Criticality in living matter: a universal mechanism of charge transport in biomolecules

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Abstract

In recent experimental works using metallic contacts attached to proteins, an anomalously large, temperature-independent long-range conductance has been measured across numerous proteins with no known role in electron transfer processes. The exact mechanism by which this phenomenon occurs is unknown, although several recent theoretical works suggest that proteins belong to a larger class of biomolecules tuned precisely to a metal-insulator critical point, where decoherence plays a pivotal role for the robust conductance measured in proteins. Along with having strong dependence on molecular conformation, the ubiquitous nature of the phenomenon suggests that it was evolutionarily selected for, as the probability to find even a single critical molecule by chance is astronomically low. In this paper, we discuss the current modeling efforts which realize the physics for this phenomenon, their relation to experiment, as well as potential evolutionary roles.

1 Introduction

Based on their chemical composition, it has generally been thought that biological proteins are great insulators [1], as the hydrophilic outer shell of a protein acts as a barrier to charge injection. Although proteins assume a very active role in electron transfer processes, a protein to be relevant for electron transport is scarcely found to be relevant to biological processes. An important distinction that is sometimes unclear, charge transfer is the process by which an electron or hole is transferred to/from some site on a protein (in many cases where an electron can reside for some time) to aid in biochemical processes allowing a protein to become reduced or oxidized. Electron transport on the other hand is more akin to charge flow through a wire; the process by which electrons flow through a junction due to a potential difference between two electrodes, without residing still on the junction (in this case, a protein) itself. This distinction is shown in Figure 1. Aside from very special and specific cases (e.g. Geobacter sulfurreduccans, a deep-soil bacteria which creates long conducting filaments to rid itself of electrons [1]), there is, in general, no currently known evolutionary pressure or role for proteins to form conductive structures.

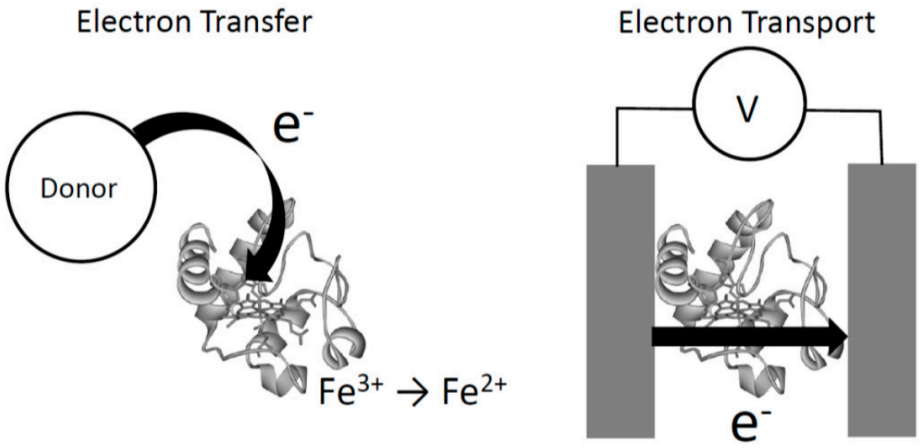

Figure 1: On the left showing electron transfer in which a protein becomes ionized (reduced or oxidized), often times for the purpose of a biochemical process. On the right showing electron transport in which electrons flow through a junction due to a potential difference between two electrodes [1]

Recent experimental findings, however, have challenged the conventional wisdom that proteins act as great insulators. In experiments of metallic contacts attached to various proteins, conductances rivaling and exceeding modern-day synthetic nanowires have been measured, which don't show significant dependence on distance between electrodes [1, 2] or temperature, with one astonishing report of a constant conductance down to 4 Kelvin in an azurin protein[3].

