Simulation of DNA Cleaved by Enediyne Anti-Cancer Antiobiotics

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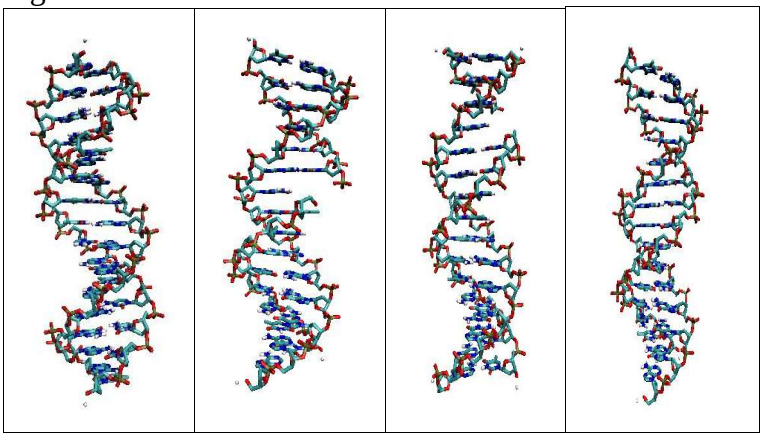
Through a collaboration with Igor V. Alabugin, Professor in the Department of Chemistry and Biochemistry at the Florida State University, we have examined gene therapy properties through computational methods. Expanding upon the principles of gene therapy, Alabugin's research is aimed at directing compounds to specified locations in DNA sequences, followed by DNA cleaving molecules.

Alabugin has explored the idea of using phosphate recognition sites in order to direct DNA cleaving agents to target sites in single polynucleotide strands. By positioning the terminal phosphate groups randomly on the target strand (Figure 1.1), he has found a better method of directing and cleaving. Once a phosphate group is positioned next to the target base, the DNA cleaving agent outfitted with lysine moiety is drawn towards the target. This has led to the creation of several different DNA constructs which have shown the potential to be useful in gene therapy.

We performed molecular dynamic simulations using AMBER8 program suite on the DNA strands in Figure 1.1. They were built in a customized manner to contain the charges and missing nucleic acids. The DNA was submersed in an octahedral periodic box of TIP3P waters, leaving a distance of 10 Å between the DNA and the edges. Sodium ions were added to neutralize the system. The Parm99 force field was used with a Langevin thermostat (nt t=3, with gamma_ln=1) to control the temperature.

As a result of the minimizations and molecular dynamic simulations, we hope to gain greater insight into the unique DNA strands prior to cleavage.

Figure 1.1



DNA I DNA II DNA III DNA IV