Consistent Rationalization of Topo II Actions

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Abstract
The mathematical basis of the hypothesis that type-2 topoisomerases (topo II) recognize and act at specific DNA juxtapositions was investigated by coarse-grained lattice and continuum wormlike chain models, showing that selective segment passages at hooked juxtapositions can result in dramatic reductions in catenane and knot populations. The lattice modeling approach has recently been extended to account for the narrowing of variance of linking number ($Lk$) of DNA circles by topo II. We established a general relationship that the steady-state variance of $Lk$, $\langle Lk \rangle_j$, of circles with the given juxtaposition. This formula allows us to demonstrate that selective segment passages at hooked juxtapositions reduce the variance of $Lk$. The dependence of this effect on model DNA circle size is remarkably similar to that observed experimentally by Trigueros et al. (2004) and Stuchinskaya et al. (2009). Their data show that topo II is less capable in narrowing $Lk$ variance for small DNA circles than for larger DNA circles. This behavior is rationalized by a substantial cancellation of writhe in small circles with hook-like juxtapositions. During our simulations, we uncovered a twisted variation of the hooked juxtaposition that has an even more pronounced effect on $Lk$ variance narrowing than the hooked juxtaposition. For an extended set of juxtapositions, there is a significant correlation between the $Lk$ narrowing potential and the logarithmic decatenating and unknotting potentials for a given juxtaposition, a trend reminiscent of scaling relations observed experimentally for topo II from a variety of organisms. The consistent agreement between theory and experiment argues for topo II actions at hooked or twisted-hooked DNA juxtapositions.

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References: Liu, Zechiedrich & Chan, J Mol Biol 400:963–982 (2010);