The mechanism behind this remarkable conductance is of current speculation and is not at all obvious. In electronic junctions composed of organic molecules which are known to conduct, the mechanism by which transport occurs depends strongly on the molecular length (the tunneling barrier) and temperature [4]. The typical mechanisms of charge transport in small molecules molecules being nonresonant tunneling in which an electron tunnels through the molecular orbitals in a single step [4], which is very weakly affected by surrounding temperature and spends no appreciable time residing on the molecule. Longer molecules typically exhibit a thermally activated hopping mechanism[4], in which the

molecule-electrode coupling is much higher than electron energy, and transport happens in steps: a charge is injected into the molecule from the first electrode and is driven along the molecular backbone via some applied field, and is then injected from the molecule into the second electrode. This leads to a series of discrete "jumps" that the charge takes along its journey, and is heavily dependent on surrounding temperature. These mechanisms are illustrated in figure 2.

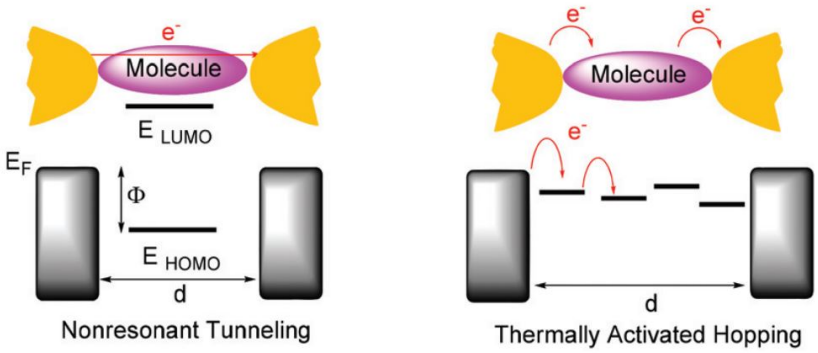

Figure 2: A brief illustration showing the mechanism of nonresonent tunneling (left) and thermally activated hopping (right) [5]

The experimental findings of an anomalously large, temperature and electrode distance independent conductance outlined above fit neither of these typical mechanisms in organic molecules. In fact, it is not at all obvious the mechanism of this protein conductance. Several theoretical works suggest that decoherence induced by the protein's environment (for example via strong coupling in vibrational states in the protein's structure) plays a very important role for this anomalous measured conductance[6, 7]; Claims very similar to the ones found in quantum biology in photosynthetic complexes [8]!

This work is structured as follows: first, we discuss in more detail the experimental results which demonstrate that proteins exhibit this anomalous conductance. Second, we go over the theoretical works which aim to capture the physics of the phenomenon, and explore the argument that proteins actually belong to a larger class of biomolecules tuned precisely to a metal-insulator critical point, which leads to the anomalous conductance. Finally, we end with a discussion of the evolutionary implications of such a mechanism among biomolecules. I.e. what would the evolutionary driving force be behind a molecule operating at a critical point?

2 Measurements of protein conductance

In this section, we expand into a bit more details around the experimental results of conductance measured in proteins.

2.1 Large conductances at long range

Several groups have showed that at distances above 7nm, proteins "sandwiched" between electrodes outperforms modern synthesized nanowire[1, 2]. Lindsay[1] summarizes the results from the laboratory of David Cahen at the Weizmann Institute in Israel[2], several experiment measuring the current density j, as a function of layer thickness of proteins, alkane chains (good conductors at small ranges), and aromatic polymers (modern

