

Joint Meeting of the Austrian Neuroscience Association (16th ANA Meeting) and
the Austrian Pharmacological Society (25th Scientific Symposium of APHAR)
Innsbruck, 25–27 September 2019

MEETING ABSTRACT

A3.7

Capacitance measurements: a tool to link functional and structural data

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Background: The transmembrane voltage is offset from that at the bulk solutions due to fixed charges at the membrane surface. The major source of these charges are phospholipid headgroups, but also charged residues of proteins that face the aqueous solution can contribute. We recently have shown that binding of charged ligands to membrane proteins result in a change in transmembrane voltage that can be monitored by capacitance measurements. It is conceivable that also rearrangement of solvent-accessible charged residues, as can occur in conformational transitions, change the surface potential.

Methods: We tested this hypothesis on the serotonin transporter (SERT) by using a multi-disciplinary approach in which structural and functional data were linked by a mathematical model. For this, the number of water-accessible charges of SERT for different conformational states were counted and fed into a kinetic model of the SERT transport cycle. By that we were able to calculate the time-dependent change of the inner and outer net surface charge densities during the transport cycle. This allowed us to simulate the expected apparent capacitance changes, which were cross-validated by experimental data.

Results: The generated *in silico* data predicted an apparent change in membrane capacitance consisting of two components: a transient decrease that is followed by an overshoot in membrane capacitance upon initiation of the transport cycle by serotonin. A similar signal pattern was seen in experimental data that was comparable in size and shape. Thus, the complex capacitance signal of the SERT transport cycle derives mainly from changes in surface potential due to conformational transitions.

Discussion: Here we show that capacitance measurements can be used to study conformational rearrangements that have an impact on the surface potential. We propose that in combination with kinetic models it might serve as a useful tool to bridge the gap between functional and structural information.

Keywords: capacitance recordings – serotonin transporter

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