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CHALLENGES OF THE NEW SENSORS: NUCLEOBASES CONTAINING MATERIALS

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Abstract. The miniaturizing is an important request nowadays. Sophisticated nano-structures are obtained by top-down or bottom-up approach, growing the number of application in various domains like biology, medicine, environmental, information technologie. Due to the simplicity and multiple H-bonding, the nucleobases are very suitable molecules for programmed self-assembled structures. Synthetic chemists encouraged by the vast potential of nucleobases application are in continuum search to apply the recognitive function of these complementary pairs in various domains like self-healing, medical diagnosis, sensors, drug delivery, information storage, purification etc.

This review highlights some important recent developments of the nucleobases applications.

Keywords: nucleobases; supramolecular; nanostructures; self-assembling.

1. Introduction

In life organism, simple molecules such as sugars, nucleobases, amino acids have an amazing capacity to assemble, creating impeccable and sophisticated structures at various scales. Hydrogen bonds play an important

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role in many systems, natural or not. The DNA molecule consists of two polynucleotide chains linked by the hydrogen bonds between complementary nucleobases. These non-covalent bonds are the key factors in the protein folding process and also in the stability of these three-dimensional structures. “Cage” molecular systems, liquid crystal, supramolecular catalysts are obtained based on the hydrogen bonds (Sengupta *et al.*, 2007; Davis and Spada, 2007; Meeuwissen and Reek, 2010).

In order to understand, reproduce or predict the biomolecular interactions, the nucleobases were the best choice by their simplicity. The adenine (A), guanine (G), cytosine (C), thymine (T) and uracil (U) are the five natural nucleobases involved in the self-assembly of biopolymers DNA and RNA. Complex multifunctional 2D and 3D nanostructures were constructed by H bonds in classical Watson–Crick pairing, Wobble motif, Hoogsteen interactions and reverse Hoogsteen patterns (Ciesielski *et al.*, 2016). Accordingly, in supramolecular chemistry many synthetic systems are based on nucleobases in order to mimic the behavior of natural compounds. The interest for the “intelligent systems” is growing hence the conclusion that it is possible to control the properties by a right manipulation of the external stimuli.

The first research in the domain of nucleobases was made by Albrecht Kossel who identifies and isolates the nucleobases, in 1880s (McHale and O’Reilly, 2012).

The molecular recognition is defined like a specific interaction between two molecules, without covalent bonds. Dynamic interactions with 10-40 kJ/mol enthalpies occur in complementary nucleobases functionalized systems like the Watson - Crick Model. In some cases, the nucleobases are losing from the specificity of interaction, forming G-A, T-A-T, U-A-U, U-A-A, C-G-G bonds or dimmers (Park *et al.*, 2008).

2. Nucleobases Containing Materials

Self-assembling process is the product of the balance between noncovalent interactions and solvent effects. The presence of large hydrophobic surface aided this process.

Based on self-assembling process, layers which can act as devices for diagnostic sensors and imaging systems were synthesized. Miyata and his group (Miyata *et al.*, 2012) have obtained, by a simple method, a thin uracil-terminated organosilane film (Fig. 1 up). This substrate can recognize the adenine into a solution and connect these by complementary hydrogen bonding (Fig. 1 down).

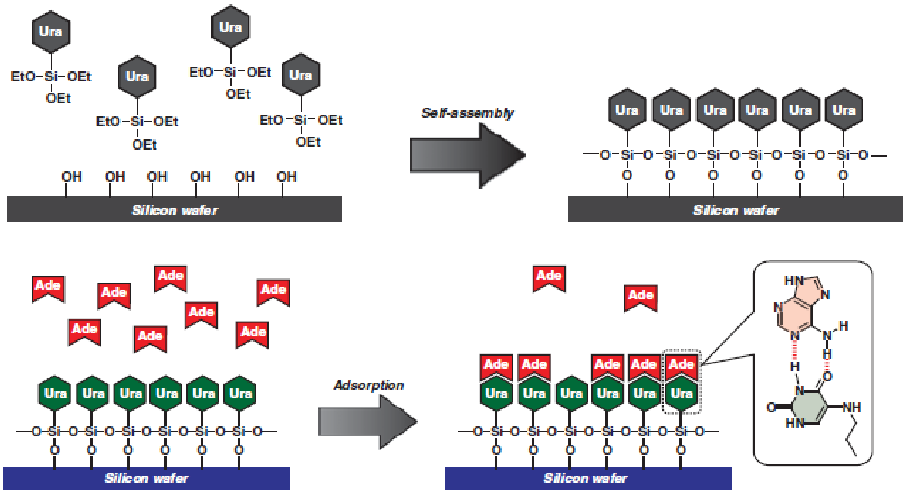
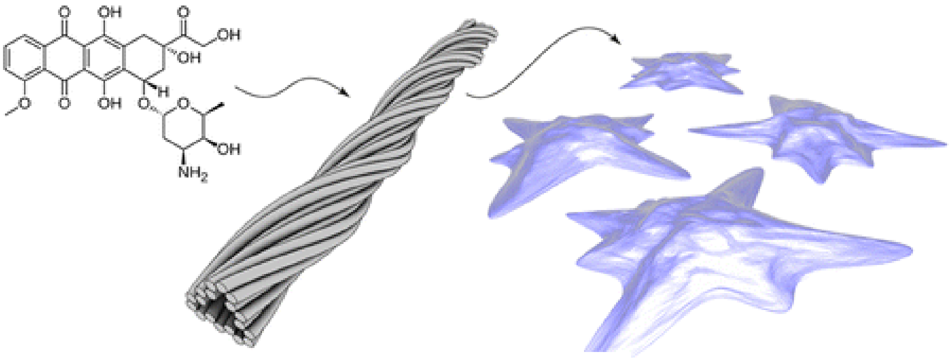