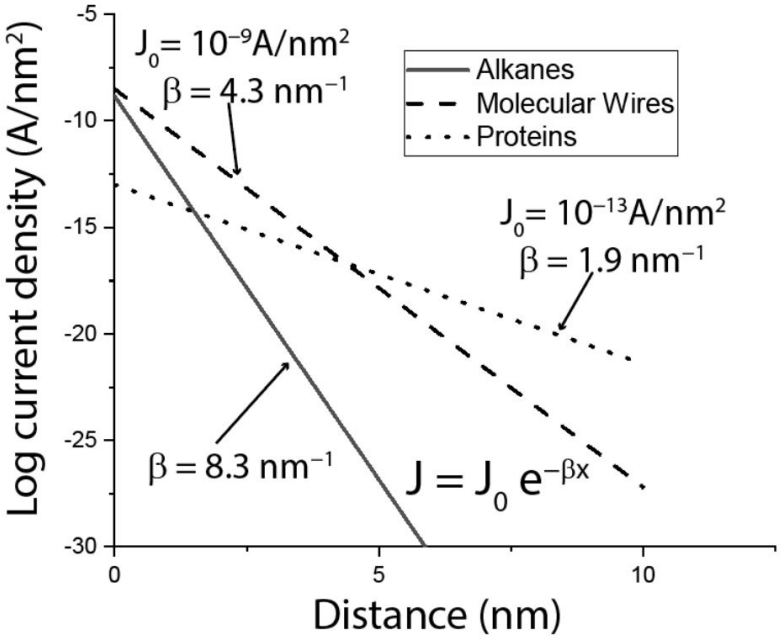

Figure 3: Plot of current density as a function of junction distance of alkanes (solid line), molecular wires (dashed line) and proteins (dotted line) [1, 2]

nanowires). Lindsay fits this data to an exponential decay of the form $J = J_0 \exp(-\beta d)$, where β is a decay constant in units of nm^{-1}, and gives the slope of the plot of $\log J$ versus d, found in Figure 3.

The immediate and striking feature of this data is that for distances greater than 7nm, proteins outperform synthetic molecular wires by a wide margin. Aside from the long conducting filaments of Geobacter sulfurreduccans as discussed in the introduction, there is no known role or driving force for proteins to exhibit long-range transport. It is for this reason alone, that this is such a surprising result.

2.2 Weak electrode gap size dependence

Lindsay also summarizes data collected on the relation between the distance between electrodes and conductance[1, 9, 10] in Figure 4. Remarkably, the conductance of the measured junction changes incredibly little (the slope of the line fitted through open circles) when compared with the molecular wire (open triangle) operating under the hopping transport regime described above, giving further evidence towards a difference in their transport mechanism.

2.3 Temperature independence

Another remarkable result is found through Kayser et al[3] in which they measured the conductance across an azurin protein to be temperature independent all the way down to 4 kelvin. Figure 5a is showing the I-V plot of a junction of the protein Azurin in between two nanowires of Gold. The overlap between the I-V curves for room temperature and 4 Kelvin ambient temperatures is apparent, demonstrating temperature independence. Figure 5b shows the same temperature independence, but for a different junction.

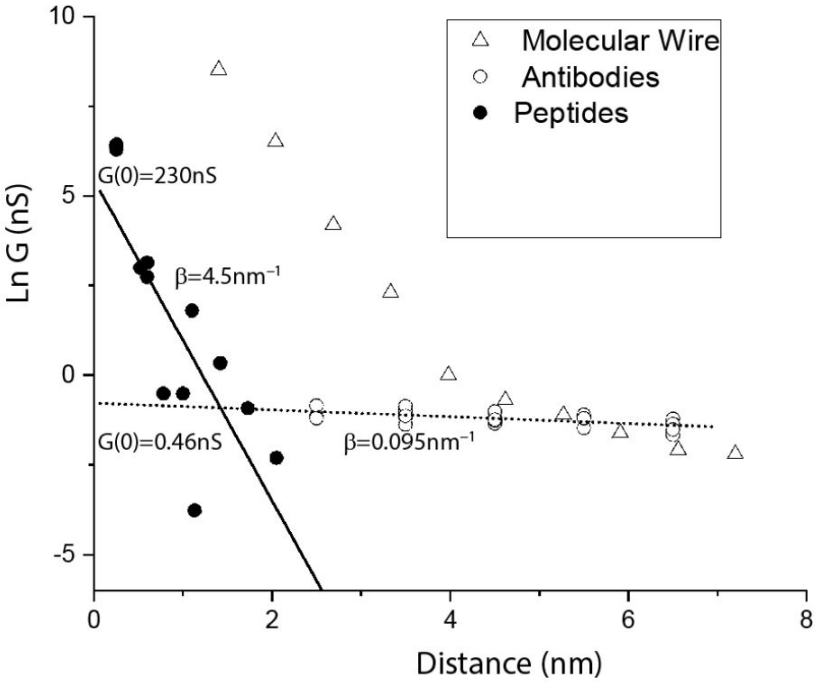

Figure 4: Plot of the natural log of conductance through single molecules as a function of the electrode gap size.[1, 9, 10]

