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Proteins as data storage devices: insights from computer models

Miguel Ortiz-Lombardía[1] and Chandra S Verma[2]

[1]Centro de Investigaciones Oncologias, C/Melchor Fernandez Almagro,3 28029 Madrid, Spain; [2]Bioinformatics Institute, 30 Biopolis Way, #07-01 Matrix, Singapore 138679

chandra@bii.a-star.edu.sg

Abstract. The ability to use charge transporting proteins such as bacteriorhodopsin in the building of data storage and transmission devices for use in computer technology is explored. Designs of mutants that lead to proteins that are more stable thermally and more efficient at data processing requires knowledge of the elctrostatics/dynamics of the molecules. We find that both the motions and the electrostatics are strongly effected when the influence of neighbouring molecules in the assembly are included, underscoring the importance of inclusion of the assemblies explicitly in computer models.

1. Introduction

Biological macromolecules, in particular proteins, carry out a vast number of different functions with dexterity whose molecular basis still eludes a completely comprehensive analysis. However, much progress has been made in the understanding of several properties of proteins. This has spurred their extensive use in the field of biotechnology, from therapeutics to bio-sensors [1]. One particular property of proteins is their ability to store and transport charges both within a protein and between proteins [2]. This forms the basis of several elementary and essential processes such as vision, respiration, general oxidation-reduction, all of which are indispensable for life. Each such process is very finely tuned and is coupled with a well defined change in the shape of a protein. It is these two properties – the ability to store/transfer charge and the accompanying change of shape that enable the use of proteins in the design of computer devices such as memories. The transfer of charge is done extremely rapidly as it has been fine tuned by evolution over millions of years. The changes in shape can be rapid but the shapes themselves can be retained for predefined periods. In recent times this has lead to the development of prototype computational devices including processing units and three dimensional memories.

The origin of this field lies in the discovery of a protein called bacteriorhodopsin (bR) which is found in bacteria that grow in salt marshes with temperatures exceeding 65° C. The protein is extremely stable to degradation, both thermally and photochemically. It uses light energy to transport charges thereby converting energy from light to chemical forms. In addition it self assembles into thin films. Together these properties make them ideal as devices that have the potential of being used as data storage devices [3]. Additionally, current advances in molecular biology imply that these proteins can be easily mass produced. The protein bR has a component (in magenta in Figure 1 below) called

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the chromophore. This molecule is the main driver of activity which is carried out through the absorption of light and the concomitant triggering of a photocycle consisting of a series of structural and chemical changes. These structural or conformational changes can be stabilized, thereby leading to the assignment of the binary code to any two long-lasting states or indeed to the assignment of some new ternary code to three such conformational states. The transition between stable states can be controlled by lasers of appropriate wavelengths; in particular the two-photon method of reading/writing data is found be the most efficient [4]. To get an idea of the conformational changes that take place please see (http://molmovdb.org/cgi-bin/morph.cgi?ID=453208-16084) or (http://www.bii.a-star.edu/~chandra/JPhys/bR.mpg) both of which show the structural changes that take place in a molecule of bR. This has formed the basis for the building of the prototype devices. While the earlier devices could only operate at very low temperatures, subsequent design strategies enable their functions at room temperatures. The next stage saw the exploitation of the three dimensional plasticity of proteins and their coupling into cubic matrices in polymer gels for building of high-density, high-speed, truly three-dimensional memories [5]. This increased the storage limit from ~10^8 bits/cm^2 in two dimensions to 10^{11}-10^{13} bits/cm^2. While the working prototypes only store information of ~18Gbytes, the theoretical limit of storage is as high as 512 Gbytes and all of it in a volume of just 5cm^3.

The properties of bR-like molecules that enable them to be used for computational devices can be summarized as: long-term thermal and chemical stability; high quantum yields; accurate and reproducible states; ability to generate thin films; ability to construct efficient 3-dimensional assemblies [3]. Of course since it is charge that these systems process, hence the electrostatic/dynamic effects of these systems are quite important and it is this that we focus on.