Fig. 1 − Self-assembly of uracil functionalized triethoxyosilane onto a silicone substrate (up), schematic representation of adsorption of adenine onto uracil layer (down) (Miyata *et al.*, 2012).

It was demonstrated that DNA-based sensors are great device to detect biomarkers (Zhang *et al.*, 2016). Acetone and ethanol are breath biomarkers for diabetes. Acetone must be less than a few hundred ppb (by volume) in the breath of a healthy person, while for diabetic patients, acetone concentration can reach 560 - 1000 ppm. High H_2S concentration can indicate cardiovascular diseases or chronic pancreatitis. HCl is a toxic gas at 50 ppm concentration. By molecular theoretical simulation and proven experimental work, the great affinity of nucleobases for the biomarker sampled before is as follows: adenine for acetone, thymine for ethanol, guanine for H_2S, and cytosine for HCl. So, DNA optimized sequence can be expected to have an important aspect in sensor domain of biological processes.

Nanomaterials have a great potential to be used in medicine in drug delivery. Based on DNA origami, Zhao *et al.* (2012) have prepared monodisperse DNA nanofilaments. These materials are loaded with anthracycline doxorubicin (Dox) by intercalation between nucleobases in order to deliver the drug in human breast cancer cells and promote apoptosis (Fig. 2). The authors have tested two DNA nanostructures with different degrees of twist on three different breast cancer lines (MDA-MB-231, MDA-MB-468, and MCF-7). The designed structures are an excellent delivery system for drugs comparing the intracellular elimination rate to free Dox, which is lower, for increased induction of programmed cell death in breast cancer cells. Therefore, the specificity of Watson-Crick base pairing used in assembling of DNA nanostructures is a powerful tool to control matter at small scale.



DNA filaments

Fig. 2 − DNA origami for drug (Dox) delivery to cancer cell (Zhao *et al*., 2012).

The supramolecular polymers containing guanine are used in electronic field due to low oxidation potential.

The special electronic, optical and thermal properties of graphene have been fructified in bio-device by functionalization with nucleobases, DNA or protein. By theoretical studies a scale of order to binding of nucleobases with graphene: G>A>T>C>U was developed (Mudedla *et al*., 2016). The interaction energy is growing when the graphene is doping with atoms like B, N, P, Si or metals. Also the presence of defects in Si - doped graphene improves adsorption strength of nucleobases on the surface. Proven evidence by DFT theoretical analysis shows that the stability of complexes is induced by the partial electrostatic and covalent interactions between lone pair of oxygen or nitrogen from nucleobases and unoccupied orbital of silicone included in graphene. The strength of the interaction is also due to π- π stacking. In consequence, these complexes are favorable to develop new sensor devices.

3. Conclusions

In summary, nucleobases have a large application in various domains. Immediate advantages of the use of nucleobases are their biocompatibility and non-toxicity in life organisms. The recognition by multiple noncovalent interactions between nucleobases is successfully used in inorganic systems.

Monitoring of medical parameters, analysis/identification of nucleic acids (using aldehyde-modified natural nucleobases (Pernagallo *et al*., 2012)), electrochemical bioanalysis(using modified nucleobases as redox probes (Hocek *et al*., 2011)), industrial and safety and security related detection (Xing *et al*., 2014; Wang *et al*., 2013; Tanaka and Taira, 2005) are possible due to nucleobases binding specificity.

REFERENCES

Ciesielski A., El Garah M., Masiero S., Samorì P., *Self-Assembly of Natural and Unnatural Nucleobases at Surfaces and Interfaces*, Small, **12**, *1*, 83-95, doi: 10.1002/smll.201501017 (2016).

