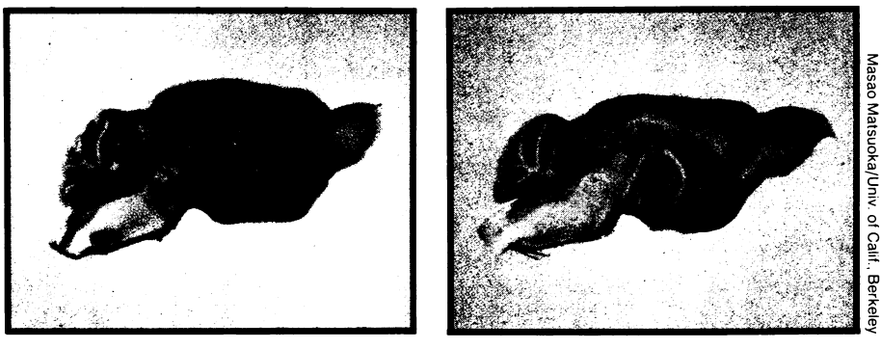
Genes May Shuffle in Developing Brain

In 1987, immunologist Susumu Tonegawa of the Massachusetts Institute of Technology won the Nobel Prize for showing that white blood cells mix and match a handful of genes to make the interchangeable parts that form the millions of different antibodies used by the body to ward off infection. However, researchers have failed to find evidence of this gene-shuffling phenomenon – called somatic, or body-cell, DNA recombination – in cells other than those of the immune system. Until now.

Nerve cells also possess the ability to dice and splice their own genes, reports an international group led by Hitoshi Sakano of the University of California, Berkeley, who worked with Tonegawa on some of the Nobel laureate's most famous experiments. Sakano and his colleagues find that neurons in the brains of mice can rearrange their genes using the same mechanisms as white blood cells. Moreover, the rearrangement accelerates during the development of young mouse pups. The group describes its work in the Oct. 4 SCIENCE.

Researchers in the group hesitate to conclude that this gene rearrangement plays a role in the specialization of the brain's different regions during early life. But they say they plan to investigate whether the shuffling process helps initiate the brain's development by turning some genes on and others off.

To make their discovery, the team created genetically engineered mice whose cells contained a backwards copy of a marker gene. In its correct orientation, this gene produces an enzyme that can cause cells to turn blue. The researchers flanked the inserted marker gene with two stretches of DNA involved in the gene rearrangement of white blood cells. They reasoned that if neurons could recombine their own genes, some of the cells would cut out the marker gene and flip it over, causing the gene-shuffled cells to stain a telltale blue.



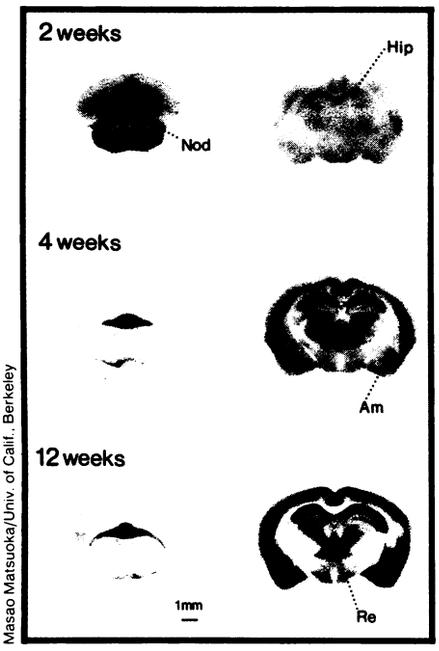
Masao Matsuoka/Univ. of Calif., Berkeley

Bluish tint appears in mouse brain regions containing the rearranged marker gene (left), but not in a brain lacking the gene (right).

To the researchers' surprise, brain neurons in the transgenic mice did reorient the marker gene. Sakano's team detected the blue stain in 78 particular areas of the mice brains – most of which they knew served to link sights, smells, sounds or pain with an appropriate response, such as eating or fleeing. The brains of older pups stained more darkly, the researchers noted, and also contained a larger number of stained regions, suggesting that neuron genes rearranged more often as a young animal matured.

"We've shown that genes can recombine in the brain," says Berkeley immunologist Linda Kingsbury, a member of Sakano's group. But she cautions that the team cannot tell how often the phenomenon occurs in normal neurons, because they studied a foreign marker gene flanked by splicing sequences used by white blood cells. "It may be that the sequences we put in are not used at all in the [normal] brain," she says.