2. Methods

We have been applying computational tools to investigate the properties of biomolecules in an attempt to enhance their usage as data storage and processing units. We have focused on either bR or the electron transporter Cytochrome-C and have been evolving strategies to make the proteins more thermally stable and to enhance their charge transfer properties through manipulation of the electrostatics of the assemblies. [6,7]. Here we apply the techniques of electrostatic potential calculations [8] to bR and complement them with normal mode analyses [9]. We have previously found that the electrostatics around Cytochrome-C is understandably influenced in a significant way when neighbouring protein molecules are included in the computations [7]. We extend this calculation to bR and couple it with dynamical information to examine the implications on charge transport by bR.

3. Results

bR converts light energy into an electrochemical proton gradient, which in turn is used for ATP production by ATP synthase. It is a light-activated proton pump, transporting protons out of the cell. The direction of proton flow is shown in Figure 1 and the residues that mediate this process are shown in Figure 2. The protein assembles into trimers which then pack with each other into larger assemblies (we have shown a 9-mer which is a trimer of trimers here). The location of the residues is shown in the context of neighbouring molecules because in contrast to the usual method of computing the electrostatics and dynamics of a monomer and extrapolating the results to interpret macroscopic observables, we investigate these properties using whole assemblies explicitly. Clearly, the amplitudes of the atomic motions will influence the distances between the atoms, which in turn will influence the electrostatic potentials, in particular those characterizing the charged residues such as Asp/Glu that are involved in the proton transfer pathway. In order to see this effect we examine the electrostatic potential that is generated on the surface of a monomer when the assembly is gradually changed from the isolated monomer to a trimer and then to a 9-mer. Figure 3 (top row) shows a sharp increase in the distribution of negative potential (red colour) upon the monomer oligomerizing to a trimer; while

subsequent change from a trimer to a 9-mer leads to little change. This suggests that the assembly process will indeed influence the rates of the proton flows and our calculations suggest that such models must include assemblies at least to the level of a trimer. However, if we examine the consequences of mutating Asp96 to Asn96 (abrogation of one unit negative charge in each monomer leading to a total increase in cationicity of +1, +3 and +9 units in the monomer, trimer and 9-mer respectively), we find that the negative patch (Figure 3 bottom row & also see slide 3 in http://www.bii.a-star.edu/~chandra/JPhys/bR.ppt) is diminished in the mutant monomer and there is increasing attenuation as the assembly size increases. This clearly suggests that although the wild type potentials suggest that assemblies larger than trimeric do not influence the electrostatics significantly, this is not the case when we examine mutants. The Asp96Asn mutant is known to be more photosensitive (by 50%) relative to the wild type and its lifetime in one of the states increases 70-fold. The proton is positively charged, therefore it would reside longer within the area of negative potential. Hence in this mutant, with a reduction of such negative potential, it is likely that the proton transits much faster. Of course there are numerous other local interactions too that contribute to the observed changes [13]. We are currently modelling this process further. Additionally, in order to examine the influence of the dynamics, we look at the lowest frequency normal modes of the bR in its various assemblies (http://www.bii.a-star.edu/~chandra/JPhys/bR.ppt). The nature of the motions is examined through the fluctuations of the Ca atoms associated with the lowest frequency motions of bR (Figure 4). It is clear that as the assembly size increases, there is a significant reduction in the amplitudes of motions. This has an immediate bearing on the charge transportations because the separations between atoms can change significantly (for example the separation between Asp36 and Asp96 fluctuates by 0.7Å during this mode) and this will lead to significant changes in the ionization characteristics of the residues implicated in the proton transport. The large changes will undoubtedly also influence the thermodynamics of the process through fluctuation-related changes in the entropy of the system. We see some nontrivial changes in the electrostatic potentials during these movements (slide 5 of http://www.bii.a-star.edu/~chandra/JPhys/bR.ppt). Dynamic influences are very important in the understanding of charge transfer rates in proteins [14].

