Simulation of DNA Cleaved by Enediyne Anti-Cancer Antiobiotics

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Within a DNA duplex, recognition sites for conjugates of lysine with a DNA-cleaving agent can be made. By annealing a single DNA strand with shorter counter-strands that are capped by one or two phosphate groups, such recognition sites are created and can direct DNA cleavage to that specific location on the DNA strand. The ability to direct DNA-cleaving agents towards a target site could potentially impact gene therapy and the design of DNA constructs that require disassembly at a specific location. In collaboration with Igor V. Alabugin of Florida State University, this project aims to investigate the possibility of using phosphate recognition for directing DNA-cleaving agents to selected target sites in single stranded DNA.

Eight different constructs of DNA, with varying lengths of DNA counter-strands and terminating phosphate groups at different locations, have been created using AMBER8. These constructs have been put through minimizations and molecular dynamics simulations within an octahedral periodic box of TIP3P waters with a distance of 10 Å between the DNA and the box. All of the simulations were run using the Parm99 forcefield. The minimizations and molecular dynamic simulations were conducted in order to understand the dynamics of the DNA constructs at realistic temperatures and to gain insight to DNA behavior post-cleavage.