

SEARCH OF SENSITIZER TO PEPTIDE NUCLEIC ACID SEQUENCE WITH ADENINE AND GUANINE BASES

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Abstract

Quantum mechanical investigations were performed to find a suitable sensitizer to peptide nucleic acid (PNA) monomer with Adenine and Guanine basis. It was shown that interaction of the orbitals of the isolated PNA sequence with Adenine-Guanine and isolated sensitizer should be present. It was found that the 3-(N,N-dimethyl)-6-(N'-acetilaminiel-N'-methyl) acridindiamine molecule could be used as a sensitizer.

Keywords: peptide nucleic acids (PNA), sensitizer, charge transfer, self-replicating.

1. Introduction

Recently, Rassmussen et al. designed a proto-organism inspired by the original concepts for a proto-cell by Luisi and coworkers. This model was different from the other ones because the authors did not start with a self-replicating container or a self-replicating gene, which was later combined and, the most important, instead of RNA peptide nucleic acids (PNA) were applied [1,2].

The PNA molecule may much easier to couple with the lipid layer than RNA due to its hydrophobic backbone and which is also easier to synthesize. On the other hand, the replication of the lipid aggregate is determined by the PNA, and it is capable of using PNA as a genomic code to guide the replication of surfactant assemblies.

The three functional structures (container, metabolism, and genes) are thermodynamically coupled in the proto-organism. The functionalities of the proposed proto-organism (to evolve, to self-reproduce, to metabolize, to be adaptive in response to environmental changes, and ability to die) are generated as the different components of this assemble. In this proto-organism each of the functionalities successively as they are generated (by the assembly of more subsystems), under the conditions that each earlier functionality is a prerequisite of the next following functionality. It implies, that proto-container is used before a redox driven proto-metabolism, and further the proto-genes require the proto-metabolism to exist. This proposed photo-driven metabolism requires a particular electron relay chain to function properly, and this electron relay is implemented within the templating polymers.

In the above-mentioned proto-organism, the synthesis of a 1,4-bis(N,N-dimethylamino)naphthalene sensitizer attached to PNA monomer took place. It is done to increase the quantum efficiency because the sensitizer coupled with an electron relay system. In this case the sensitizer could be introduced to block back the electron transfer process, and thus the increase the

quantum yield of surfactant production. The energized sensitizer causes a charge separation between the sensitizer and lipid precursor. The neutralization of the sensitizer by the delivery of an electron from the PNA electron relay chain is occurred. The precursor lipid molecule is energized and will eventually break into a lipid (carboxyl acid) and a phenyl group. However, since no adenine-sensitizer-guanine complex is available the replication process will start with the formation of functional PNA dimer consisting of both the thymine-sensitizer-cytosine and adenine-guanine complexes. So, when the sensitizer to PNA sequence with adenine and guanine (AG) bases is found, the process of the self-replication would be simplified (not necessary the above dimer formation) and it will speed up the sensitization process for the photo fragmentation reaction and as a consequence the quantum yield of surfactant production increased.

Thus, the question arises how and which sensitizer is better to be attached to PNA oligomer with adenine - guanine bases so that quantum efficiency should be as high as possible and how to simplify the appropriate sensitizer search.

It was assumed that the selection of the sensitizers could be performed basing on the relative position of the eigenvalues of the isolated sensitizer and lipid molecules. The orbital interaction strongly influences the quantum efficiency of proto-metabolic process proposed by Rassmussen et al. as in the case of sensitizer search to the PNA sequence with cytosine and thymine [3-8]. It implies, that the HOMO of a sensitizer molecule must be higher than that of lipid and the same for the LUMO placement of this molecules. However these conditions are not enough when the sensitizer is searched to the PNA sequence with A and G. Without going into details, we may state that the interaction (coupling) of sensitizer orbital with one of the PNA sequence with adenine and guanine is important in this case. The obtained performances are in agreement with these predictions.

2. Computational methodology

The quantum chemical ab initio Hartree-Fock (HF) and density functional theory (DFT) investigations were applied with the geometry optimization to gain structural information on the investigated compounds [8-14]. Geometrical and electronic structures of the single photo-donor molecules substituted by a specific group to provide an attachment of the molecule to a PNA fragment with the AG bases to propose as a suitable sensitizer and a lipid molecule were investigated applying B3LYP exchange-correlation functional with 6-311G** basis set [15, 16] (Fig. 1).

