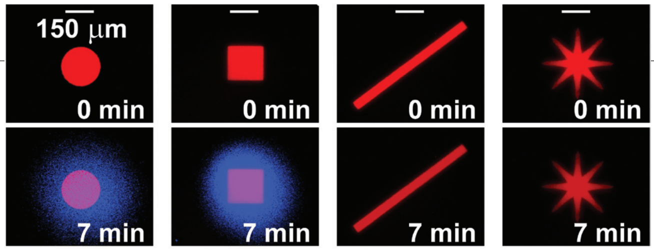
Spotlight

The Shape of Things



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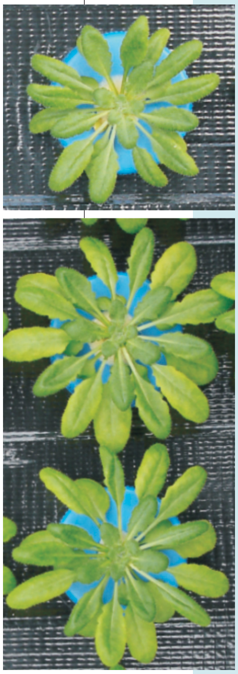
At the molecular level, chemistry dictates biological processes, and the shapes of the molecules involved play a profound role in guiding these processes. Less is understood, however, about how shapes govern events at the cellular and organismal levels. For example, what fundamental processes guide insects to respond to the outline of a flower, or human white blood cells to take action against invading pathogens? Kastrup *et al.* (*Angew. Chem., Int. Ed.* 2007, *46*, 3660–3662) investigate this mysterious phenomenon by exploring the initiation of coagulation of human blood plasma after exposure to various shapes of a clotting stimulus.

Using photolithography, the authors patterned distinct shapes of the blood-clotting stimulus tissue factor in a microfluidic chamber. Plasma was exposed to the shapes, which were a circle, rectangles of varying dimensions, and a star. They determined the initiation of blood clotting by using bright field and fluorescence microscopy to monitor the formation of fibrin and thrombin, respectively. As expected, clotting initiation occurred on circular patches, provided they were above a threshold size. However, other shapes had striking effects on clotting initiation; wide but not narrow rectangles initiated clotting, and the star-shaped patch initiated clotting only half of the time. To examine the mechanism behind this phenomenon, the authors first used 3D numerical simulations of a simple reaction-diffusion system and then a simplified chemical model system of blood clotting. Their results indicated that the dynamics of the clotting network are regulated by a threshold response in which the initiation of clotting requires a certain threshold concentration of clotting activators, a threshold that was not attained, for example, with narrow rectangles. They further demonstrated that response to shape not only is dictated at the organismal level but also can emerge at the level of a biochemical network. Additional studies will address the generality of their findings and may help explain the fundamental processes that govern responses of complex biological systems. **Eva J. Gordon, Ph.D.**

Tolerating Manganese



Peiter, E., *et al.*, *Proc. Natl. Acad. Sci., U.S.A.*, *104*, 8532–8537. Copyright 2007 National Academy of Sciences, U.S.A.

Manganese is an essential micronutrient for all living things. However, too much Mn can be toxic, and many plants and animals have developed mechanisms for tolerating high Mn concentrations. Though not extensively characterized, it is generally thought that Mn levels in plants are controlled mainly through export across the plasma membrane or compartmentalization in vacuoles, in contrast to animals, which also utilize secretory vesicles to eject Mn from cells. Peiter *et al.* (*Proc. Nat. Acad. Sci. U.S.A.* 2007, *104*, 8532–8537) now report the previously unobserved finding that plants also employ the secretory system to regulate Mn levels with the help of a cation diffusion facilitator called MTP11.

Scientists first discovered that MTP11 from *Arabidopsis* selectively restored Mn tolerance to wild-type levels in yeast mutants that were hypersensitive to Mn. To verify that MTP11 played a similar role in plants, the authors generated *Arabidopsis* mutants lacking functional MTP11, and these plants were indeed hypersensitive to Mn. In addition, plants overexpressing the protein were found to be hypertolerant of Mn. Notably, MTP11 from poplar rescued the Mn-hypersensitive *Arabidopsis* mutant, an indication of a general role for the protein in Mn homeostasis in plants. The authors investigated the mechanism by which MTP11 regulates Mn levels by expressing fluorescent MTP11 fusion proteins and examining their localization patterns. Surprisingly, MTP11 was found to localize to the Golgi apparatus and not the plasma membrane or vacuoles, where other transport systems involved in metal tolerance reside. Furthermore, compared with wild-type plants, mutant plants had a higher Mn content. This suggests that plants, like animals, also use the secretory pathway to manage Mn concentrations and prevent the toxic effects associated with elevated Mn levels. **Eva J. Gordon, Ph.D.**