Sequence-dependent flexibility of DNA*

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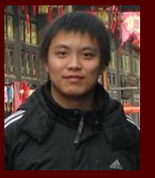

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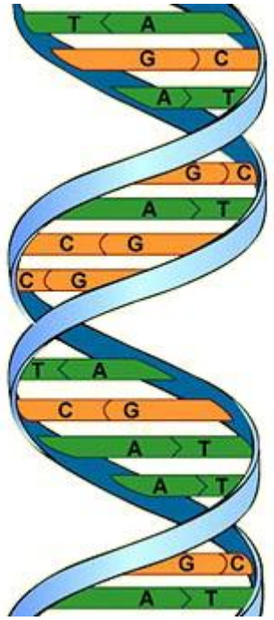
Introduction

- DNA is the most important material for eukaryotes in that it carries most of the genetic information. It is a long double-strand composed of 4 types of nucleotides, adenine (A), thymine (T), cytosine (C), and guanine (G). Only A and T, C and G can form standard base pairs.
- DNA is of meters long, and highly condensed in cells. On the other hand, when DNA needs to be replicated or transcribed, it can be efficiently located.
- Local mechanical property of DNA (such as bending and twist stiffness) is highly sequence-dependent, and determines these biological events.



* Full paper of this slide set is available on ACS Nano (DOI: 10.1021/acsnano.5b06863). Funding in part by NIH R01GM087677.

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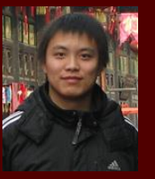

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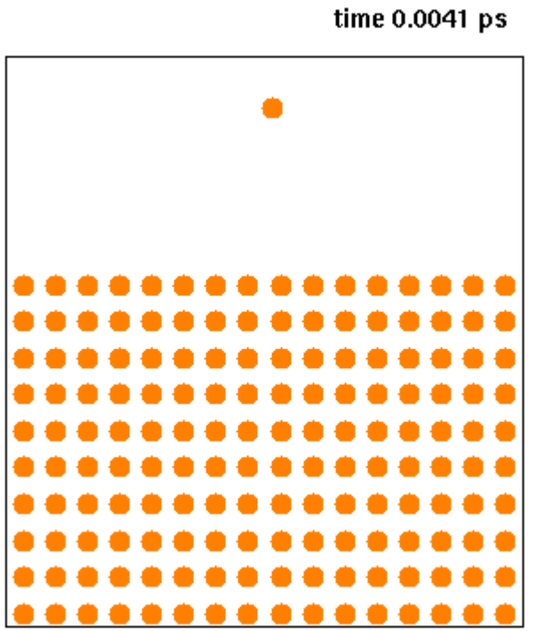
Molecular Dynamics

- Atomistic MD simulation provides “ultimate details” of motional phenomena of molecules, and therefore is an ideal method to study DNA motion and flexibility at molecular level.
- All-atom molecular dynamics (MD) simulation was used to study the local motion of many DNA segments. Properties calculated from our simulation are consistent with diverse experimental observations.



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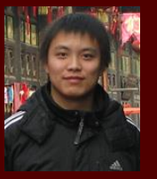

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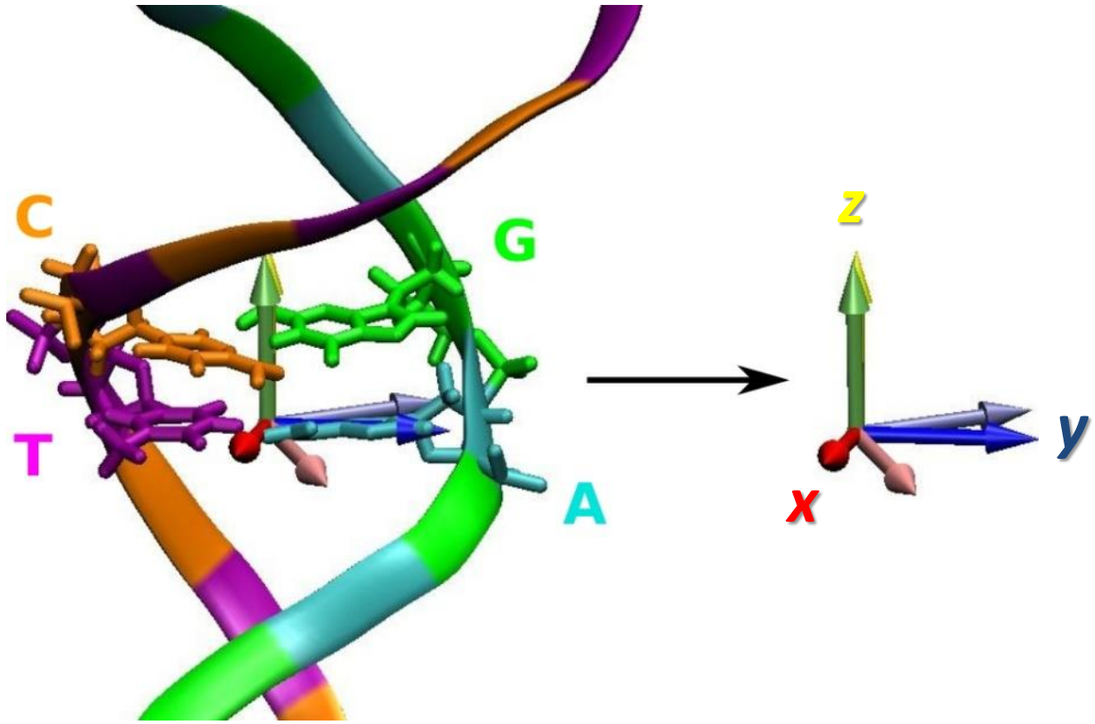
Triad Vectors