David T. Larue of Berkeley, a neuroanatomist on the team, adds that researchers cannot determine whether gene rearrangement plays a role in brain development until they can find that one of a neuron's own genes is shuffled before birth and as a mouse pup matures. Until then, "we won't know if this is occurring as part of any real developmental sequence," he says.



Masao Matsuoka/Univ. of Calif., Berkeley

Slices from the hindbrain (far left) and midbrain (left) reveal larger bluish areas of gene rearrangement as mouse pups mature after birth. Abbreviations denote specific brain regions.

Nevertheless, "one can't help but feel very excited and intrigued by [Sakano's team's] results," says David G. Schatz of Yale University. Two years ago, Schatz and several colleagues reported identifying the gene that activates the genetic swap in immune-system cells. Schatz's team also found that the gene, named recombination activating gene-1, is turned on in neurons. But he cautions that Sakano's team needs to rule out the possibility that the brain DNA might recombine randomly. "It's absolutely essential that their experiments be repeated in other strains of mice," Schatz says. – *C. Ezzell*

Saturn's white spot: Driven by the sun?

A puzzling white spot mars Saturn's normally featureless face about every 30 years. Astronomers now report data suggesting that a seasonal change in solar heating may trigger storms that produce this short-lived phenomenon.

The most recent giant spot erupted over Saturn's equator last October, catching many astronomers by surprise (SN: 10/13/90, p.228). But Agustin Sanchez-Lavega and his colleagues were ready. They had predicted the spot's occurrence based on the frequency of the last four to blemish the ringed planet. By June 1990, the researchers had one telescope in Japan and three more in France trained on Saturn, awaiting the spot's debut.

Their 48 nights of observations, made over a range of visible-light and near-infrared wavelengths from late September through November, provide the most detailed information yet on the phenomenon, asserts Sanchez-Lavega, of the University of Pais Vasco in Bilbao, Spain.

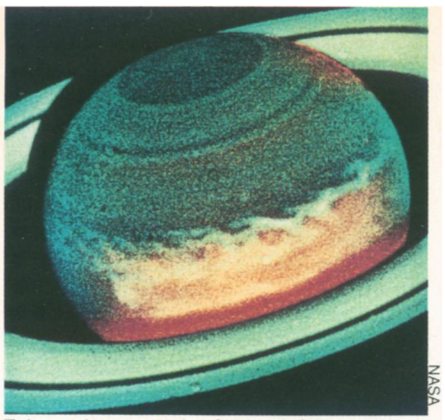
One widely accepted theory attributes the spot to storms that shoot a blob of warm gas up from Saturn's lower atmosphere and through a thick upper mantle of old, smog-stained ammonia ice. As the

gas expands in the upper atmosphere, fresh crystals of ammonia condense on the cooling vapor, forming the white region visible from Earth.

Observations made during early October 1990 – soon after the spot appeared – uphold that idea, the researchers report in the Oct. 3 NATURE. For example, the spot remained bright in blue and violet light – even though the old ammonia clouds in Saturn's hazy atmosphere readily absorb these wavelengths. This seems to indicate that the spot sits above the older ammonia clouds, where the theory says such a storm plume should emerge. Observations last November with the Hubble Space Telescope confirm these and other ground-based findings by Sanchez-Lavega's team, says Chris Barnet of NASA's Goddard Space Flight Center. His team will report its findings in an upcoming ICARUS.

Sanchez-Lavega's team was the first to link the spot's appearance to Saturn's orbital period around the sun – 30 Earth years. Although spots appear alternately over the equator and at higher latitudes, they always form during summer in Saturn's northern hemisphere.

This suggests the sun may drive the formation of Saturn's spots, which typically last several months, the astronomers say. Indeed, they note, the northern summer season comes some 15 Earth years after the equator receives its least sunlight and soon after the sun begins warming the upper atmosphere over the equator. These factors may conspire to create an unusually strong temperature gradient between the upper and lower layers of Saturn's atmosphere at the equator, triggering the sudden updrafts of gas believed responsible for the spots.



False-color portrait of great white spot, taken last November by Hubble Space Telescope. Blue denotes low-altitude clouds; higher clouds appear red.

