STM STUDIES OF HYDROGEN-BONDED DNA BASE AGGREGATES

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Hydrogen bonding between DNA bases is one of the main interactions that control the conformation and hence the biochemical function of nucleic acid molecules [1]. The exact physico-chemical nature of these bonds, and the importance of charge transfer contribution to the stabilization energy associated to hydrogen bonding in NA molecules have recently been the subject of an intense debate [2-4], motivated by the discovery that a hydrogen bond formation is not necessary for the specificity in DNA replication [5]. Experiments to quantify the charge transfer associated with hydrogen bonding between nucleic acid bases are nevertheless difficult to design and interpret for systems consisting of DNA and RNA molecules in buffer solution.

Here we have combined STM experiments and DFT calculations to study the geometry and bonding of self-assembled hydrogen-bonded islands of the DNA bases guanine (G), cytosine (C), adenine (A) and binary mixtures of the complementary bases G and C and the non-complementary bases A and C, deposited under UHV conditions onto a Au(111) substrate by means of thermal evaporation.

Interestingly, G molecules self-assemble into a hydrogen-bonded network of G-quartets, whose structure corresponds perfectly with the quartet structure of telomeric DNA [6] determined by X-ray crystallography [7] (see Figure 1a). The interplay between STM experiments and DFT calculations shows that the strong preference of G molecules to form quartets can be explained by a cooperative effect that strengthens the hydrogen bonds within the G-quartet network over the hydrogen bonds in isolated dimers (see Figure 1b). The results constitute the first experimental evidence that cooperative charge transfer effects in the DNA base interaction are fundamental for the formation and stability of G-quartet structures.

We have also investigated the molecular recognition effects in 2D binary mixtures of complementary (G-C) and non-complementary (A-C) DNA bases. Molecular recognition events between complementary nucleic acid bases are fundamental for many biological processes, like DNA replication, and are currently being exploited for self-assembling DNA-based nanostructures. The DNA replication fidelity in living organisms is maintained by a complex molecular machinery of polymerases, exonucleases, etc. On the other hand, in the case of replicating NA molecules in the prebiotic soup, the basic physico-chemical mechanism to steer the replication process is the hydrogen bonding between DNA bases. The fidelity of this replication process implies that Watson-Crick pairing must be favored over others, like “wobble” or “deviant” pairing.

Our results show that after gentle annealing to 80°C, the non-complementary bases segregate into islands of pure A and a network of pure C, whereas the complementary bases G and C form a network that cannot be separated by annealing up to the desorption temperature for C (see Figure 2). High-resolution STM images allow us to identify the structures for the enhanced thermal stability as structures that contain G-C bond, possibly with the same structure as the Watson-Crick pairs in DNA molecules. We have thus demonstrated that the

hydrogen-bonding interaction alone can steer the molecular recognition process necessary for high-fidelity DNA replication even in the absence of polymerases, exonucleases, etc. The result could be relevant in order for us to understand the origin and nature of the first self-replicating molecules in the prebiotic soup.

References:

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Figures:

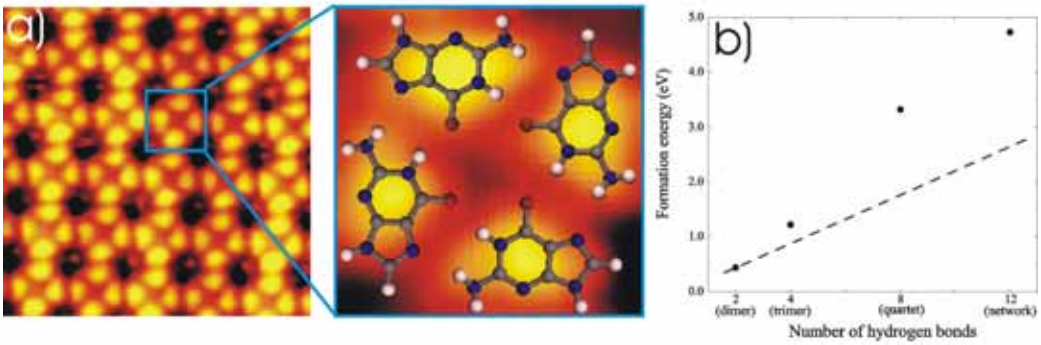

Fig. 1. a) STM image (8 × 8 nm2) of the self-assembled G molecules on Au(111), and a zoom-in image of the unit cell compared with the structure of the G-quartets. b) DFT-calculated formation energies as a function of the number of H-bonds.

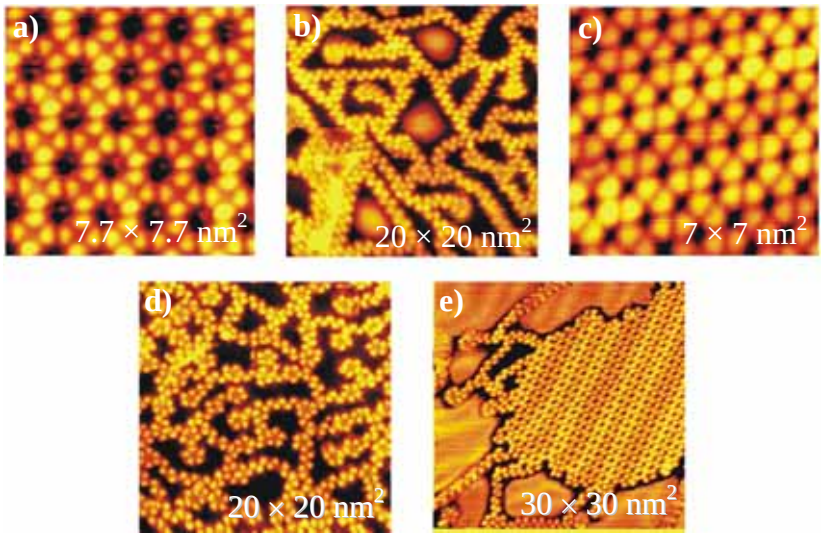

Fig 2. a), b) and c) display STM images of guanine (G), cytosine (C) and adenine (A), respectively. d) and e) show STM images of the binary mixtures G + C and A + C. Whereas the complementary bases for a network are more stable than those of the G and C molecules separately, the non-complementary bases segregate into regions of pure A and regions of pure C.