- Triad vectors can be used for studying flexibility of DNA sequence. By projecting one vector from one triad to the previous triad, we can obtain the relative motion pattern of local structure.
- (x, y, z) vectors for the lower pair are indicated in (red, blue, yellow) color, and (orange, gray, green) for the upper pair.



Local coordinate is extracted from base-pair

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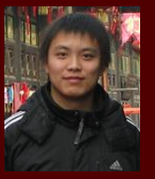

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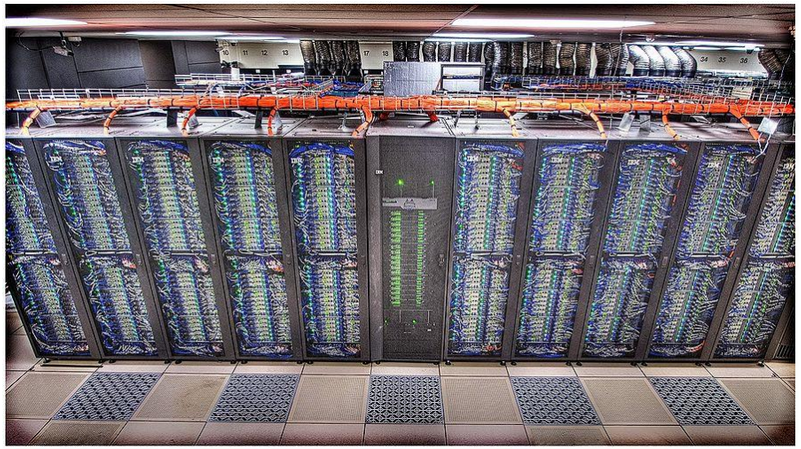
Computing Set Up

- Simulations performed on the ADA cluster (ada.tamu.edu) at the Texas A&M High Performance Research Computing Facility.
- Each 100-ns simulation (~60,000 atoms) used 280 CPUs and about 170 hours of run time.
- Software Used: CHARMM (Chemistry at HARvard Molecular Mechanics).
- Visualization: VMD (Visual Molecular Dynamics).



CHARMM

VMD
Visual Molecular Dynamics

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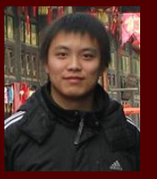

