

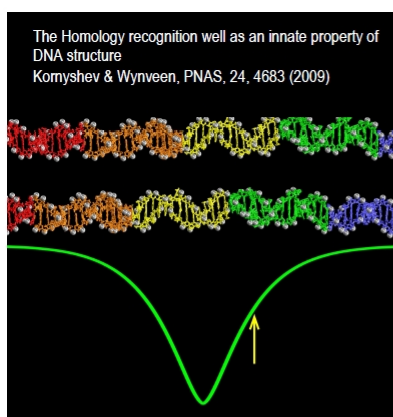
~~Special Polymer Physics Seminar ~~

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10:00 AM Monday, April 5th, 2010
301 Steidle Bldg.

Unravelling new abilities encoded in the structure of DNA



Recombination of genes is a process in which sequences are exchanged between two DNAs. In *homologous recombination* fragments of the same homology are swapped. This makes possible gene shuffling between two parental copies of DNA, crucial for evolution and genetic diversity; a similar process is utilized in DNA repair, and its accuracy warrants the robustness of life. It is generally accepted that understanding recombination of genes is one of the key challenges of the "post-genomic era".

"Decades of research into homologous recombination have unraveled many of the details concerning the transfer of information between two homologous sequences. By contrast, the processes by which the interacting molecules initially co-localize are largely unknown. How can two homologous needles find each other in the genomic haystack?" (Barzel & Kupiec, Nature Rev, 2008)

This talk will discuss a physical explanation of this enigma, which suggests that the structure of DNA can provide one more function: recognition of homology.

The key point in homologous recombination is the swapping of correct genes: only regions with homologous sequences should be exchanged or used as a template for repair. Recombination mistakes are known to cause a variety of severe genetic diseases and contribute to aging. Fortunately, such errors are rare. The recognition of homology occurs with amazing precision, but it was established that at least 50-100 bp homology is required for it; this ensures that the fragments belong to two alleles of the same gene rather than to different genes. Still, to learn how we might assist nature in further reduction of recombination errors, diminishing their unhealthy consequences, is a challenging task. But for this we need to understand the recognition mechanism in depth. In 2001, we suggested a simple, but nontrivial electrostatic mechanism of homology recognition of intact DNA duplexes without any assistance of proteins [1]. This mechanism resulted from a detailed theory of the interaction of biomolecules with helical charge patterns in solutions [2] - for review of the theory development see [3]). Evidence for the existence of the recognition effect acting between intact DNA duplexes from a distance in a *protein-free* pure electrolytic solution has been recently experimentally shown [4]. This talk will overview the principles of the theory and discuss the existing experiments, as well as possible new single molecule experiments, including those related with DNA translocations.

* <http://www3.imperial.ac.uk/people/a.kornyshev>

¹ Kornyshev AA, Leikin S (2001) Sequence recognition in the pairing of DNA duplexes. *Phys Rev Lett* 86:3666-3669.

² The first papers -- Kornyshev AA, Leikin S: (1997) Theory of interaction between helical molecules. *J Chem Phys* 107:3656-3674; (1998) Symmetry laws for interaction between helical macromolecules. *Biophys J* 75:2513-2519. Electrostatic interaction between helical macromolecules in dense aggregates: An impetus for DNA poly- and mesomorphism. *Proc Natl Acad Sci USA* 95:13579-13584; (1999) Electrostatic zipper motif for DNA aggregation. *Phys Rev Lett* 82:4138-4141.

³ Kornyshev AA, Lee DJ, Leikin S, Wynveen A (2007) Structure and interactions of biological helices. *Rev Mod Phys* 79: 943-996.

⁴ Baldwin GS, Brooks NJ, Robson RE, Wynveen A, Goldar A, Leikin S, Seddon JM, Kornyshev AA, (2008) DNA double helices recognize mutual sequence homology in protein free environment. *J Phys Chem B* 112:1060-1064.