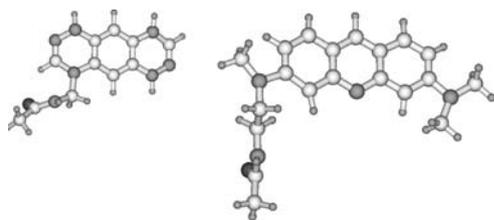


Fig. 1 The view of the molecules under investigations substituted by bridge fragment. On the left, the views of the 8-acetylaminomethyl-1,4,5,8-tetrahydro-1,2,4,5,6,8-hexaazaanthracene (called as **I**) and on the right 3-(N,N-dimethyl)-6-(N'-acetylaminel-N'-methyl)akridindiamine molecule (**II**).

As it was mentioned above, there was assumed, that selection of the sensitizer could be based on the investigation of the relative positions of eigenvalues and their interaction. Firstly, we try to find the explanation why the 1,4-bis(N,N-dimethylamino)naphthalene molecule selected as sensitizer for the PNA sequence with thymine-cytosine (TC) bases is not suitable in the case of adenine-guanine one. The study of the relative positions of the eigenvalues indicates the interaction LUMO+1 of the lipid molecule and the LUMO of the PNA sequence with A and G. (Fig. 2). Due to the interactions, these orbitals split and mix in the compound consisting of the lipid molecule and the PNA sequence with AG. Therefore the LUMO of the above compound could be originated from the orbitals of the lipid and PNA sequence with AG and it could be the reason the absence of charge transfer from the PNA sequence to lipid despite the necessities for self-replication processes proposed by Rassmunsen et al. Due to it the quantum efficiency of proto-metabolic process would be very low. Thus, it was assumed that the above orbital interaction should be avoided. Following the line of thought it is predicted that the sensitizer for the PNA sequence with A and G bases should be chosen in accordance with these criteria:

- 1) the HOMO of a sensitizer molecule must be higher than that of lipid one;
- 2) the LUMO of the lipid would be lower than that of the PNA sequence with AG and sensitizer;
- 3) the orbitals of the PNA sequence with A and G should (or lipid) interact with the orbitals of sensitizer.

Without going into the theoretical and formal details here the essence of the third step is very important because due to the above orbital interaction these orbitals split and mix in the compound consisting of the sensitizer attached to the PNA sequence with AG. It leads to avoiding of the orbital interaction of lipid and the PNA sequence. Therefore it is more probable that in the PNA with A-sensitizer-G and lipid the HOMO will be mostly originated from atomic orbital of PNA sequence while the LUMO one will be generally depicted from the atomic orbital of the lipid. Hence, it is possible to predict that the self-replication processes proposed by Rassmunsen et al. will occur.

To place the sign problem in a better perspective we

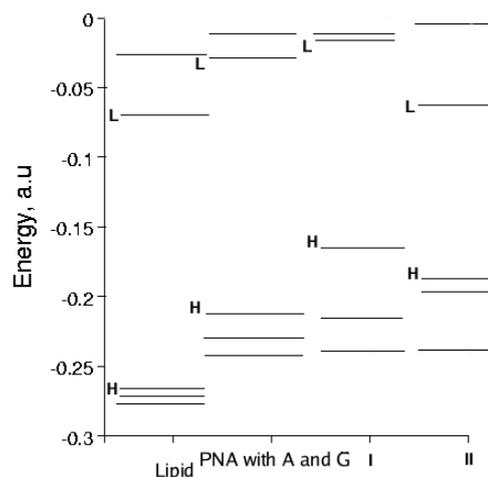


Fig. 2. The placement of the molecular orbitals of the lipid, PNA sequence and the molecules that are under investigations. The HOMO (**H**) and LUMO (**L**) of the investigated derivatives are marked.

investigated two molecules 8-acetylaminomethyl-1,4,5,8-tetrahydro-1,2,4,5,6,8-hexaazaanthracene and 3-(N,N-dimethyl)-6-(N'-acetylaminel-N'-methyl)akridindiamine that in our notation are called **I** and **II** to simplify discussion (Fig.1). The molecules are chosen not-accidentally because the investigated molecule orbitals interact differently with orbital of PNA sequence. It is necessary to mention that orbitals of the **I** molecule interact with the orbitals of the PNA sequence in the resonance manner of the lipid one, while LUMO of **II** molecule interact slightly with LUMO of lipid (Fig.2). It is noted, that the placement of LUMO and HOMO of the selected sensitizers with respect to of lipid of those is satisfied, i.e. the HOMO and LUMO of sensitizer are higher than that of lipid respectively.