4. Conclusions

We find that in attempts to design protein-based devices to process information in computers, it is important to understand the role of electrostatics and dynamics from the computational models. In this process, the inclusion of assemblies explicitly in the calculations is crucial. We hope that our current findings will spur interest in this rapidly evolving field.

References

[1] Clark J, Singer EM, Korns DR, Smith SS 2004 **36** 992, 998.

[2] Gray HB and Winkler JR Electron tunneling through proteins. 2003 *Q Rev Biophys* **36** 341

[3] Hampp N (2000) Bacteriorhodopsin as a photochromic retinal protein for optical memories 2000 *Chem Revs* **100** 1755

[4] Birge R (Ed) 1994 *Molecular and Biomolecular Electronics*, Birge, Robert R. Ed., American Chemical Society, Washington D.C. 162

[5] Birge RR Protein-based optical computing and memory 1992 *Computers* **25** 56.

[6] Renogopalakrishnan V, Ortiz-Lombardia M and Verma CS Electrostatics of Cytochrome-C assemblies. 2005a *J Mol Modelling* **11** 265

[7] Renugopalakrishnan V, Garduno-Juarez R, Narasimhan G, Verma CS, Wei, X and Li, P Rational design of thermally stable proteins: relevance to biotechnology. 2005b *J Nanosci Nanotech* **5** 1759

[8] Baker NA, Sept D, Joseph S, Holst MJ and McCammon JA. 2001 *Proc. Natl. Acad. Sci. USA* **98** 10037

[9] Suhre K and & Sanejouand YH 2004 *Nucleic Acids Research* **32** W610
[10] DeLano WL 2002 The PyMOL Molecular Graphics System on http://www.pymol.org
[11] Subramaniam S and Henderson R. Molecular mechanism of vectorial proton translocation by bacteriorhodopsin 2000 *Nature* **406** 653
[12] Pettersen EF, Goddard TD, Huang CC, Couch GS, Greenblatt DM, Meng EC and Ferrin TE 2004 *J. Comput. Chem.* **25** 1605
[13] Brown LS, Kamikubo H, Zimanyi L, Kataoka M, Tokunaga F, Verdegem P, Lugtenberg J and Lany JK 1997 *Proc Natl Acad Sci USA* **94** 5040.
[14] Balabin IA and Onuchic JN. 2000 *Science* **290** 114.

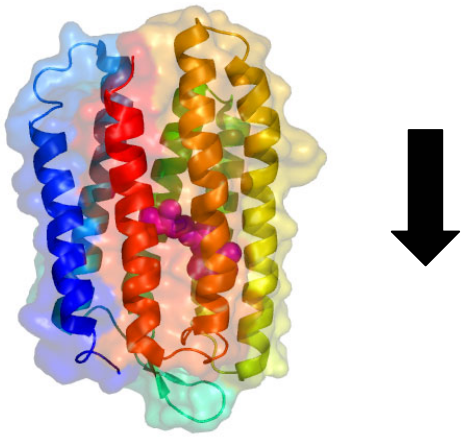

Figure 1. The structure of bacteriorhodopsin, the transmembrane protein with the alpha helical segments shown as ribbons and the chromophore retinol shown as magenta spheres. The figure was drawn using Pymol [10] and is based on the coordinates taken from the crystal structure with entry 1FBB [11] in RCSB. The top end is towards the intracellular side while the bottom end is towards the extracellular side and the photon travels from the top in the direction shown by arrow.

