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# Phosphonate Tubules

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*Tubules are stable, hollow, cylindrical crystalline tube-like structures a few micrometers (millionths of a meter) in size, with potential applications in nanofabrication and medical encapsulation. Stringent control of the kinetics of the process by which these tubules self-assemble is necessary to control the dimensions and qualities of the tubules. An alternative control mechanism involves subtle chemical modifications made to the self-assembling molecules. By using x-rays produced at the National Synchrotron Light Source, scientists have studied both control pathways to understand better how subtle changes made to lecithin, a molecule found in egg yolks and the plasma membrane of plant and animal cells, causes rigid, hollow tubules to form.*

Scientists are currently studying how to build novel materials the size of a few nanometers (a few billionths of a meter, or the size of a few atoms), and the conditions under which these tiny materials could self-assemble spontaneously into specific configurations. Understanding the self-assembly process is one of the most important objectives of nanotechnology, because this process could lead to materials with completely novel properties.

Perhaps the most familiar example of self-assembly is the formation of vesicles from phospholipids (lipids typically found in cellular plasma membrane) placed in water. The vesicles form under the action of divergent forces on the phospholipid's long, water-insoluble (hydrophobic) hydrocarbon tails, and its compact, water-soluble (hydrophilic) "headgroup." These divergent forces drive self-assembly. For example, the hydrophilic headgroups lie exposed upon the inner and outer surfaces of spontaneously formed spherical vesicles, while their hydrophobic tails lie sheltered in between the two hydrated surfaces.

We are now learning that factors far more subtle than the simple "hydrophobic" and "hydrophilic" forces can have profound consequences upon the morphology of a self-assembled material. For example, small, inflexible sections can be inserted in the phospholipid's otherwise flexible hydrocarbon tails by creating triple bonds in the tails. When this change to the tail's shape is made, then cooling the resulting spherical vesicles leads to the creation of rigid, hollow 30-by-0.5 micrometer (millionth of a meter) vesicles of an astonishing cylindrical symmetry (**Figure 1**).

Close examination of these cylinders, called tubules, reveals two unusual features: the tubules are coaxially nested sets of cylinders, also called lamellae, and the tubules possess a helical, hence chiral, substructure.

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Tubules form through the helical winding of a uniform-width phopholipid bilayer ribbon, which creates a cylinder that serves as a "nucleus" for subsequent coaxial windings. Interestingly, the tubule's helical sense of handedness depends upon the chirality of the tubule-forming molecule: molecules of one chirality produce tubules possessing a right-handed helical structure, while molecules of the opposing chirality al-

ways produce left-handed helices.

To understand better tubule formation, we have made synthetic perturbations to tubule-forming molecules and characterized the new products. While it is clear that the tails' diynes are required for tubule formation, the remarkable helical handedness-molecular chirality correspondence suggests that by altering the molecule near its chiral center, significant changes to tubule morphology could result. Indeed, we have found that removing the phosphoryl oxygen that links the headgroup to the tails of the tubule-forming molecule called 1,2-bis(10,12-tricosadiynoyl)-sn-glycero-3-phosphocholine, we have doubled the tubule diameter (**Figure 2**). This change in tubule diameter is significant, since previous studies have succeeded in changing tubule length, but not its diameter.

Tubule gross morphology can be quickly measured by microscopy, but such measurements are both static and insensitive to the tubule's *interior* structure. The high intensity of the x-rays produced at beam line X10A of the NSLS has allowed us to perform kinetic small-angle x-ray scattering (SAXS) studies of the transition between spheres and tubules. These studies revealed that: (1) the transition is of the first order (spheres and tubules are in equilibrium during the transition) and is reversible; (2) tubular interlamellar spacing is tightly conserved when tubule diameter is doubled; and (3) the number of lamellae is *halved* when the tubule diameter doubles. These surprising results about tubule interior structure give important clues about intrinsic membrane curvatures and bending moduli, which are unobtainable by any other means.

Tubule dimensions and morphology suggest a host of potential technological applications, ranging from nanofabrication and purification to medical encapsulation. Our work is one step into realizing this technological potential, which will ultimately require optimizing the tubule's morphology for a given application, and understanding not only its "gross" structure but its interior structure as well.

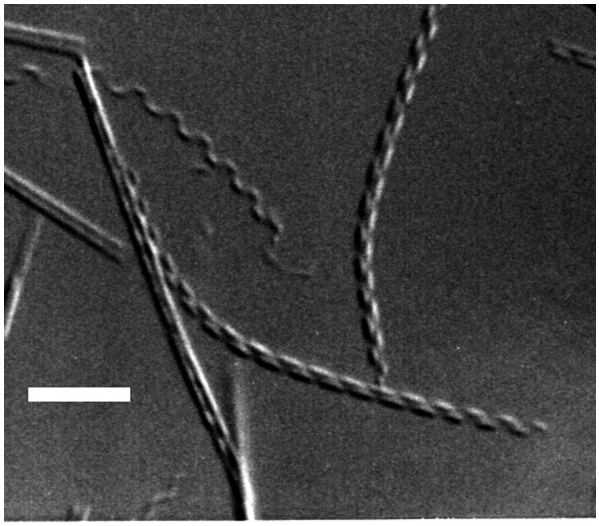

***Figure 1.*** *Some phosphonate tubules observed with an optical microscope.*

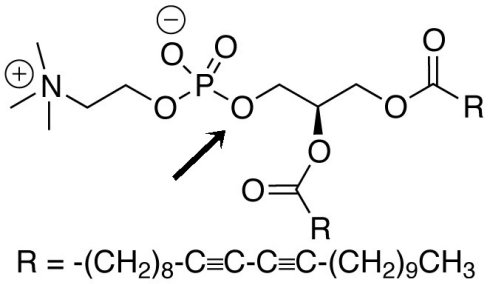


***Figure 2.*** *The tubule-forming 1,2-bis(10,12-tricosadiynoyl)-sn-glycero-3-phosphocholine. The arrow indicates the oxygen atom removed to make the tubule derivative investigated in this study. The molecule's chiral center lies two atoms at the right of that of this oxygen.*