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DENDRITIC PEPTIDES FORM HELICAL PORES

Self-assembling building blocks offer general path to functional pores

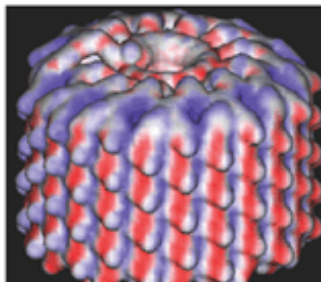
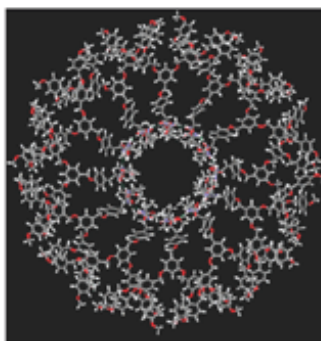
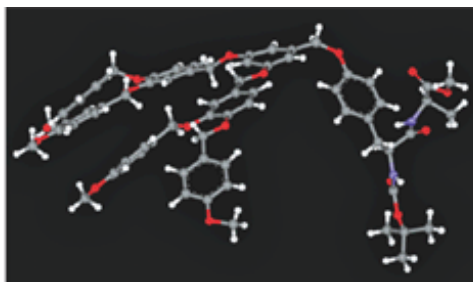
[MAUREEN ROUHI](#)

Dipeptides covalently linked to dendritic units (dendrons) have been found to assemble into helical structures containing a pore that mimics channels produced by pore-forming proteins. Because the self-assembly tolerates variations to the structure of the peptidic dendrons, these molecules offer access to functional synthetic pores for diverse applications [*Nature*, **430**, 764 (2004)].

Preparing synthetic mimics of protein pores has been a research goal for decades but has had limited success, notes [Virgil Percec](#), a chemistry professor at the University of Pennsylvania, Philadelphia. He led the team that carried out the years-long effort to design and prepare the peptidic dendrons and to examine the structure and properties of the supramolecular structures they form. The peptidic dendrons offer a more general solution than has been achieved so far, he adds.

The work is "simply beautiful," comments [M. Reza Ghadiri](#), a chemistry professor at Scripps Research Institute who has designed cyclic peptides that assemble into tunable nanotubes that can selectively disrupt bacterial cell membranes. Ghadiri notes that the supramolecular structures formed by the peptidic dendrons are much larger than his peptide nanotubes and that the way they assemble reminds him of rod-virus assembly. "The number of examples is breathtaking and suggests the

SPIRAL Peptidic dendrons such as those shown at top organize like the steps of a spiral staircase into porous supramolecular structures that are clearly helical when viewed from the top (center) or the side (bottom).



generality of this approach. This type of virus-inspired assembly will have very interesting biological and material applications," he says.



IMAGES COURTESY OF VIRGIL PERCEC

Each peptidic dendron is shaped like a wedge. From the peptide at the narrow end, the dendron spreads out. Self-assembly occurs through hydrogen bonding between the peptides, but in a manner contrary to their natural tendency because of the presence of the dendrons. Instead of hydrogen bonding in an antiparallel arrangement as peptides do, the peptidic dendrons arrange in a parallel manner. "The mechanism of organization is different from those known in biology," Percec says.

Although in the examples so far reported the peptide consists of only two amino acids, the number of amino acids can be varied. Depending on the amino acid composition, the diameter of the pore formed can be varied from 1 to 24 Å. The pores can assemble to almost any length in solution. In a membrane, though, the pores span only the bilayer thickness.

The self-assembly is indifferent to the stereochemistry of the amino acids. In Ghadiri's self-assembling cyclic peptides, for example, the amino acids must have alternating stereochemistries. With the peptidic dendrons, self-assembly occurs with any combination of amino acid stereochemistries, forming channels with different characteristics.

When the peptide consists of hydrophobic amino acids, a hydrophobic channel is formed, regardless of the sequence or the stereochemistries of the amino acids. Percec and coworkers have shown that the hydrophobic channels can mediate proton transport in the same way that the pore formed by the natural protein gramicidin does.

Percec is exploring various applications. Self-assembling peptidic dendrites could be incorporated into human cell membranes as artificial channels to complement the body's natural protein channels. Large pores could be inserted into bacterial cell membranes to kill pathogens.

Sensing is another application. Percec notes that the protein α -hemolysin is already being used to detect single-stranded DNA. But that protein has a pore diameter of only 16 Å. Larger pores would extend applications to larger analytes, such as double-stranded DNA.

Because the supramolecular structures can form films, their use in membrane separation is yet another possibility. Percec is excited about making membranes that allow both rapid and selective passage of specific molecules, such as water. A current dogma in separations is that increasing the selectivity of a membrane decreases the rate at which the analyte passes through. Yet water passes rapidly through natural protein channels that are selective for water. Preliminary experiments suggest that peptidic dendrons can mimic what happens in nature.

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