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BIOMIMETICS

MODELING BLOOD VESSEL'S BAND-AID

Microfluidics and a simple chemical system mimic complex hemostasis

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Chemists at the University of Chicago are ingeniously mimicking the human body's ability to patch a damaged blood vessel without obstructing normal blood flow. Their work takes advantage of microfluidics and biomimetics to offer a novel approach for modeling complex biological reaction networks [*Angew. Chem. Int. Ed.*, published online Feb. 24, http://www3.interscience.wiley.com/cgi-bin/abstract/107629156].

The body's dynamic reaction network for maintaining blood flow is called hemostasis. It consists of about 80 coupled reactions that put to work a host of enzymes, clotting factors, fibrinogen, and platelets. Mimicking such a complex system might seem extraordinarily involved, if not impossible, says Rustem F. Ismagilov, a professor of chemistry at Chicago. But Ismagilov has found a way to create a simple model. He likens it to mimicking an enzyme with a small molecule. "We are not going to worry about every single reaction in the network, just as we don't worry about every single atom in the enzyme."

Ismagilov and students Bethany Johnson-Kerner and Matthew Runyon pared hemostasis down to three core kinetic parts: initiation, inhibition, and precipitation. In normal blood flow, the reactions that induce blood clotting (initiation) are balanced by the reactions that prevent clotting (inhibition). When a blood vessel is damaged, the initiation reactions dominate, triggering clot formation (precipitation). This third step patches the damaged blood vessel.

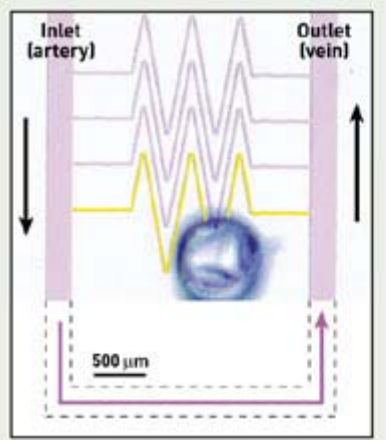
Instead of using biochemical reactions, Ismagilov and coworkers used an inorganic acid-base reaction system to mimic the complex network. An autocatalytic chlorite-thiosulfate reaction produces hydronium ions (initiation) and is balanced by one that consumes hydronium ions (inhibition). The third reaction--precipitation--kicks in when the concentration of hydronium ions rises above a threshold level, causing sodium alginate to gel.

Because vessel geometry and flow are crucial aspects of hemostasis, the Chicago group also designed an artificial capillary bed to test their model. Their microfluidic channels resemble biological vasculature. Narrow tubes (capillaries) of soft silicone rubber meander between

two broader tubes: an inlet (similar to an artery) and an outlet (similar to a vein).

The scientists poked a hole in a capillary to simulate the damaging of a blood vessel. Hydronium ions built up because of the disrupted flow, and sodium alginate gelled and plugged the capillary. Ismagilov was excited to see that the precipitation reaction did not spread to the larger vessel--a critical property of normal hemostasis.

Ismagilov and colleagues hope that their microfluidics model eventually will lead to synthetic vessels that do not induce clotting (for dialysis or heart bypass surgery, for example). Primarily, however, they see this experiment as a prototype for studying other complex reaction networks. "This is just the beginning," says Daniel T. Chui at the University of Washington. Ismagilov concurs. In its capacity to be modeled by a simple chemical system, he says, "hemostasis is not unique."



PATCHED **In this hemostasis model, a simulated rupture in one capillary (yellow) is plugged by the gelling of sodium alginate (blue) without blocking normal flow in the other channels.**

ADAPTED FROM ANGEWANDTE CHEMIE/COURTESY OF RUSTEM ISMAGILOV

NETWORKERS
Runyon (from left), Johnson-Kerner, and Ismagilov collaborated to model hemostasis.

COURTESY OF RUSTEM ISMAGILOV

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