In order to obtain more results to confirm our assumptions the above-mentioned molecules were joined to PNA fragment with a adenine and guanine bases (Fig.3)

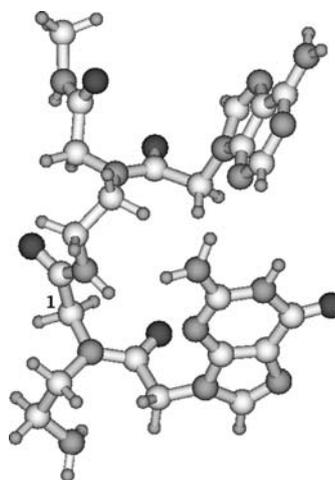


Fig. 3. The view of the PNA sequence with Adenine and Guanine bases. The number marks the position where sensitizer could connect to this sequence.

To obtain the geometrical structure of the molecule as sensitizer (S) attached to the PNA with A and G bases, the HF method with 6-31G basis set was applied. The sensitizer molecule was attached to the PNA sequence in the position that was obtained in the case of PNA sequence with Thymine and Cytosine. In this case the sensitizer is attached near Guanine (Figs. 3, 4) [17-20]. The geometry optimization was performed by HF/6-31G. In order to obtain more accurate results more elaborate ab initio treatment such as DFT, MP2 and the similar are required, but this requires too much computation resources for such large molecules with C1 molecular symmetry. On the other hand, our investigation of the PNA sequence with cytosine base and lipid molecule indicates, that the geometry of such kind compounds obtained by DFT and HF approach coincide enough well and most important, obtained performances are in agreement with an experiment [8]. Additionally, it is shown that HF calculations agree well with the experimental bond lengths and very well with angles [21]. Hence, the HF approach is used to avoid too large computational time and memory resources. The nature of molecular orbitals and transitions will be evaluated applying GUGA/6-31G method. It is remarkable, that in this paper we presented only the successful cases of our investigated sensitizers excluding others which were worse from the quantum mechanical point of view.

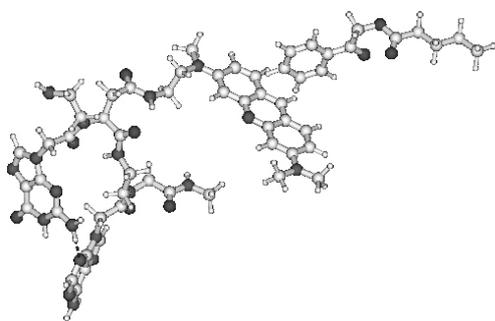


Fig. 4. The view of structures of the investigated compound consist of the lipid and the PNA sequence with A and G basis substituted by **II** molecule to exhibit where the sensitizer is connected more properly. The views of the investigated compound are possible to see in Fig.5 and 6 also.

3. Obtained performance

The primary purpose of these investigations to find the sensitizer to PNA sequence with Adenine and Guanine because of potential application in the self-replication processes. In an effort to shed light on the subject, the investigation of the compounds consisting of lipid precursor molecule and the PNA sequence with AG and sensitizer is performed. The above mentioned compounds with a lipid precursor are investigated to guide the excited charge transfer. Several aspects of this purpose deserve special comment following from our investigation described in [8]: 1) during photo-excitation the charge redistribution in the PNA fragment should take place and then the charge is slowly transferred to lipid, and 2) later it is transferred to sensitizer due to rotation and vibrations. It is more

appropriate to say, that the HOMO-LUMO transition should be forbidden and correspond to transition from sensitizer to lipid.

Guided by analogy, one might guess that the **II** investigated molecule is not suitable sensitizer. The conclusion is based on the investigation of the HOMO and LUMO nature of the compound consisting of lipid and the PNA sequence with A and G bases substituted by sensitizer (see Fig. 5).