3 Theoretical evidence for a universal mechanism of biomolecule conductance

3.1 Arguments from Random Matrix Theory

This section is based on the work of Vattay et al[7]. Wherein, the authors tackle the question of protein conductivity starting from the Anderson model, a robust model for the understanding of conduction in condensed matter.

The Anderson Hamiltonian on a 3D lattice with randomly distributed on-site energies $\epsilon_i \in [-W, W]$ is given as

$$H_A = \sum_i \epsilon_i a_i^+ a_i - \sum_{<ij>} a_j^+ a_i$$

the critical level of disorder in such a Hamiltonian is $W_c = 16 \pm 0.5$ [11]. When $W < W_c$, one finds the system in a disordered metal with extended states [7]. For $W > W_c$, the states are localized characteristic of insulating behavior.

Next, to analyze the statistical properties of the Hamiltonian, Vattay et al employs a current main tool to do so in the literate [7], random matrix theory (RMT). Take the distance between any two levels to be $\sigma_n = E_{n+1} - E_n$, with the average spacing between levels as $\Delta(E)$. The level spacing for a given level n is then defined as $s_n = \sigma_n/\Delta(E_n)$, with the distribution of level spacings given by $P(s)$. RMT predicts different, but specific, functional forms for $P(s)$ for systems exhibiting localized, delocalized and critical behavior [12]. These distributions are believed to be independent of microscopic details and universal. The level spacing distribution for the delocalized metallic phase is

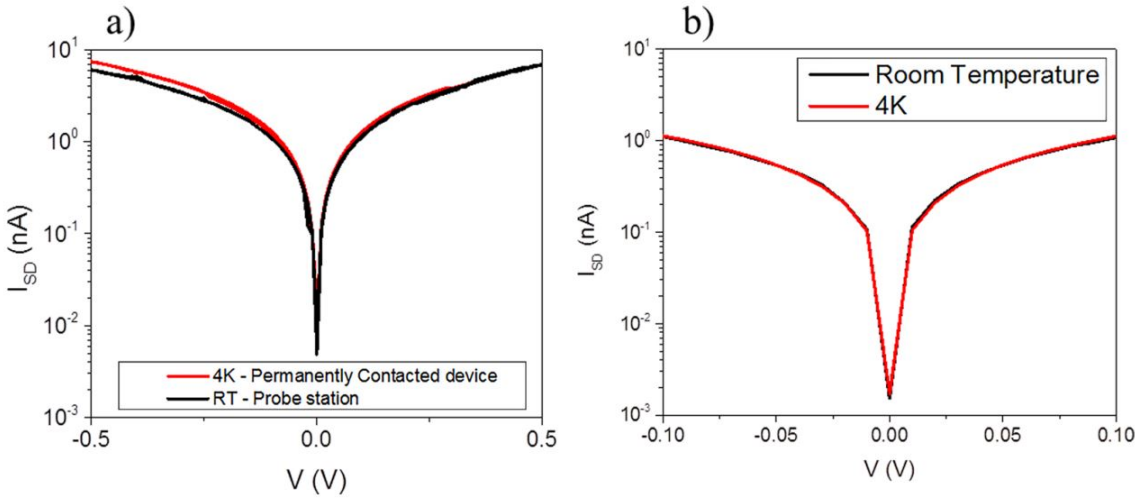

Figure 5: (a) Plot of the $I-V$ characteristcs for a gold-Azurin-gold junction at room temperature (black) and 4 Kelvin (red). (b) Shows the same as left, but for a different junction [3]