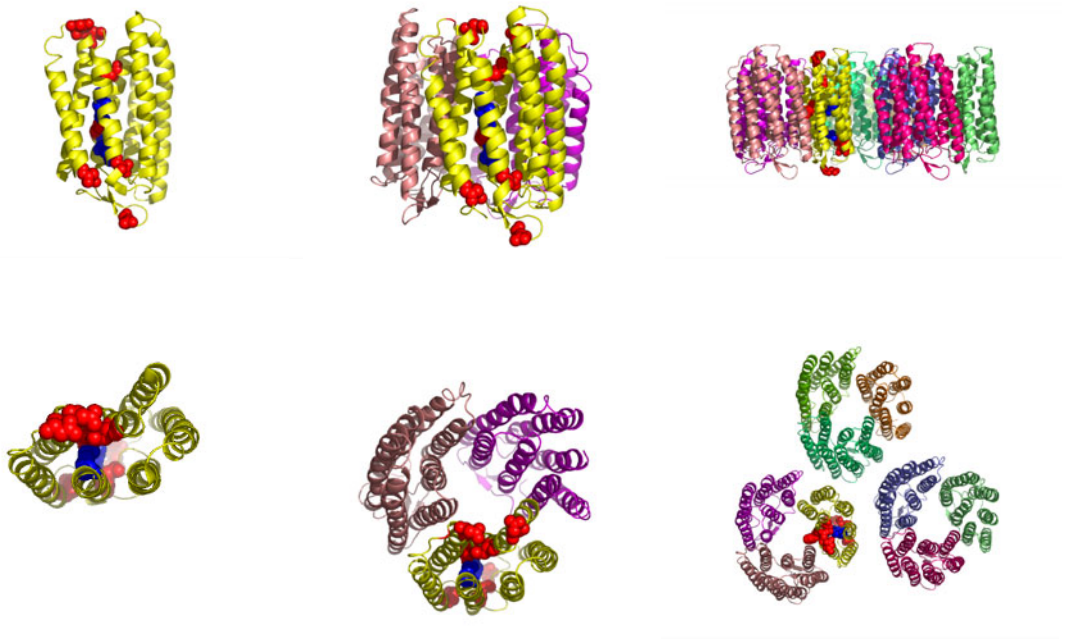

Figure 2. The structure of bacteriorhodopsin, the transmembrane protein with the alpha helical segments shown as ribbons and the residues involved in the proton transfer process shown as spheres (the residues are Asp36, Asp38, Asp96, Lys216, Asp85, Arg82, Glu204, Glu9, Glu74 with the Asp/Glu shown in red and the Arg/Lys shown in blue; the numbering is not sequential as this is the sequence in 3-dimensional space from the top to the bottom following the proton pathway). The figure was drawn using Pymol [10] and is based on the coordinates taken from the crystal structure with entry 1FBB [11] in RCSB. The top end is towards the intracellular side while the bottom end is towards the extracellular side and the photon travels from the top in the direction shown.