In our described case the HOMO and LUMO of the above compounds consist of the π orbitals of sensitizer mostly (Fig. 5). Hence, it is more appropriate to say that allowed transition should be obtained from HOMO to LUMO that leads to charge redistribution only, i.e. the charge transfer to lipid due to vibration and rotation absent.

We would like to point out that the described situation is not conventional for self-replication process although not fully conclusive because the other phenomenon is omitted in this work, but it could influence to this process also. Let us remember, that in this case the both sensitizer and lipid LUMO interact. Consequently, the choosing sensitizer is not correct if one makes the assumption that the lipid and sensitizer orbitals should interact.

Completely different situation arise in the case of the **I** molecule. Let us remember that orbital of this molecule interact with one of the PNA sequence with AG. In this case the HOMO of the compound (lipid, the PNA sequence with A and G bases joined with **I**) is described by the atomic orbital of the sensitizer atoms while the LUMO one consist of the atomic orbital of certain atom of the lipid (Fig. 6).

The nature of HOMO-LUMO orbitals and their placement allow us to foresee that the HOMO-LUMO transition should be forbidden and correspond to transition from sensitizer to lipid. Roughly speaking, we have situation that is necessary for the described self-replication processes. Although not fully described the charge transfer in the compound the comparing performances of the investigations of the PNA sequence with cytosine and thymine bases and the PNA sequence with guanine and adenine bases conclude that

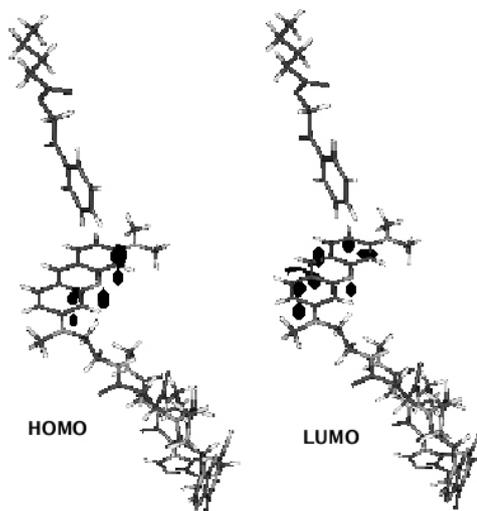


Fig. 5. Molecular orbitals of the compound consist of the lipid and the PNA sequence with A and G basis substituted by **II** molecule.

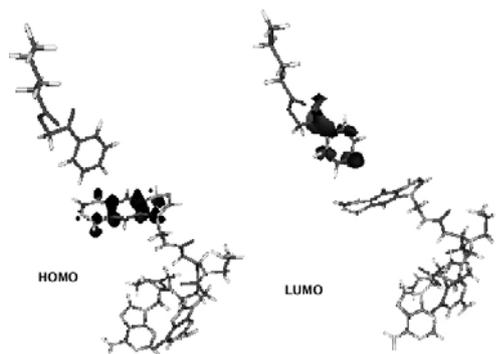


Fig. 6. Molecular orbitals of the compound consist of the lipid and the PNA sequence with A and G basis substituted by I molecule. In this case the molecule is joined to the PNA sequence with A and G near Adenine basis.

the I molecule could be applied as sensitizer. The sensitizer coupled with an electron relay system and could be introduced to block back the electron transfer process. Hence, - the quantum yield of surfactant production will be increased. On the other hand our prediction that the sensitizer to the PNA sequence with A and G basis should be chosen so that these molecule orbitals interact is confirmed also.

4. Conclusions

Basing on the investigation results it is evident that the account of the relative positions of single molecule orbital and their interaction help us in the selection of the sensitizer for the PNA sequence with A and G bases. The comparison investigation performances of the PNA sequences with both AG and TC basis allow us to conclude that I molecule (8-acetylaminomethyl-1,4,5,8-tetrahydro-1,2,4,5,6,8-hexaazaanthracene) could be applied as sensitizer to this sequence with A and G basis. So the self replication process is simplified. The choosing of the sensitizer joined to the PNA sequence with Adenine and Guanine bases should be performed in accordance with these criteria:

- 1) the HOMO of a sensitizer molecule must be higher than that of lipid one;
- 2) the LUMO of the lipid would be lower than that of the PNA sequence with AG and sensitizer;
- 3) the orbital of the PNA sequence with A and G (interacting with that of lipid) should also interact with orbitals of sensitizer.

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