End-to-End Stacking and Liquid Crystal Condensation of 6- to 20- Base Pair DNA Duplexes

Science **318** (2007) 1276

Authors: Michi Nakata, Giuliano Zanchetta, Brandon D. Chapman, Christopher D. Jones, Julie O. Cross, Ronald Pindak, Tommaso Bellini, and Noel A. Clark

Recommended and a commentary by Randall D. Kamien, University of Pennsylvania

Crystalline order is inevitable when rigid molecules are allowed to equilibrate at high enough densities. Liquid crystalline phases, on the other hand, are more delicate and depend crucially on the molecular geometry. Inspired by Langmuir [1], Onsager developed the now celebrated theory of nematic ordering in rigid rods [2]. He established that when the aspect ratio of the rods, L/d, was large, nematic order ensued when the volume fraction exceeded (roughly) four times d/L. From this point of view it is not surprising that long, stiff biomolecules adopt liquid crystalline ordering in the crowded cell. The beautiful works of Bouligand [3] and Livolant [4] elucidating complex liquid crystalline ordering in a variety of cellular contexts serve as both inspiration and fodder for the liquid crystal community, from nematics and cholesterics to blue phases and other defect-laden phases. New work, out of the Boulder group, proposes a novel step forward: liquid crystalline order is not just inevitable in a biophysical context, but it is essential for life, creating a crucible for autocatalytic reactions.

Working with very small quantities of short fragments of single-stranded DNA, this group discovered, to their surprise, nematic ordering for molecular lengths too short to form this mesophase. (It is worth having a look at the gorgeous micrographs of these phases taken by the late Michi Nakata). How is this possible? One system they studied used so-called palindromic sequences, *e.g.* AACGCATGCGTT. Recall that there are four DNA base pairs, labeled A,C, G, and T; A and T form a pair and C and G form a pair. In solution by themselves, these strands first bind to themselves forming double-stranded segments. At this point, they are roughly $L = 4$nm long and $D = 3.3$nm wide, too stout to form nematics. However, hydrophobic effects promote the stacking of base pairs, even in the absence of the sugar-phosphate backbone, and these fragments stick together, end-to-end, in a process aptly known as living polymerization. Both nematic and columnar phases form.

Their insight came from a slightly different experiment. Consider a mixture of (non-palindromic) sequences in solution, *e.g.* CCTCAAAACTCC and GGAGTTTTGAGG. In a 1:1 mixture these complementary strands find their partners, form double helices and stick end-to-end in much the same way as before. However, when changing the ratio to 10:1, the authors continue to find liquid crystalline order, despite the low concentration of the double-helical strands. At such a low concentration, it would be hard to imagine that these short segments could find each other to stick or that the Onsager criterion for nematic order could be satisfied. How does this happen? Through a dramatic phase separation between the rigid, double-helical strands, and the flexible single-helical strands which remain unpaired. The phase separation allows the double-helical stumps to find

each other and stick and, at the same time, allows for the formation of the nematic phase. To quote the authors, "An immediate inference is that molecules that complementarily aggregate and assemble into larger units that phase separate have a potential advantage in a chemical race to grow in size and specificity over those that cannot phase separate." In other words, molecules that can form liquid crystalline mesophases are preferentially selected in the evolution of molecules. No longer need we view the liquid crystallinity as a by-product of the rigidity of the biopolymers, but rather as an essential part of their ontogeny.

---

[1] I. Langmuir, J. Chem. Phys. **6** (1938) 873.
[2] L. Onsager, Ann. N.Y. Acad. Sci. **51** (1949) 627.
[3] Y. Bouligand, M.O. Soyer and S. Puiseux-Dao, Chromosoma **24** (1968) 251.
[4] F. Livolant, Physica A **176** (1981) 117.