Computer Modeling of Extended E-Motif Structures in DNA

Kathryn Iverson

School of Pharmacy, University of Southern California, Los Angeles, CA 90089
SoCalBSI, California State University, Los Angeles, CA 90032

Introduction
The E-Motif structure is a unique structure that may form because of an expanded GCC repeat in the promoter region of DNA. In this structure mismatched cytosines become extra-helical and interact with one another outside the helix. Experimental evidence suggests one of the extra-helical cytosines becomes protonated and this may promote extra-helical interaction between the mismatched C-C pairs1. Using in-house programs, commercial energy minimization software and other bioinformatics tools I was able to model possible structures of an extended E-motif (eE-Motif) structure with up to 30 GCC repeats.

Methods

Generation of PDB Files
To create the PDB files I wrote a python script that output several input files for the in house program NASDAC, which generates PDB files. The input files consisted of parameters the user can vary within a set range. The parameters that can be varied include the length of the GCC repeat, the angle of the axis and various angles of atoms and bonds within the structure.

Molecular Dynamics Modeling with AMBER
Using the proprietary software AMBER8, energy minimization and molecular dynamics modeling were done in silico to generate a minimized structure. Special attention was given to distances between the extra-helical cytosines, and the distance between the stacking of the G-C base pairs. Restraints were added to the minimization and molecular dynamics modeling to generate a more accurate structure.

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Bibliography