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Counterintuitive physics property found to be widespread in living organisms

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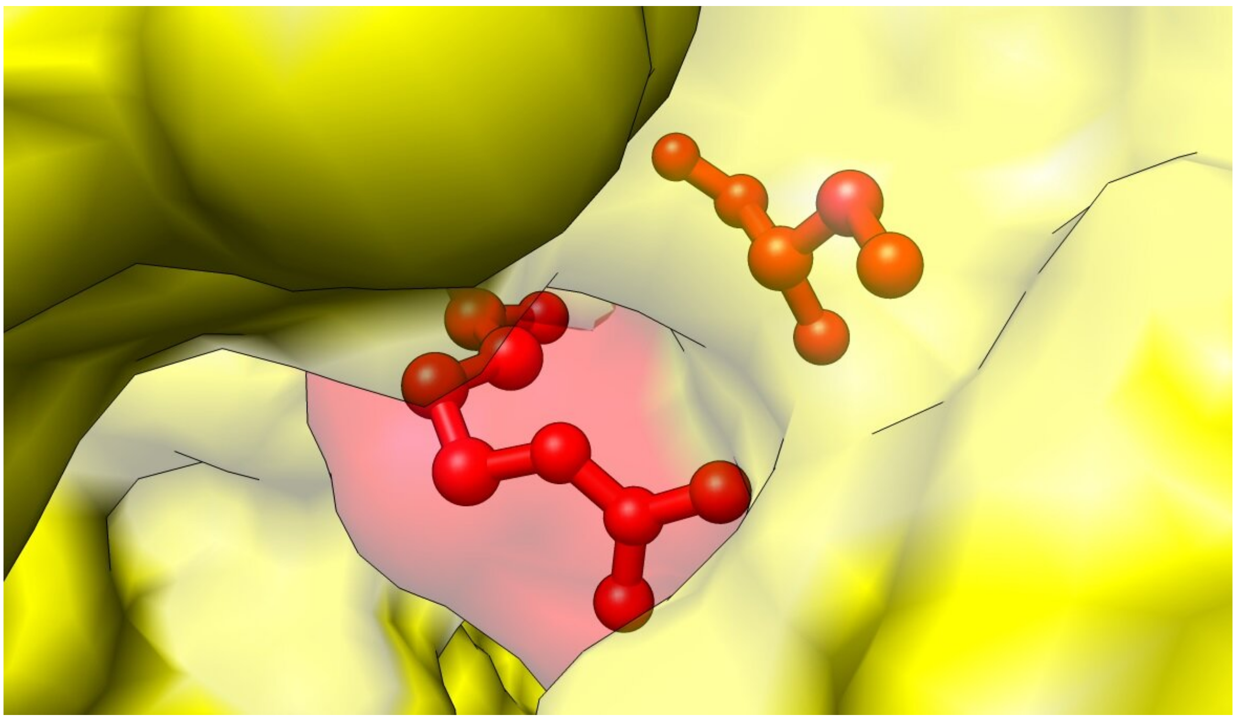

A negative differential response occurs in substrate inhibition, a process that occurs in about 20% of all known enzymes. Credit: Khopkins2010, Wikimedia Commons

Ever since the late 19th century, physicists have known about a counterintuitive property of some electric circuits called negative resistance. Typically, increasing the voltage in a circuit causes the electric current to increase as well. But under some conditions, increasing the voltage can cause the current to decrease instead. This basically means that pushing harder on the electric charges actually slows them down.

Due to the relationship between current, voltage, and resistance, in these situations the resistance produces power rather than consuming it, resulting in a "negative resistance." Today, negative resistance devices have a wide variety of applications, such as in fluorescent lights and Gunn diodes, which are used in radar guns and automatic door openers, among other devices.

Most known examples of negative resistance occur in human-engineered devices rather than in nature. However, in a new study published in the *New Journal of Physics*, Gianmaria Falasco and coauthors from the University of Luxembourg have shown that an analogous property called negative differential response is actually a widespread phenomenon that is found in many biochemical reactions that occur in living organisms. They identify the property in several vital biochemical processes, such as enzyme activity, DNA replication, and ATP production. It seems that nature has used this property to optimize these processes and make living things operate more efficiently at the molecular scale.

"This counterintuitive, yet common phenomenon has been found in a wealth of physical systems after its first discovery in low-temperature semiconductors," the researchers wrote in their paper. "We have shown that a negative differential response is a widespread phenomenon in chemistry with major consequences on the efficacy of biological and artificial processes."

As the researchers explained, a negative differential response can occur in biochemical systems that are in contact with multiple biochemical reservoirs. Each reservoir tries to pull the system to a different equilibrium point (like a balance point), so that the system is constantly exposed to competing thermodynamic forces.

When a system is in equilibrium with its surroundings, any small perturbation, or noise, affecting the reservoirs will typically cause an increase in the production rate of some product, in accordance with positive entropy. The production rate of a product can be thought of as a chemical current. From this perspective, the increase in noise that causes an increase in chemical current is analogous to the "normal" case in electric circuits in which an increase in voltage causes an increase in electric current.

But when a system in contact with multiple reservoirs becomes out of equilibrium, it may respond differently to noise. In an out-of-equilibrium system, additional factors come into play, so that an increase in noise decreases the chemical current. This negative differential response is analogous to the case in which electric circuits exhibit negative resistance.

In their work, the researchers identified several biological processes that have negative differential responses. One example is substrate inhibition, which is a process used by enzymes to regulate their ability to catalyze chemical reactions. When a single substrate molecule binds to an enzyme, the resulting enzyme-substrate complex decays into a product, generating a chemical current. On the other hand, when the substrate concentration is high, two substrate molecules may bind to an enzyme, and this double binding prevents the enzyme from producing more product. As an increase in substrate molecule concentration causes a decrease in the chemical current, this is a negative differential response.

As a second example, the researchers showed that a negative differential response also occurs in autocatalytic reactions—"self-catalyzing" reactions, or reactions that produce products that catalyze the reaction itself. Autocatalytic reactions occur throughout the body, such as in

DNA replication and ATP production during glycolysis. The researchers showed that negative differential responses can arise when two autocatalytic reactions occur simultaneously in the presence of two different chemical concentrations (reservoirs) in an out-of-equilibrium system.

The researchers also identified negative differential responses in dissipative self-assembly, a process in which energy is needed for a system to self-assemble, making it far from equilibrium. Dissipative self-assembly occurs, for example, in the ATP-driven self-assembly of actin filaments—the long, thin microstructures in the cytoplasm of cells that give cells their structure.

Nature does everything for a reason, and the presence of negative differential response in living organisms is no exception. The researchers showed that this property imparts advantages for biochemical processes mainly in terms of energy efficiency. In substrate inhibition, for example, it allows a system to reach homeostasis with less energy than would otherwise be required. In dissipative self-assembly, the negative differential response allows the system to realize a nearly optimal signal-to-noise ratio, ultimately increasing the efficiency of the self-assembly process.

More information: Gianmaria Falasco et al. "Negative differential response in chemical reactions." *New Journal of Physics*. DOI: 10.1088/1367-2630/ab28be