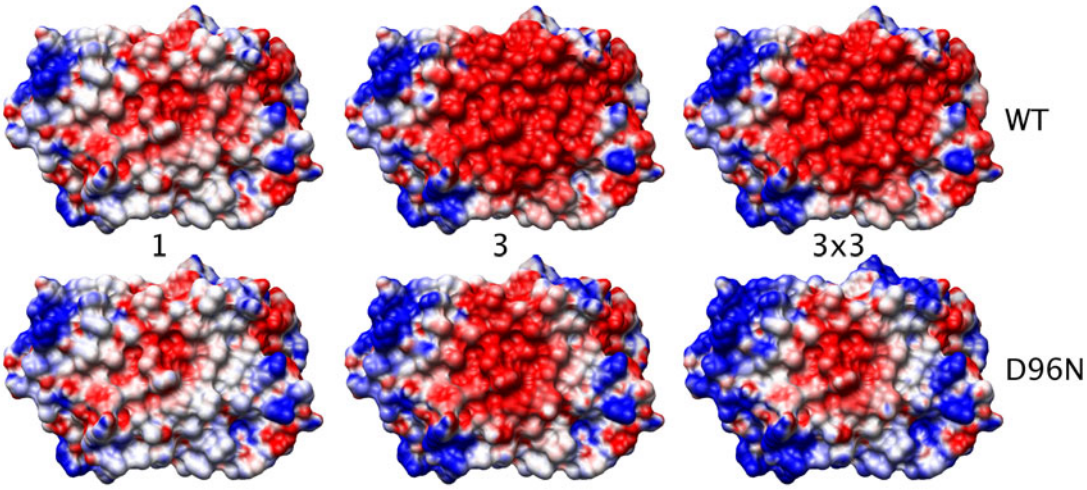

Figure 3. The electrostatics of bR and its modifications in assemblies. On the left is the electrostatic potential on the surface of the bR monomer, in the middle is the electrostatic potential on the same monomer which is now part of a trimer and on the right is the electrostatic potential of the same monomer which is now part of the trimer of trimers. The top row is the potential computed for the wild type bR while the bottom row is the potential computed for the mutant Asp96Asn. Red denotes a negative potential while blue denotes a positive potential. The potentials are contoured between -10kT and +10kT. The calculations were done using APBS [8] while the figures were drawn using UCSF Chimera package from the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco (supported by NIH P41 RR-01081) [12].

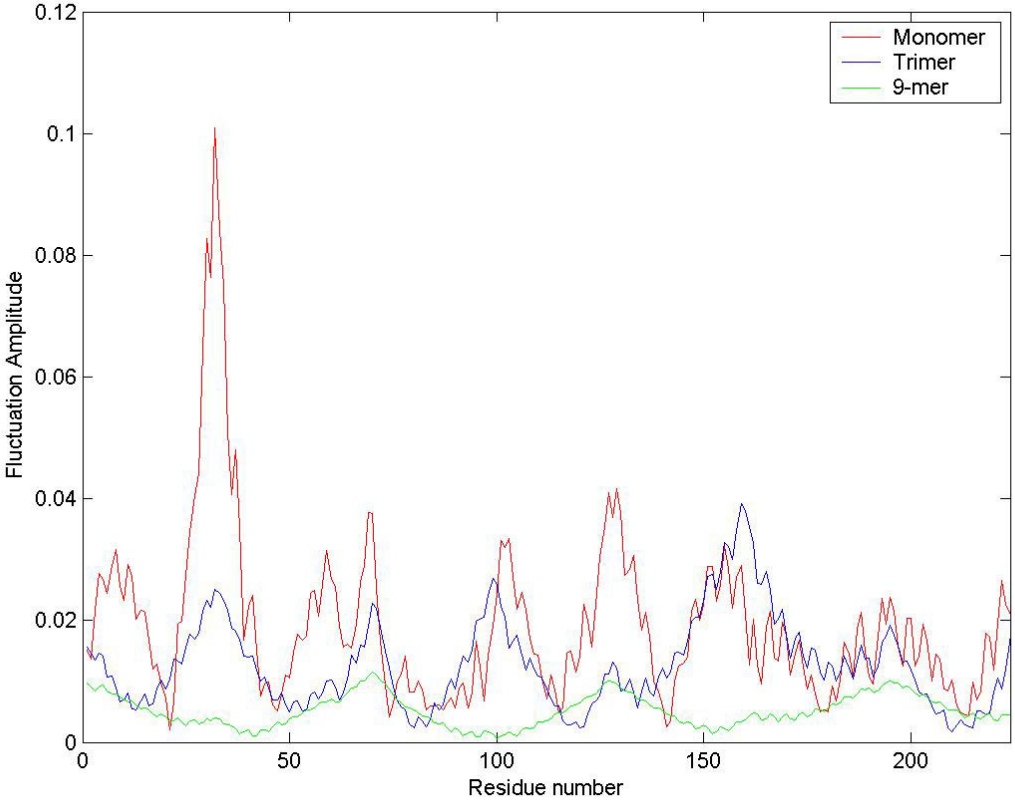

Figure 4. Fluctuations of the Cα atoms of the bR monomer along the lowest frequency modes as computed from normal mode analyses as the assembly increases from monomeric to trimeric to 9-meric. The fluctuations amplitudes are in units of $Å^2$.