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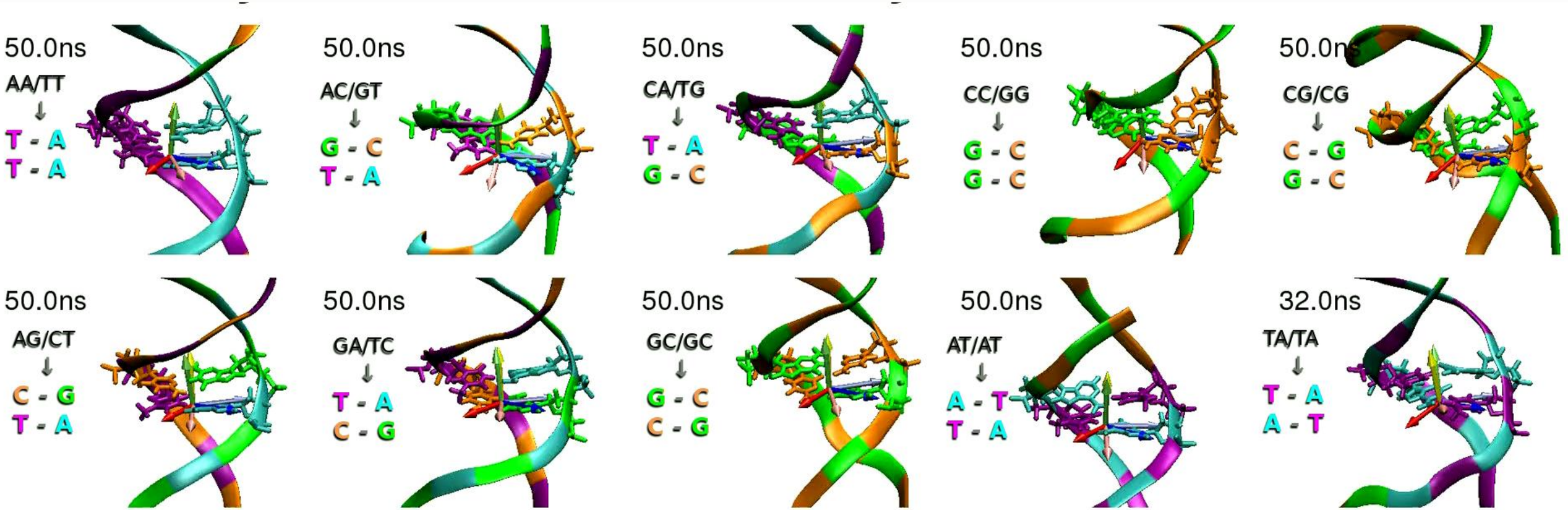
Sequence-Dependent Flexibility of DNA by All-Atom Molecular Dynamics Simulation



Example trajectories of 10 possible DNA base pair steps
Arrows: Triad vectors used for tracing local deformation

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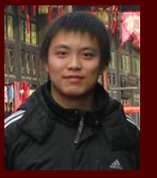

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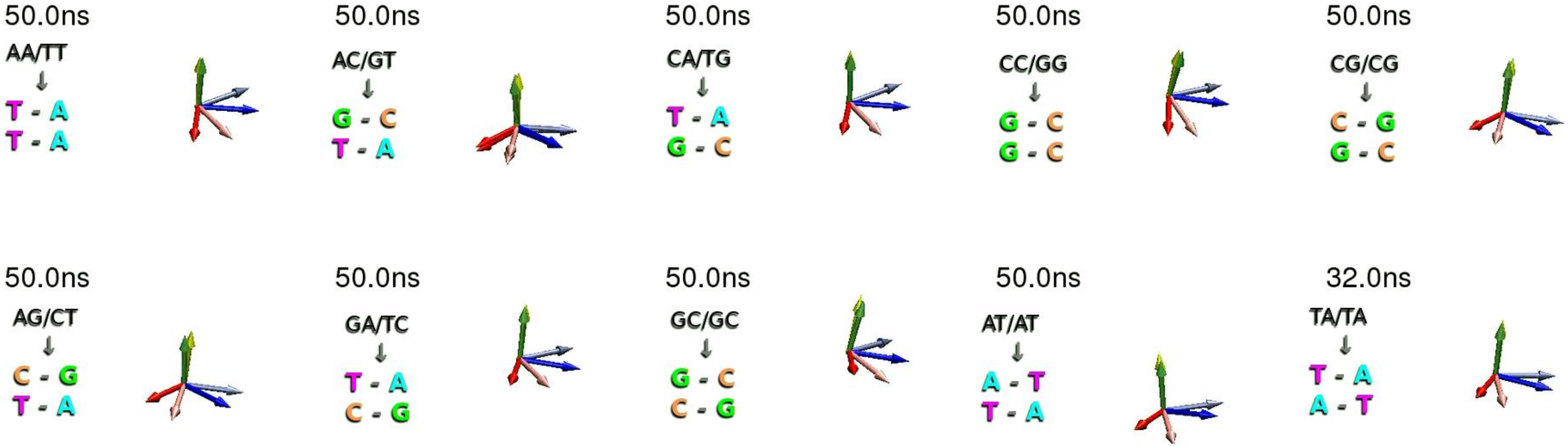

Example trajectories of 10 possible DNA base pair steps
Arrows: Triad vectors used for tracing local deformation

Lower pair: (x, y, z) → (red, blue, yellow)
Upper pair: (x, y, z) → (orange, gray, green)

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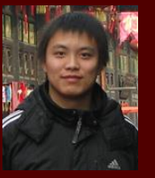

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Results

- Result shows different base pair steps have diverse stiffness and flexibility. Organism can adopt these properties to fulfill various purposes (packaging, ligands binding, initiation of transcription etc).
- A simplified model of DNA molecules can be established to further study phenomenon of long DNA segments (thousands base-paris) at large time scale (~ms).