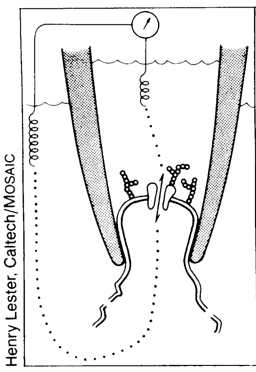
Cell channel finders garner medical Nobel

Two German cell physiologists won the 1991 Nobel Prize in Physiology or Medicine this week for proving that tiny pores dot the outer membranes of cells and allow the cells to take up and excrete charged atoms.

Erwin Neher of the Max Planck Institute for Biophysical Chemistry in Gottingen and Bert Sakmann of the Max Planck Institute for Medical Research in Heidelberg, who will share the $1 million prize, showed how such channels regulate a cell's internal levels of sodium, potassium, calcium or chloride ions. Channel defects underlie disorders such as diabetes, epilepsy, cystic fibrosis and some forms of heart disease.

Neher and Sakmann proved the existence of ion channels in the late 1970s after developing a technique called "patch clamping." This procedure, now widely used in studies of cell communication, allowed them to isolate and study the activity of a single channel. Ten years ago, they reported monitoring the opening and closing of 15 types of channels among more than 20 different cell types (SN: 11/7/81, p.295).



Henry Lester, Caltech/MOSAIC

In patch clamping, researchers use suction to clamp a tiny pipette (shaded areas) against a patch of cell membrane. As ions traverse pore-like channels on the membrane, they create a measurable electrical current.

The researchers "conclusively established with their technique that ion channels do exist, and how they function," states the Nobel Assembly of the Karolinska Institute in Stockholm. "Neher and Sakmann's contributions have meant a revolution for the field of cell biology, for the understanding of different disease mechanisms, and opened a way to develop new and more specific drugs."

Together, Neher and Sakmann found that specific channels only accept ions of the correct size, and that the channels contain charged regions used to filter out ions bearing the wrong charge. The Nobel committee noted that Neher independently worked out the process used by cells to secrete substances such as hormones and neurotransmitters. By measuring electrical changes at the cells' surfaces, he determined that secretory cells spew out their products after inner-membrane vesicles bubble to the surface and fuse with the cells' outer membranes.

— C. Ezzell

Electric fields orient chilled molecules

Just as a bully likes to have his victim pinned down so he can deliver his blows straight-on, chemists want their molecules lined up properly for chemical reactions. Head-on hits, sideswipes and rear-end collisions have different effects on reaction rates, and those differences can make it difficult for researchers to analyze the dynamics involved when two chemicals combine.

Now, two teams report success in controlling simple polar molecules by cooling and then orienting them in an electric field. One group, led by physicist Hansjürgen Loesch at the University of Bielefeld in Germany, went on to study how beams of iodide compounds interact with beams of potassium. The other, led by Harvard University chemist Bretislav Friedrich, used laser spectroscopy to characterize this orientation. "They figured out a way to measure the effect," comments Steven Stolte, a chemist at Vrije University in Amsterdam.

Both groups study chemical reactions by generating two beams of molecules and aiming those beams so that they intersect. The scientists then monitor what happens to molecules that collide where the beams cross. The use of beams enables them to control the type of molecules involved and the angle and speed of the collisions, but not the orientation of the molecules.

The molecules pack in energy that causes them to spin and tumble. To understand this motion in a two-atom molecule, for instance, it helps to envision the molecule as a barbell, with each weight representing an atom and the connecting bar representing the bond between them. The atomic barbell's rotational state — how fast and how frequently it turns — depends on its energy, which varies from molecule to molecule.

Normally, most molecules tumble so wildly that electric fields cannot control them. Certain molecules known as "symmetric tops" represent an exception; scientists can orient them with a technique called electric field focusing. But until now, researchers believed it would take millions of volts to orient other molecules effectively, Loesch says.

In independent studies, the German and U.S. groups have now demonstrated that if they cool the atomic barbells by shooting a stream of them into a vacuum, they do not need to use such a strong electric field. The cooling forces the molecules to settle down into low rotational states, in which they tumble more slowly.

Once the molecules have cooled, even a moderate electric field is strong enough to stall the slowed atomic barbells in mid-tumble, Friedrich explains. The barbells wind up swinging back and forth like pendulums and pointing in the same general direction.

Friedrich and Harvard colleague Dudley R. Herschbach use a pulsed orange-red laser to illuminate the molecules in the electric field. The oscillating molecules absorb light of a certain wavelength. Moments later, they fluoresce, radiating light back to a detector. The intensity of the fluorescence reflects the degree to which all of the molecules share the same orientation, and the position of the spectral lines creates a spectroscopic signature for the oriented molecules, report Friedrich and Herschbach in the Oct. 3 NATURE. "There is a close linkage between spectroscopy and orientation," Friedrich says. "You can do spectroscopy and learn about the orientation."

Loesch and his student Andreas Remscheid initially tested this technique on a symmetric-top molecule, an iodide hydrocarbon (CH_3I). In the Oct. 17 JOURNAL OF PHYSICAL CHEMISTRY, they say their iodide hydrocarbon experiment verifies that the angle at which a potassium beam strikes the axis of the molecule determines the likelihood of a reaction taking place.

When the potassium gets close enough to the molecule, an electron jumps from the potassium to the molecule and causes it to explode. The iodine heads off one way and the CH_3 heads in the opposite direction, but both travel along the axis of the original molecule. Potassium iodide is most likely to form in a collision when the iodine directly faces the potassium, and least likely to form if the iodine faces in the opposite direction, Loesch explains.

The German team has since extended its work to a barbell molecule. Their soon-to-be published findings indicate that the orienting technique works for studies of iodide monochloride, Loesch told SCIENCE NEWS. "That's a linear molecule which cannot be oriented by any other means," he adds.

At this point, neither research team has managed to orient a very high percentage of the molecules, but both Loesch and Friedrich say they expect to improve their percentages. Then researchers can study molecules whose orientations produce much more subtle effects on reactions. That ability is quite tantalizing, notes Stanford chemist Richard N. Zare.

"What's exciting is how easy it might be to orient molecules," he says. "That seems to be what the major payoff might be."

— E. Pennisi