Microscopic modeling of charge transport in sensing proteins

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INTRODUCTION AND MOTIVATION

• CHARGE TRANSPORT IN BIOLOGICAL MATERIALS: WHICH MECHANISMS?

• MONITORING SENSING PROTEIN OF THE GPCR FAMILY THROUGH ITS ELECTRICAL PROPERTIES

• CORRELATION BETWEEN PROTEIN STRUCTURE AND ELECTRICAL PROPERTIES

• CONVERTING A BIOLOGICAL CHAIN OF DETECTION INTO A CHANGE OF AN ELECTRICAL SIGNAL

• WIDE APPLICATIONS IN MOLECULAR DEVICES CONTROLLING THE QUALITY OF LIFE
PHYSICAL SYSTEM OF INTEREST

G Protein Coupled Receptor (GPCR) as sensing protein

Typical sensing action to: light, odours

For light: Bovine Rhodopsin, Bacterio-Rhodopsin

For odours: rat OR-I7, Human OR 1740, Scimpanzee OR-7D4
GPCR AS A TRANSMEMBRANE PROTEIN WITH 7 HELICS
OR 7D4 HUMAN - Protein code

MEAENLTEL SKFLLLGLSDDP ELPV VLFGLFLS MYLVTVLGN LIIILAVSSDSH LH T PMYFFLSNL SFVDIC FISTT VP KMLVN IQAR SKDI SY MGCL TQVYFLMMFAG M DTFLLAVMAYDRFVAICHPLHYTVIMN PCLCGLLVLASWFIIFWFSLVHILLM K RLTFS TVEI PHFFCEPAQVLK VACSNTLLNNIVLYVATA LLGVFPA GILFSYSQ IVSSLMRMSS TE GKY KAFSTCGSHL CVVSLFYGTGLGVYLV SSATHSSQSSSMA SVMYAMVTPMLNPFIYSLRN KDVKGALERLLSRADSCP
SCHEMATIC OF BOVINE RHODOPSINE AMINO ACID STRUCTURE
A REALISTIC VIEW OF KNOWN GPCRs

- Active bovine rhodopsin
- Native bovine rhodopsin
- B2 Adrenergic
- Adenosine
Transduction cascade of the signal. Capture of the ligand leads to a conformational change - monitored by a G protein - that initiates a biological chain of detection – finally collected by the brain.
OR-7D4: native state in red and active state in green
AVAILABLE EXPERIMENTS ON THE ELECTRICAL PROPERTIES OF SENSING PROTEINS

CURRENT VOLTAGE CHARACTERISTICS ON NANOLAYERS OF MACROSCOPIC CROSS SECTIONAL AREA (-1 +1 V)

CURRENT VOLTAGE CHARACTERISTICS ON NANOLAYERS CARRIED OUT WITH AN AFM TECHNIQUE ON NANO AREA (-10 +10 V)

ELECTROCHEMICAL IMPEDANCE SPECTROSCOPY ON SELF ASSEMBLED MONOLAYERS OF MACROSCOPIC AREA (mV at 0.1 – 10^5 Hz)
I-V ON MACRO AREA

APTMS-modified Al/AlO\textsubscript{x} bR monolayer junctions
Jin et al 2006
$A = 2 \times 10^{-3} \text{ cm}^2$
h = 5 nm
Schematic of the AFM technique and of the measurement chain.
Gomila et al at IBEC Barcelona 2007

$I$ (nA)

$10^1$ $10^0$ $10^{-1}$ $10^{-2}$ $10^{-3}$ $10^{-4}$ $10^{-5}$

$0$ $2$ $4$ $6$ $8$

bias (V)

$1.2$ nm $2.8$ nm $4.6$ nm

A=0.1-0.01 nm²

h in figure
Schematic of a three electrode electrochemical cell
Formation of self-assembled multilayer

- Rhodopsin or I7
- Biotinylated antibody
  - neutravidin
  - Goat IgG
  - Biotinyl-PE
  - HS(CH₂)₁₅COOH
  - Au

Biotinyl-PE

Thiol

HSCH₂(CH₂)₁₃CH₂−C−OH

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Nyquist plot of a functionalized layer with rat OR I7 in the presence of the specific odorant octanal at different concentrations.
THEORETICAL MODEL
Protein Data Base ([link](www.pdb.org))
Reconstruction from a known model (GPCRautomodel@INRA)
Elementary mechanism of charge transfer is the overlap between two aminoacids and the equivalent circuit element. $C_{\alpha i}$ identifies the center of the sphere corresponding to the alpha carbon atom of the $i$-th aminoacid.
Interaction radius $R_c$ to determine the connection between nodes

The network is solved with a standard procedure based on Kirchhoff’s law
Basic state of Rhodopsin and Metarhodopsin II as constructed from the protein data base (PDB): backbones in scale:
1 – C-terminus.
2 – Transmembrane core
3 – N-terminus
RESULTS AND DISCUSSION
Correlation between I-V and the associated variance of current fluctuations.

A colossal increase of current fluctuations is predicted at the cross over between direct and Fowler Nordheim tunnel regimes.
Prediction of the sensitivity of the AFM measurements to the presence of green light
Rat OR I7
D5.5: Modeling Nyquist plots on the basis of the conformation of a given sensing protein

Available data: OR I7, OR 17-40

\[ \frac{Z_{\text{im}}}{Z_{\text{Re}(0)}} \]

\[ \frac{Z_{\text{Re}}}{Z_{\text{Re}(0)}} \]

E. Alfinito, J-F. Millithaler, L. Reggiani, N. Zine, N. Jaffrezic-Renault, submitted to JAP

Fig. 3. Sensor responses to the injection of $10^{-10}\text{M}$ helional (A) and $10^{-10}\text{M}$ heptanal (B). Measurements were performed in PBS pH 7.0 at 20 °C.
CONCLUSIONS AND PERSPECTIVES

Sensing proteins exhibit detectable charge transfer properties.

As microscopic mechanisms we suggest overlap between neighbouring aminoacids.

Static I-V are dominated by tunneling mechanism of charge transfer, direct at low voltages Fowler Nordheim at high voltages.

Conformational change due to capture of the ligand leads to a detectable change of the electrical properties both as I-V and EIS characteristics.

The change of electrical response of a protein due to its sensing action is promising for the development of a new family of sensors which mimics the mammalian light and olfact senses carried out at a cellular (nanosize) level.

The Impedance Network Protein Analogue (INPA) we have developed has been validated by comparison with experiments and proved to be a valuable first step towards a microscopic interpretation of the electrical properties of a given protein.
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