found to be

$$P_W(s) = \frac{\pi s}{2} \exp\left(\frac{\pi s^2}{4}\right)$$

And for the localized insulating phase, the level distribution is

$$P_P(s) = \exp(-s)$$

At the transition point, $W = W_c$ many works show a sort of intermediate distribution exists called the semi-Poissonian distribution given as

$$P_{SP}(s) = 4s \exp(-2s)$$

A distribution that physical systems display when the strength of its disorder is tuned to a critical point. Operating under standard procedure the cummulative spacing, $I(S) = \#\{s_i < S\}/N = \int_0^S P(s)ds$ is calculated for each distribution, leading to the cummulative spacings, $I_{SP}(S) = 1-(2S+1)e^{-2S}$, $I_P(S) = 1-e^{-S}$ and $I_W(S) = 1-e^{-\pi S^2/4}$ corresponding to semi-Poissonian, Poissonian and Wigner statistics respectively [7].

By numerically calculating the molecular orbitals of various biomolecules via the Extended Huckel (EH) Molecular Orbital Method (the details of which, is beyond the scope of this work), Vattay et al [7] has been able to show that the energy level spacing statistics follows with incredible precision the distributions for I_W, I_P, and I_{SP} shown above! These results, we will briefly go over.

Vattay et al [7] first calculated energy level spacing of Myoglobin, human profilin and human apolipoprotein; Three proteins with known biochemical function. The results of the calculation are striking, with level spacing following with incredible precision the semi-Poissonian distribution, as seen in Figure 6, without any external tuning to their Hamiltonians!

Vattay et al then goes on to extend this calculation to many additional quasi-randomly selected (randomly choosing molecules in major databases based on size and availability of 3D crystallographic data) organic molecules found throughout biology, the results of

