

## CARBOHYDRATE-CARBOHYDRATE INTERACTION PROMINENCE IN 3D SUPRAMOLECULAR SELF-ASSEMBLY

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Self-association in water of biologically significant carbohydrate molecules is a controversial topic due to the strong solvation of these molecules in this solvent and the difficulty to experimentally detect these very weak intermolecular forces by biophysical techniques. Carbohydrate-carbohydrate interactions are implied in biological phenomena as important as the cellular adhesion or the morula compacting.<sup>1,2</sup> Interaction between carbohydrates in water is usually considered to be non-stabilizing due to the strong solvation of these molecules by the excess of water. Recently it has been demonstrated that the interaction between multiple carbohydrate molecules is specific and stabilizing<sup>3</sup>, however, these molecules were chemisorbed on gold surfaces. Herein we report the tremendous ability of amphiphilic carbohydrate molecules to form complex three-dimensional architectures which are based only on weak interactions<sup>4</sup>. We have experimentally observed the 3D self-assembly into multilayers of disaccharide neoglycolipid dimers on graphite by means of non-contact AFM. Such long-range associations between amphiphilic carbohydrates in water have never been observed before. We have also theoretically modeled the interaction between two dimers in order to learn about the structure and composition of these layers. A simple bilayer structure as observed for many amphiphilic lipids was discarded by the experiments. Instead, based on the good agreement between experiments and calculations, we propose that multilayer formation takes place through the assembly of building blocks consisting of two dimers each. We propose that, in addition to hydrophobic effects and van der Waals interactions between alkyl chains, carbohydrate-carbohydrate interactions are a fundamental key in the organization of this supramolecular structure. Moreover, the results indicate that H-bonding does not play an important role in this carbohydrate-carbohydrate interaction, as it is commonly stated.

### References:

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### Figures:

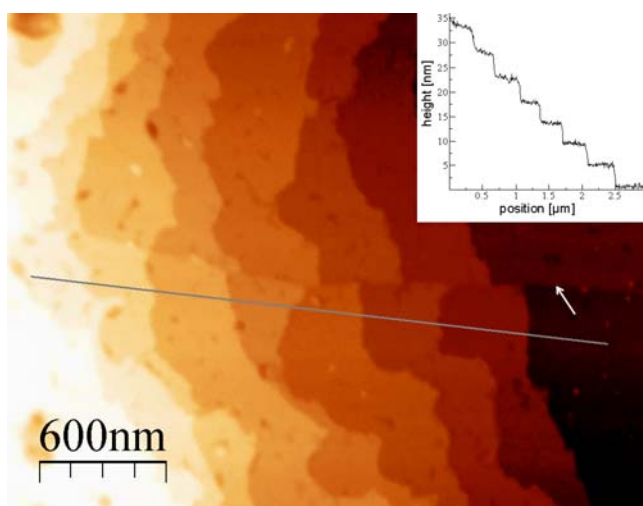
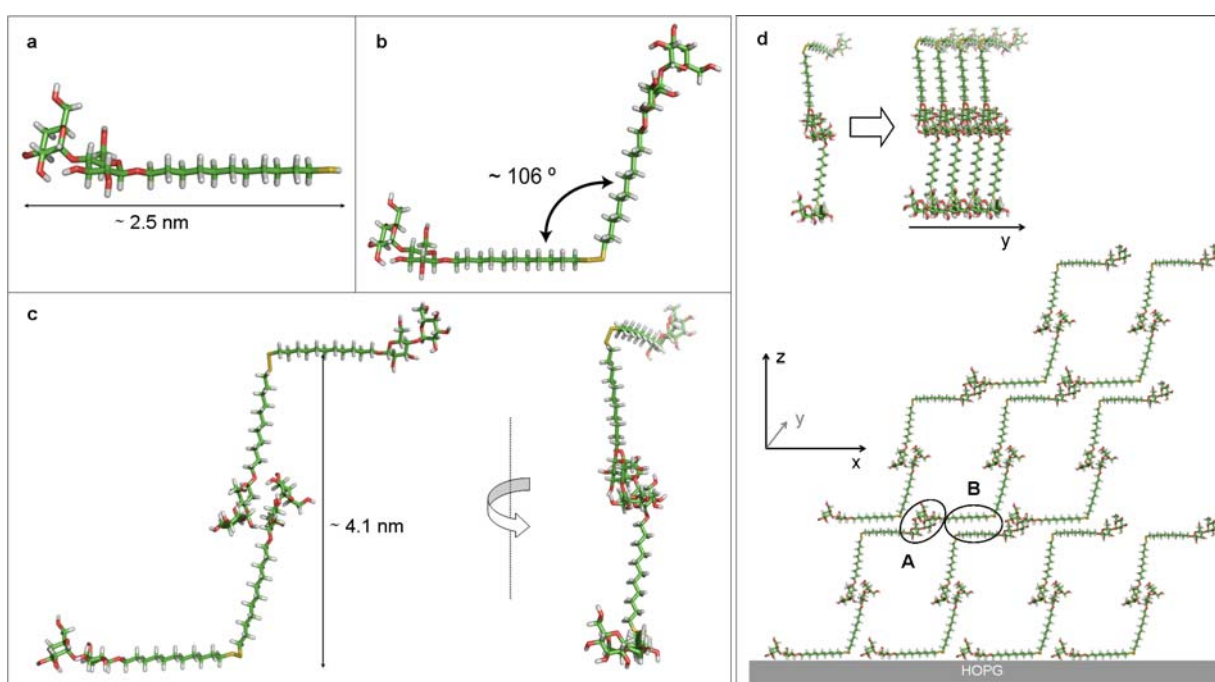


Fig. 1.  $(\text{maltoC}_{11}\text{S-})_2$  molecules self-assembled into multilayers on graphite (HOPG) imaged by non-contact AFM. A graphite terrace (indicated by the arrow) can be seen crossing the image from side to side under at least nine layers of maltose disulfide molecules formed from the  $(\text{maltoC}_{11}\text{S-})_2$  solution. In the inset, a profile drawn just below the graphite terrace (grey line) shows the uniform height of the multilayers ( $\sim 4.2\text{nm}$ ).



(a-c): Conformations calculated for (a) the maltose neoglycolipid and (b) the corresponding dimer  $(\text{maltoC}_{11}\text{S-})_2$  (1). (c) Repetitive unit (“building block”) obtained by theoretical calculations showing the interactions between two neoglycolipid dimers. In this minimum energy configuration, intermolecular interactions take place between the two disaccharide units leading to a bottom-to-top distance of 4.1 nm. (d): Cartoon of the proposed model for the multilayer formation of 1 on graphite. In  $y$ -direction, pairs of dimers as shown in (c) align in a parallel fashion. A suggested assembly in the  $x$ - $z$ -plane is shown in the lower part of (d). Hydrophobic forces between the alkyl spacers and further carbohydrate interactions between the maltose units are thought to be responsible of self-assembling in all three directions. Together, they could provide the cohesion necessary both in  $x$ -direction and between layers (vertically) through the interactions at A and B.