KNOTTED AND LINKED BIOPOLYMERS IN BIOLOGICAL SYSTEMS BY COARSE-GRAINED COMPUTER SIMULATIONS

Dusan Racko[a,b,c,*], Fabrizio Benedetti[a,b], Julien Dorier[a,d], Yannis Burnier[a,e], Andrzej Stasiak[a,b,*]

[a] Center for Integrative Genomics, University of Lausanne, 1015-Lausanne, Switzerland
[b] SIB Swiss Institute of Bioinformatics, 1015-Lausanne, Switzerland
[c] Polymer Institute of the Slovak Academy of Sciences, 842 36 Bratislava, Slovak Republic
[d] Vital-IT, SIB Swiss Institute of Bioinformatics, 1015-Lausanne, Switzerland
[e] Institute of Theoretical Physics, Ecole Polytechnique Fédéral de Lausanne (EPFL), 1015-Lausanne, Switzerland

Due to helical structure of DNA the process of DNA replication is topologically complex so that freshly replicated DNA molecules are entangled with each other and are frequently knotted. For proper functioning of DNA it is necessary to remove all these entanglements. This is done by DNA topoisomerases that pass DNA segments through each other using cutting and pasting mechanism. However, it has been a riddle how DNA topoisomerases select their places of action, since in highly crowded DNA in living cells random passages between contacting segments would only increase the extent of entanglement. Using molecular dynamics simulations we observed that in actively supercoiled DNA molecules the entanglements resulting from DNA knotting or DNA catenation spontaneously approach sites of nicks and gaps in the DNA. Type I topoisomerases that preferentially act at sites of nick and gaps are thus naturally provided with DNA-DNA juxtapositions where cutting and pasting operation results in an error-free DNA unknotting or DNA decatenation. By means of Monte Carlo simulations we also show that Topoisomerase IV can unknot right-handed knots and decatenate right-handed catenanes without acting on right-handed plectonemes in negatively supercoiled DNA molecules, based on geometrical specificity of juxtapositions.

---

[1] D. Racko, F. Benedetti, J. Dorier, Y. Burnier, A. Stasiak (2015) “Generation of supercoils in nicked and gapped DNA drives DNA unknotting and postreplicative decatenation” *Nucleic Acids Res.* **43**(**15**) 7229-7236. DOI:10.1093/nar/gkv683

[2] E. Rawdon, J. Dorier, D. Racko, KC Millet, A. Stasiak (2016) "How topoisomerase IV can efficiently unknot and decatenate negatively supercoiled DNA molecules without causing their torsional relaxation” *Nucleic. Acids Res.* **44**(**10**) 4528-4538. DOI: 10.1093/nat/gkw311

---

* dusan.racko@unil.ch, andrzej.stasiak@unil.ch