

## TAUTOMERISATION OF THE A·T WATSON-CRICK BASE PAIR VIA THE DOUBLE PROTON TRANSFER AS A POSSIBLE SOURCE OF POINT MUTATIONS IN DNA: QM AND QTAIM PERSPECTIVES

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Combining theoretical investigations at the MP2 and DFT levels of QM theory with QTAIM analysis of the electron density, the tautomerisation of the A·T Watson-Crick base pair by the double proton transfer (DPT) was comprehensively studied *in vacuo* and in the continuum with a low dielectric constant ( $\epsilon=4$ ) corresponding to a hydrophobic interface of protein–nucleic acid interaction. Basing on the sweeps of the electron-topological, geometrical and energetic parameters, which describe the course of the tautomerisation along its intrinsic reaction coordinate (IRC), it was proved that the A·T→A\*·T\* tautomerisation through the DPT is a concerted (i.e., the pathway without an intermediate) and asynchronous (protons move with a time gap) process.

For the first time, the nine key points along the IRC of the A·T base pair tautomerisation, which could be considered as electron-topological "fingerprints" of the concerted asynchronous process of the DPT tautomerisation, have been identified and fully characterized. These key points are used to define the reactant, reaction and product regions of the DPT in the A·T base pair.

Considering the energy dependence of each of the three H-bonds, which stabilize Watson-Crick and Löwdin's base pairs, along the IRC of tautomerisation, it was found that these H-bonds are cooperative in the A·T base pair, reinforcing each other, and the C2H...O2 H-bond behaves anti-cooperatively in the A\*·T\* base pair, that is it weakens at the strengthening of the two others.

From a quantum mechanical point of view it was found that the A\*·T\* Löwdin's base pair is dynamically unstable and therefore the tautomerisation of the A·T Watson-Crick base pair *via* the DPT cannot be a source of spontaneous point errors in DNA replication.

Additionally, it was demonstrated using the conductor-like polarizable continuum model (CPCM) that the effects of biomolecular environment ( $\epsilon=4$ ) cannot ensure dynamic stabilization of the Löwdin's pair of DNA bases and does not affect qualitatively the course of the tautomerisation reaction.

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