Davis J.T., Spada G.P., *Supramolecular Architectures Generated by Self-Assembly of Guanosine Derivatives*, Chem. Soc. Rev, **36**, *2*, 296-313, doi: 10.1039/B600282J (2007).

Hocek M., Fojta M., *ChemInform Abstract: Nucleobase Modification as Redox DNA Labeling for Electrochemical Detection*, Chem. Soc. Rev, **40**, *12*, 5802-5814, doi: 10.1039/c1cs15049a (2011).

McHale R., O'Reilly R.K., *Nucleobase Containing Synthetic Polymers: Advancing Biomimicry via Controlled Synthesis and Self-Assembly*, Macromolecules, **45**, *19*, 7665-7675, doi: 10.1021/ma300895u (2012).

Meeuwissen J., Reek J.N.H., *Supramolecular Catalysis Beyond Enzyme Mimics*, Nature Chemistry, **2**, *8*, 615-621, doi: 10.1038/nchem.744 (2010).

Miyata T., Kawamura A., Meotoiwa T., Matsumoto M., Uragami T., *Synthesis of Novel Nucleobase-Terminated Organosilane and its Self-Assembly on a Substrate*, Polymer Journal, **44**, 625-631, doi:10.1038/pj.2012.41 (2012).

Mudedla S.K., Balamurugan K., Kamaraj M., Subramanian V., *Interaction of Nucleobases with Silicon Doped and Defective Silicon Doped Graphene and Optical Properties*, Phys. Chem. Chem. Phys., **18**, 295-309, doi: 10.1039/C5CP06059A (2016).

Park S.J., Yamaguchi K., Hong J., *Supramolecular Capsule Based on Complementary Adenine-Thymine Base Pairing*, Bull. Korean Chem. Soc., **29**, *1*, 205-207, doi: 10.5012/bkcs.2008.29.1.205 (2008).

Pernagallo S., Ventimiglia G., Cavalluzzo C., Alessi E., Ilyine H., Bradley M., Diaz-Mochon J.J., *Novel Biochip Platform for Nucleic Acid Analysis*, Sensors, **12**, *6*, 8100-8111, doi:10.3390/s120608100 (2012).

Sengupta J., Mukhopadhayay R., Bhattacharjya A., *Bis- and Trisuracil Nucleosides with Nucleobases Anchored to 11-, 12-, and 16-Membered Macrocyclic Scaffolds: Synthesis and Aggregation Study*, J. Org. Chem., **72**, *13*, 4621-4625, doi: 10.1021/jo062554b (2007).

Tanaka Y., Taira K., *Detection of RNA nucleobase metalation by NMR spectroscopy*, Chem. Commun., **16**, 2069-2679, doi: 10.1039/B415137M (2005).

Wang F., Liu B., Huang P-J J, Liu J, *Rationally Designed Nucleobase and Nucleotide Coordinated Nanoparticles for Selective DNA Adsorption and Detection*, Anal. Chem., **85**, *24*, 12144-12151, doi: 10.1021/ac4033627 (2013).

Xing C., Yuan H., Xu S., An H., Niu R., Zhan Y., *Nucleobase-Functionalized Conjugated Polymer for Detection of Copper(II)*, ACS Appl. Mater. Interfaces, **6**, *12*, 9601-9607, doi: 10.1021/am502978w (2014).

Zhang W., Wang M. L., Cranford S. W., *Ranking of Molecular Biomarker Interaction with Targeted DNA Nucleobases via Full Atomistic Molecular Dynamics*, Scientific Reports, **6**, 18659 doi: 10.1038/srep18659 (2016).

Zhao Y.-X., Shaw A., Zeng X., Benson E., Nyström A. M., Högberg B., *DNA Origami Delivery System for Cancer Therapy with Tunable Release Properties*, ACS Nano, **6**, *10*, 8684–8691, doi: 10.1021/nn3022662 (2012).

PROVOCĂRILE NOILOR SENZORI: MATERIALE CARE CONŢIN NUCLEOBAZE

(Rezumat)

Miniaturizarea este o cerinţă importantă în zilele noastre. Nanostructuri sofisticate sunt obținute prin tehnici top-down sau bottom-up, mărindu-se astfel numărul de aplicații în diverse domenii precum biologie, medicină, mediu, tehnologia informației. Datorită simplității şi a multiplelor legături de hidrogen pe care le formează, nucleobazele sunt molecule potrivite pentru structurile auto-asamblate programate. Chimiștii sinteticieni, încurajați de vastul potențial de aplicații al nucleobazelor, sunt într-o continuă căutare de a aplica funcția de recunoaștere a acestor perechi complementare în diferite domenii precum cel de auto-vindecare, diagnostic medical, al senzorilor, eliberarea de medicamente, stocarea informației, purificarea etc.

Acest review evidențiază câteva din importantele progrese recente ale aplicațiilor nucleobazelor.