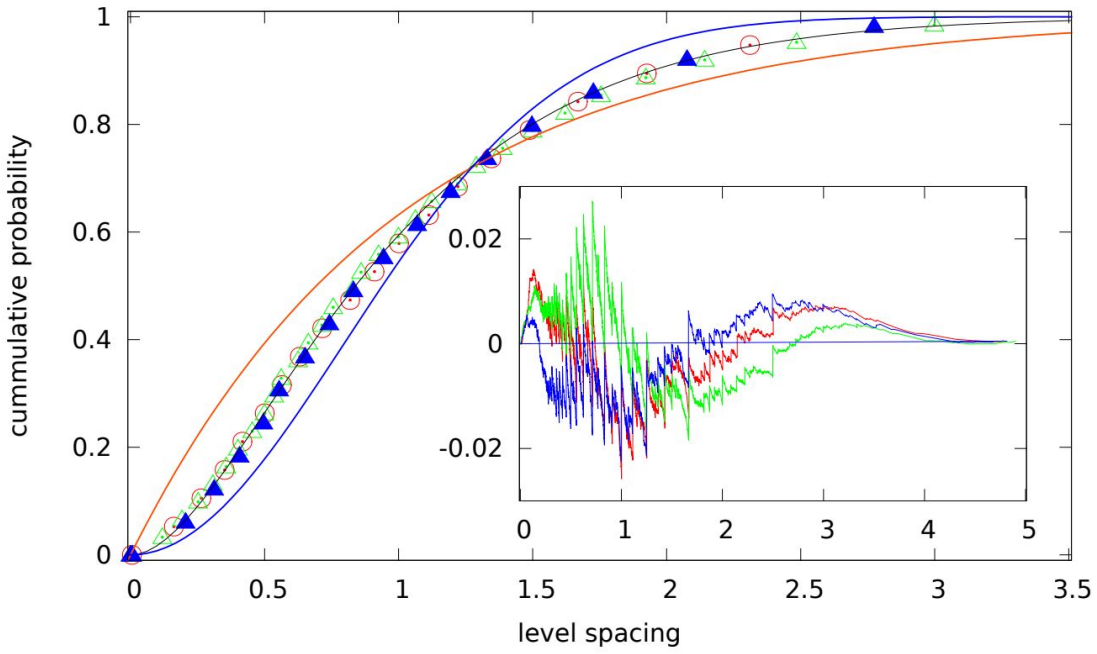

Figure 6: Shown is a plot of $I(S)$ for Myoglobin (blue triangles), human apolipoprotein E (green circles) and Profilin (red circles). Also shown, are the theoretical curves $I_{SP}(S)$ (black line), $I_P(S)$ (red line) and $I_W(S)$ (blue line). In the inset is shown the difference between the protein data curves, and $I_{SP}(S)$. Note the agreement between data and $I_{SP}(S)$ curve [7]

which are found in Figure 7. The most striking observation with these results is just how "cleanly" each biomolecule fits into each cumulative spacing functional form, I_P, I_W and I_{SP}. Intermediate distributions are certainly not forbidden in RMT and quantum chaos [7], so it is quite curious as to how the distributions fit so nicely. Perhaps the Hamiltonians of each biomolecule are not random, but instead evolved over time to be tuned to one of the spacing classes? This gives a first taste of evidence that evolution has selected for structures which exhibit these "clean" statistics. Of course the next question, the answer to which is not at all obvious, is what evolutionary driving force could have selected for such finely tuned Hamiltonians? This, of course, is a principle question which will require further experimental and theoretical analysis of in the future.

One clue, is that among the molecules tested and plotted in Figure 7, nearly every molecule that actively take part in biochemical processes exhibited the semi-Poissonian distribution characteristic of their Hamiltonian being tuned to the transition point, and are critical conductors. Nearly all other biomolecules which do not actively take part in biochemical processes (for example, silk, a structural material) exhibited Poissonian and Wigner level spacing statistics characteristic of insulating and conducting properties respectively.

These results are highly suggestive of a mechanism of conductance for biochemically active molecules different from the mechanism one sees in metals [7]. In metallic conductors, an electric field accelerates floating charges as they scatter from impurities, leading to a constant average charge propagation velocity. As stated before, this is a mechanism almost never seen in biological systems. The more likely mode of conductance, for which there is an abundance of evidence for in photosynthetic light harvesting systems as well[8],

