

## Comment to the Editor

### On the Impossibility of Nonzero Reversal Potentials of Passive Pores Separating Symmetric Solutions: Comment on *Haemophilus influenzae* Outer Membrane Protein P5 Is Associated with Inorganic Polyphosphate and Polyhydroxybutyrate

In their recent article, Zakharian and Reusch (1) “unpredictably” measure a nonzero reversal potential when reconstituting NTHi P5 channels into a lipid bilayer separating identical solutions. They then attempt to explain this “unexpected asymmetry” by invoking an asymmetric association of polyanions with this passive pore. Although such an association may influence NTHi P5’s selectivity, it cannot be responsible for generating a nonzero reversal potential across a membrane separating symmetric solutions. Any potential arising from a surface charge generates an asymmetry in the distribution of ions near the membrane that in turn creates a transmembrane potential of equal magnitude and opposite sign. The measured reversal potential, which represents the voltage difference between the bath electrodes on the two sides of the membrane, will therefore always be zero in symmetric solutions at equilibrium (2).

But a much more potent argument can be made—one that does not rely on the subtleties of electrostatic theory of surface charges—for why this observation cannot be correct: it violates the second law of thermodynamics. By connecting the system described by Zakharian and Reusch to an external device, one could construct a perpetual motion machine of the second kind, in which thermal energy is converted to work without any change in the universe (3,4). This impossibility explains why the authors would not have previously

read about such an effect in any other passive pore similarly reconstituted, which in turn probably accounts for their description of their result as unexpected and unpredictable. Indeed, this odd finding should have been a clarion call to both the authors and reviewers to search for a source of systematic error in the experimental setup rather than for the “molecular basis” of the finding.

#### REFERENCES

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