

Institute for Materials Science, Chair of Materials Science and Nanotechnology

Electronic signatures of DNA with oxidative damage (8-oxoguanine)



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Motivation

8-Oxoguanine: most common form of oxidative DNA damage



How DNA repair enzymes recognize 8oxoG lesions within the entire genome?

Electronic differences \rightarrow damage recognition?



T. Z. Markus et al., J. Am. Chem. Soc. 131, 89 (2009); X. Gheng et al., J. Am. Chem. Soc. 127, 13906 (2005)



Methodologies: how to include dynamical effects?



- System: DNA+solvent+counterions
- Solvent and dynamical effects are included in MD trajectory



Methodologies





Methodologies





G:C sequence:

5'-TT G TTT G TTT G TT-3' 3'-AA C AAA C AAA C AA-5'

3 OG:C sequence:

5'-TTOGTTTOGTTTOGTT-3' 3'-AA C AAA C AAA C AA-5'



Average structure over 20 ns MD trajectory

Structural RMSd =1.25 Å G:C (cyan) vs 30G:C (red)

There is no major conformational changes due to the replacement of G:C by OG:C.







Base-localized MO energy level alignment depends on the site.

Overall coupling is slightly reduced when oxoG is placed in the sequence.











 $\langle T(E,t) \rangle_{AM}$ biases the mean to higher value.





 $\langle T(E,t) \rangle_{GM}$ dampens the effect of very high transmission as well as reduces the fluctuation.





Transport properties

Averaged transmission and current for two sequences

$$\left| T(E,t) \right\rangle_{\rm GM} = \exp\left(\frac{1}{N} \sum_{i=1}^{N} \ln(T(E,t_i))\right) \qquad I = \frac{2e}{h} \int dE\left(\left(f\left(E - E_F - \frac{eV}{2}\right) - f\left(E - E_F + \frac{eV}{2}\right) \right) \left\langle T(E,t) \right\rangle_{\rm GM} \right)$$



- Transmission is slightly reduced for the sequence with 8-oxoG.
- Current is reduced by a factor of 2~11 when oxoG is placed in the dsDNA sequence.





Transport properties

Averaged transmission and current ratio for different part of the sequence



- Suppression of transmission is observed for the sequence with 8-oxoG.
- Current is reduced by a factor of 2~4.



- Solvent and dynamical effects were fully taken into account in charge transport calculation of DNA via multi-scale modeling (classical MD, QM/MM electronic structure calculation, model Hamiltonian).
- When 8-oxoG is placed in the dsDNA sequence,
- Transmission is suppressed.
- Current is reduced by a factor of 2-11.

Thank you for your attention!



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M. H. Lee, G. Brancolini, R. Gutierrez, and G. Cuniberti, in preparation