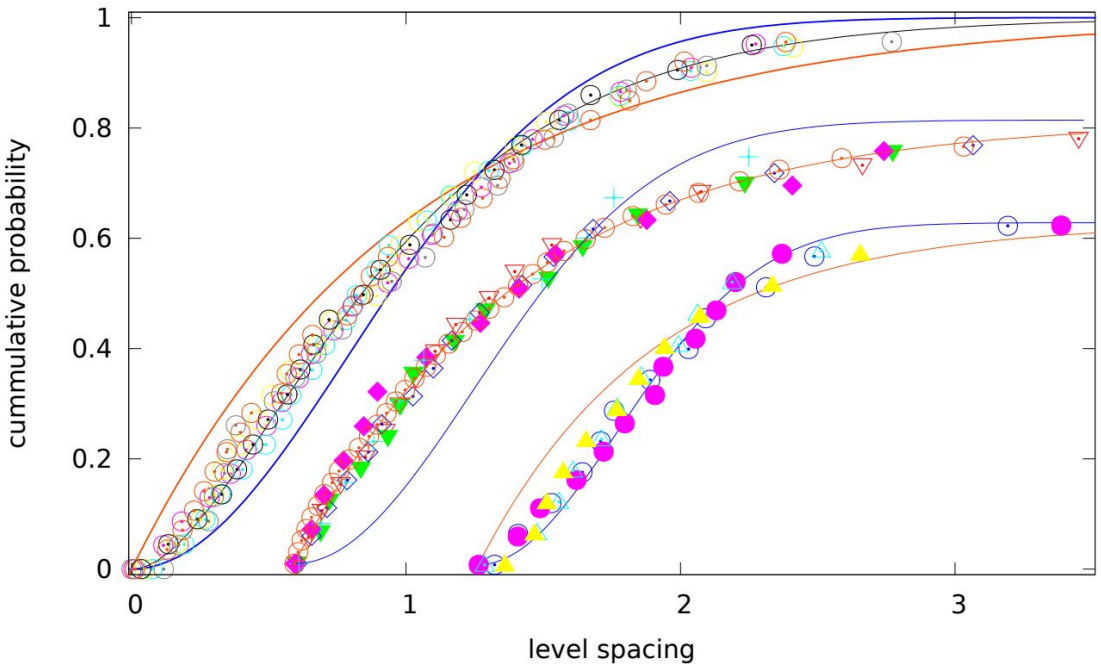

Figure 7: (Left most curve) Critical cumulative level statistics $I_{SP}(S)$ for Vitamin D3, Vitamin B12, Linoleic Acid, Primary fluorescent chlorophyll catabolite, Leucine and finally Sucrose. (Middle Curve) Silk, Dextrin, Gefarnate, Octadecane, and a 21 base pair DNA sequence with Poissonian level statistics $I_P(S)$ are shown. (Right-most Curve) Progesterone, Testosterone, Aristolochic Acid and Dibenzo(a,e)pyrene with Wigner cummulative statistics are shown $I_W(S)$ [7]

is that as a charge enters a "critical" biomolecule, it is influenced by both the quantum Hamiltonian, as well as the decoherence brought on by the environment. This mode of conductance, otherwise coined "Environment Assisted Quantum Transport" (ENAQT) is a large focus of research in quantum biology [8]. In ENAQT, put simply, a conducting system is tuned such that environmental decoherence leads to a boost in the spread of excitations over the system.

The treatment of the problem discussed above can readily lead us to the hypothesis that biochemically active molecules exhibit a different mechanism of conductance, but it tells us very little of the details behind such a mechanism. This, as one would expect, is a very prohibitive task considering most biomolecules in question can contain thousands of atoms.

3.2 Vibrational mode coupling via the Landauer formula

To tackle this immense complexity, approximate methods can be useful. In a recent theoretical work, Papp et al [6] develops a generalization of the low temperature Landauer formula in an attempt to account for the joint effect of decoherence and tunneling. In their original paper [6], they first discuss the theoretical derivation from their approximation, and then use it to compare with known anomalous experimental results. We will show the main result of the calculation, and then discuss in a bit more length the comparison with experiment. In a system of a biomolecule attached to two contacts, Papp et al [6] start from a quantum master equation, approximated with the Markovian Redfield equation (representing the main approximation)

$$\partial_t \rho_{nm} = \frac{i}{\hbar}(\epsilon_m - \epsilon_n + i\Gamma_n/2 + i\Gamma_m/2)\rho_{nm} + \sum_{kl} R_{nmkl}\rho_{kl} + J_n\rho_{nm}$$

where R_{nmkl} is the Bloch-Redfield tensor which describes transitions brought on by phononic vibration couplings $\epsilon_n + i\Gamma_n/2$ is the level broadening due to the metallic contacts, and J_n is external current. Under the assumption that bioelectronic systems have highly localized electronic states as well as the assumption that the HOMO-LUMO gap is large, Papp et al are able to replace the Fermi distribution of states with the Boltzmann distribution. This along with other novel methods leads the authors to the main result of the paper to an expression for the conductance, G,

$$G = \frac{e^2}{2\hbar}\sum_n D_n(E_F, T)\left[\Gamma_n^L + \Gamma_n^R + \frac{1}{\hbar}\sum_k (\Gamma_k^L - \Gamma_k^R)L^{-1}_{kknn}(\Gamma_n^L - \Gamma_n^R)\right]$$

Using this expression for conductance, Papp et al then go on to recreate the temperature independence found in experiment. Raichlin et al[13] experimentally show temperature independence for a current measured through Myoglobin found in Figure 3 of [13]. Papp et al reconstruct these results both with good agreement in figure 8, in which, temperature independence for low temperatures can be readily seen, consistent with results we've shown in section 2.

