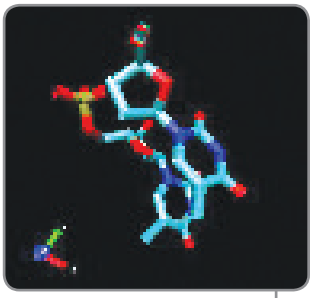

Demystifying UV light damage

By employing molecular dynamics simulations, an Ohio State University researcher is investigating how DNA is damaged by ultraviolet (UV) light.

The most typical type of damage created by UV light radiation is the cyclobutane pyrimidine dimer (CPD). CPDs interfere with normal cell processing of DNA, which can lead to mutations that cause diseases such as cancer. Recent studies have shown that it takes less than a picosecond, or one-trillionth of a second, for UV light to damage two specific adjacent bases of DNA, thymine-thymine, and create a CPD.

"Because we know the cell's DNA is dynamic, and motions such as helix bending or stacking and unstacking of bases occur relatively slowly, we suspected CPDs form only when the adjacent pyrimidine bases of DNA are favorably aligned for dimerization when excited by photons," said Yu Kay Law, a graduate research associate in biophysics at Ohio State. "Simulating the movements of DNA bases using supercomputers will clarify how CPDs are formed."

Law and his advisor, professor Bern Kohler, Ph.D., verified this hypothesis by using molecular dynamics simulations to model conformational changes of thymidylyl-thymidine in water and with various organic co-solvents, computing at each timestep the distance between the two C5=C6 double bonds and their improper torsion angle.

The two parameters were used to find the reactive conformations, which then were used to determine the structure of the dimer precursor. This structure, determined from molecular dynamics simulations, has many similarities with the structure of actual CPDs determined from experiments using nuclear magnetic resonance and X-ray crystallography. The simulations have revealed the motions that make DNA vulnerable to damage, and help to explain why CPDs are formed more readily at certain sequences.

"Conventional experimental means can't be used when investigating a reaction that occurs so quickly," Law said. "With access to OSC's P4 and Itanium clusters, we could simulate these computation-intensive reactions and conduct statistical sampling on a variety of structures."

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For more information:
www.chemistry.ohio-state.edu/~kohler/dna.html