Abstract for MMSG Problem

Microscopic investigations of DNA molecular complexes: Understanding the impact of the substrate on complex morphology

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In-vivo, deoxyribonucleic acid (DNA) molecules rarely exist on their own, and are normally complexed with a range of molecules ranging from small inorganic molecules to large proteins. The formed complexes and molecular condensates are integral to many cellular processes including DNA replication and molecular compaction within the nucleosome. For this reason much recent attention has focussed upon microscopic techniques that are able to investigate the structure of such complexes. To this end our group has utilized the atomic force microscope (AFM) to investigate the morphology of a range DNA molecular complexes including complexes with small intercalating dye molecules, proteins and with polymers intended for gene therapy applications (see Figure 1).

Implicit to many of the microscopic techniques required to visualize these molecules is their deposition or immobilization onto a flat surface. The impact of the surface upon the morphology of the condensate however, remains poorly understood. The study group is thus asked to develop mathematical models to tackle the following problems:

(1) Do the structures of the molecules visualized on the surface reflect those in solution?
(2) For a given population of DNA molecular complexes (with a range of charges/charge densities) is there any preferential adsorption of a particular species on to a defined surface?

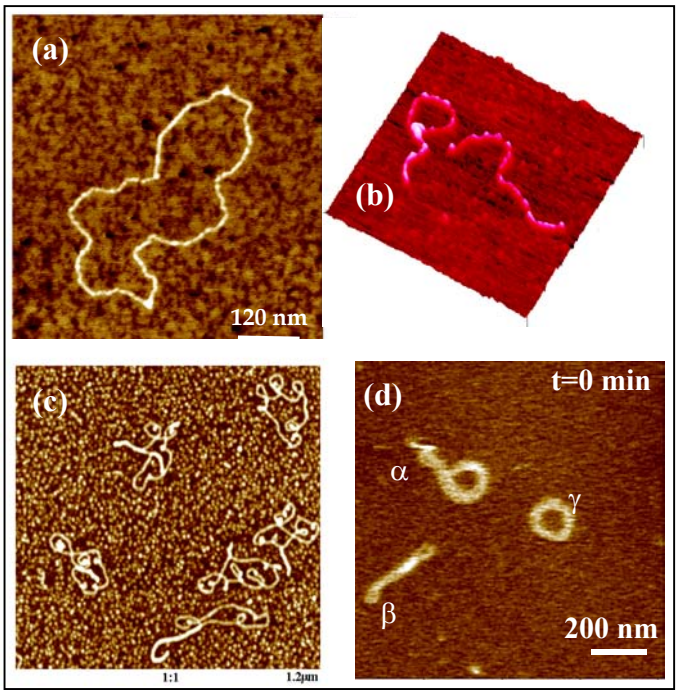

Figure 1 A selection of AFM images displaying (a) a single DNA plasmid molecule, (b) two plasmid-protein complexes, (c) a range of complexes formed between DNA and ethidium bromide (1:1 DNA:bp ratio) and (d) three different types of condensate formed between DNA plasmids and a cationic polymer