This calculation importantly shows through the inclusion of the Bloch-Redfield tensor R_{nmkl}, that decoherence via strong coupling to vibrational modes is very important to the high conductance measured inside these biomolecular structures, giving further evidence of the intuition from section 3.1 that decoherence could be a very relevant parameter. Approximate analytical methods are of course very usable to do get predictions for new experiments without the need for high-performance computing, however they tell us very

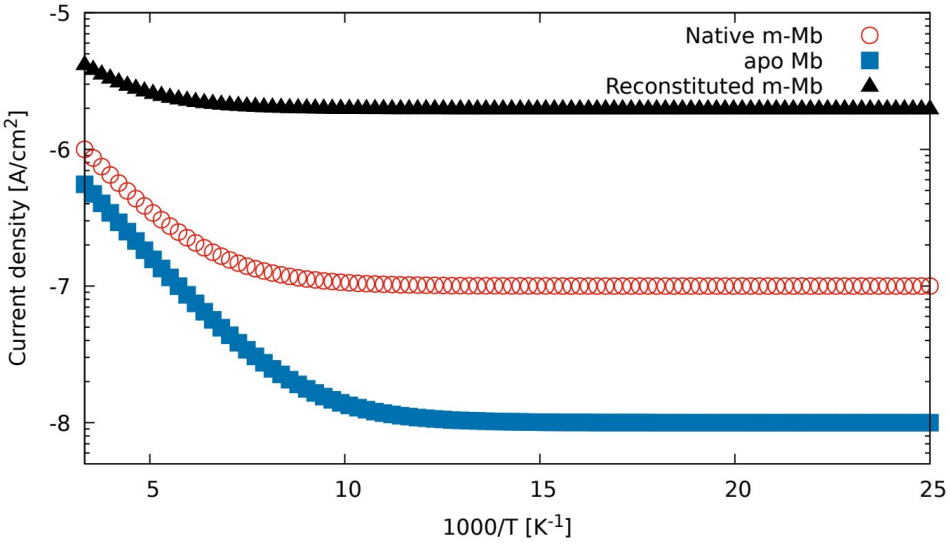

Figure 8: Theoretical reconstruction of experimental data from [13] conductance calculated from [6] in section 3.2 [6]

little about the exact molecular mechanism responsible. To get a completely precise picture of what is going on, robust computational methods will need to be employed.

4 Evolutionary implications

Through a simple statistical argument[7], Vattay et al estimates that through evolution, only an incredibly small fraction $p \sim 10^{-50}$ of chemically feasible, small organic molecules and proteins were selected for. The idea that numerous biomolecules have Hamiltonian's tuned to a critical point, coupled to the notion that the probability to find even a single critical molecule by chance is astronomically low suggests that criticality was selected for.

As hinted at throughout this paper, the principle question in regards to the evolution of such a conductance is, what evolutionary driving force would be responsible for the making of many biomolecules with no known role for biological conductance to be better conductors than engineered nano-wires? Like many questions posed in this paper, the answer is not at all obvious. The key, could perhaps lie in the evidence that only biochemically active molecules exhibited this anomalous conducting behavior, as discussed in section 3.1. Molecular conformation is vital for many biochemically active processes, so it might be reasonable to suggest that if such a function is not merely coincidence, then it might depend on conformation, as Lindsay [1] postulates for proteins. Zhang et al [14] show that the conformational change brought on by the binding of biotin to streptavidin changed the conductance drastically. It is difficult to say with certainty if this change in conductance was due to a change in the supramolecular structure of the protein, or if it truly did have to do with the resulting conformational change.

These results are incredibly new, numerous gaps exist in the literature, and there is much work to be in this area for the coming years. On the application front of such a phenomenon, however, Lindsay [1] remarks that the outlook is clear. Given their remarkable conductance properties coupled to the fact that they self assemble at the nano-scale, proteins make excellent electronic components and are poised to surely find application in bioelectronics.

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