If so, Barnet says, spots also should form 30 degrees south of the equator, where computer simulations suggest an even higher temperature gradient occurs. A full test of the theory, however, awaits exploration by spacecraft, since Saturn's rings would block the view of such spots. – *R. Cowen*

Alcohol gene: A wider scope

A gene linked to alcoholism apparently does not cause the disorder, but may increase the severity of its symptoms, as well as the symptoms of several other psychiatric and neurological conditions.

The new findings follow several studies suggesting that the same gene – which orchestrates the functioning of brain-cell receptors for the chemical messenger dopamine – intensifies the severity and medical consequences of alcoholism (SN: 9/21/91, p.190).

An increased prevalence of the dopamine receptor gene – ranging from 42 percent to 55 percent – appeared among study participants with alcoholism, autism, hyperactivity, Tourette's syndrome or post-traumatic stress disorder, geneticist David E. Comings of City of Hope National Medical Center in Duarte, Calif., and his colleagues report in the Oct. 2 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

The gene did not display an increased prevalence among participants with severe depression, panic attacks, Parkinson's disease or obesity, Coming's group asserts. About one in four healthy controls possessed the gene, they note.

The dopamine receptor gene may worsen symptoms of disorders caused by other genes, the researchers say. □

Computer model shows tiny drops still drip

Raindrops falling on a waxed car hood bead up and roll away. But should those drops hit a cotton rag used to buff that metal, they flatten and stick, dampening the fabric.

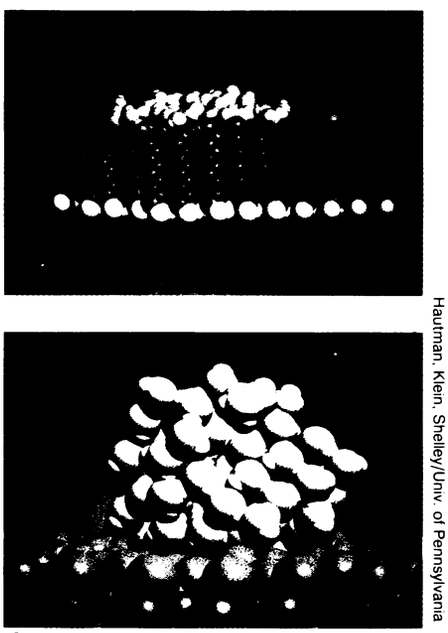
Now two chemists have shown that what people observe in their everyday encounters with water also happens on a molecular scale. Using sophisticated computer software that they developed, Joseph Hautman and Michael L. Klein of the University of Pennsylvania in Philadelphia studied the behavior of water on charged and neutral surfaces. Even when present in small numbers, water molecules on a neutral surface form microscopic droplets that look and act like their much larger counterparts, they report in the Sept. 23 PHYSICAL REVIEW LETTERS.

"That's the surprise, the scaling, that it maps so nicely," says Klein. "You need relatively few molecules to produce macroscopic behavior." Raindrops, with more than a quintillion molecules, dwarf the researchers' minuscule computer droplets, which contain fewer than 100 molecules.

For their surfaces, Hautman and Klein simulated long hydrocarbon molecules called alkylthiols. In real life, when scientists dip a thin gold-covered plate into a solution of these molecules, the alkylthiols line up on the plate and "self-assemble" into a single layer that coats the plate. This "monolayer" serves as a surrogate for a simple membrane, says Klein.

For their study, they had the computer model make two kinds of monolayers. They created one monolayer where the molecules align with a charged end sticking out and also a slightly different one with neutral tips facing outward. The scientists then introduced 90 supercooled water molecules on top of each layer. For the simulation, they heated the wetted monolayer. Then, using graphics software developed by graduate student John Shelley, they watched the reorganization of these computer-generated water molecules on a computer screen.

On the neutral surface, "the [water] droplet arises spontaneously," says Klein. Also, the droplet does more than look like visible drops (SN: 3/16/91, p.165). Scientists often assess the hydrophilic (water-loving) nature of a material by measuring the angle between the surface and the droplet. The more water beads up, the larger this contact angle, and the less wettable the material. Hautman and Klein found that this angle in their simulations also correlated to wettability. Thus, one can use this computer model to predict a new material's hydrophilic properties, says Klein.



Computer simulation reveals that even a few water molecules (yellow) flatten out on charged surfaces (top), but form droplets on neutral surfaces (bottom).

This study represented one of the first steps toward developing computer models of membranes and, ultimately, of cells, he adds. – *E. Pennisi*