Relating microscopic charge movement to macroscopic currents: The Ramo-Shockley theorem applied to ion channels

Wolfgang Nonner[1]*, Alexander Peyser[1#], Dirk Gillespie[2§] and Bob Eisenberg[2¶]

[1] Department of Physiology and Biophysics, University of Miami School of Medicine, P.O. Box 016430, Miami, FL, 33101-6430, USA

[2] Department of Molecular Biophysics and Physiology, Rush University Medical Center, 1750 West Harrison Street, Suite 1291, Chicago, Illinois 60612, USA

Running title: Gating Charge and Ramo-Shockley

Key words: gating charge, electrical coordinate, displacement current, voltage-dependent gating, simulations of charge movement

[#] email address: wnonner@chroma.med.miami.edu
[#] email address: a.peyser@umiami.edu
[§] email address: dirk_gillespie@rush.edu
[¶] email address: beisenbe@rush.edu

Monday, June 14, 2004

ABSTRACT

Since the discovery of gating current, electrophysiologists have studied the movement of charged groups within channel proteins. The relation of the atomic-scale movements of charged groups to the gating current measured in an external circuit is not obvious, however. Here we use the Ramo-Shockley theorem to relate atomic motions and the macroscopic current measured in an external circuit. The relation is concise and generally applicable to any charged system. Even without any calculation, the Ramo-Shockley theorem eliminates a class of interpretations of experimental results. The theorem calculates gating charge that would result from movements of protein charges and can be applied at varying levels of approximation. In comprehensive particle simulations (including simulations of ionic currents in channels), the theorem computes external current with less noise than the counting of particle crossings.

INTRODUCTION

Since Schneider and Chandler (1973), electrophysiologists have investigated the internal movements of channel proteins by measuring "gating current" (reviewed by Hille, 2001). Gating current is the capacitive current produced by the movement of charged atoms in a channel protein when the voltage between the electrodes is changed. It is distinct from the conduction current produced by the flow of ions through the open channel. Experiments using site-directed mutagenesis have since identified charged amino acid residues of channels that contribute to voltage-dependent gating (Stühmer *et al.,* 1989) and gating current (Aggarwal and MacKinnon, 1996; Seoh *et al*., 1996).

To interpret any of these measurements quantitatively, one must know the relationship between the atomic-scale charge movements and the externally recorded current. This problem is not trivial; it requires coupling disparate time and length scales and computing nonlinearly-coupled charge movements in heterogeneous dielectric media. The Ramo-Shockley theorem solved this problem in simple charged systems (Shockley, 1938; Ramo, 1939). Recent generalizations of the original theorem directly relate microscopic charge movements and macroscopic current in complex systems. The generalized theorem provides a concise and model-independent method that is applicable to many biophysical problems. In this paper, the generalized Ramo-Shockley theorem is applied to gating current and gating charge experiments. With the theorem, certain interpretations of experimental results can be ruled out categorically, and gating currents for specific charge movements can be predicted. More generally, with the Ramo-Shockley theorem external currents of simulated systems can be computed with high efficiency from atomic motions.

THE RAMO-SHOCKLEY THEOREM

In voltage clamp experiments used to study currents through a biological membrane, two electrodes impose a controlled voltage across a domain that contains dielectrics and charged particles (ions in the baths and channels, and charged groups in the protein) (Hodgkin *et al.,* 1952). The charged particles move because of thermal agitation (heat) and the applied electric field. The current measured by the external circuit has two components: the particle current carried by ions entering or leaving the electrodes and the displacement current. The displacement current is the movement of charge (electrons) in

the electrodes induced by changes in the electric field caused by the movement of all the charged particles that do *not* reach the electrode (Jackson, 1999; Purcell, 1985, p. 371; Feynman, 1964, for example, Ch. 23, p. 2). The Ramo-Shockley theorem equates the total current (particle and displacement) measured in the external circuit with the microscopic motion of the charged particles in the domain between the electrodes.

Voltage-clamp experiments measure the total current I flowing into an electrode held at voltage E_m with respect to a grounded electrode. The Ramo-Shockley theorem (references given below) states that this current is

$$I = \frac{1}{1\,\text{volt}} \sum_j q_j \mathbf{W}\left(\mathbf{r}_j\right) \cdot \mathbf{v}_j \ . \tag{1}$$

We use the nomenclature of Yoder *et al*. (1997) where $\mathbf{v}_j$ and $\mathbf{r}_j$ are the instantaneous velocity and position vectors, respectively, of the particles j with charge q_j when the clamped voltage E_m is applied. $\mathbf{W}$ is the electric field that would be generated by removing *all* particle charges (mobile and fixed) from the domain and setting the clamped voltage to 1 volt. The only charges contributing to $\mathbf{W}$ are the charges needed to impose ground potential and 1 volt at the electrodes and charges induced by the electrode charges on and in the dielectrics of the domain. $\mathbf{W}$ is *not* the field that is present when the clamped voltage E_m is applied and the current is observed. The field resulting from the clamped voltage E_m enters the equation indirectly, through the positions $\mathbf{r}_j$ and velocities $\mathbf{v}_j$ that it imparts to mobile charged particles. The sum in Eq. 1 is over all mobile particle charges q_j in the domain, including those that belong to the channel protein and all ions in the bath solutions and the pore of the channel.

The measured current *I* of Eq. 1 is converted to charge by integrating over arbitrary trajectories that connect known starting locations $\mathbf{r}_j'$ of the particles to known en d-ing locations $\mathbf{r}_j''$. This integration yields the externally measured gating charge:

$$Q = -\frac{1}{1\,\text{volt}} \sum_j q_j \left[U\left(\mathbf{r}_j''\right) - U\left(\mathbf{r}_j'\right) \right] \tag{2}$$

where $U\left(\mathbf{r}\right)$ is the potential at location $\mathbf{r}$ that would be generated by removing *all* particle charges (mobile and fixed) from the domain and setting the clamped voltage to 1 volt. Again, the potential field present while the clamped voltage is held at E_m enters the equation only indirectly; it determines the locations of the charged particles.

The theorem was derived independently by Shockley (1938) and Ramo (1939) and is commonly used in computational electronics as a generalization of Kirchoff's current law that includes displacement current. The original derivations assumed negligible magnetic and radiation effects (that is, quasi-electrostatics) to describe electron transport in vacuum tubes. The theorem has subsequently been generalized to systems containing inhomogeneous linear dielectrics (Pellegrini, 1986; Kim *et al.,* 1991). An extended version for the full electrodynamic regime has been derived (Yoder *et al.,* 1996, 1997). We use the generalized quasi-electrostatic version of the theorem.

To illustrate the theorem, we give a simple derivation for a capacitive linear circuit that applies to a voltage-clamped system. Imagine that a vanishingly small conductive sphere *j* is placed at location $\mathbf{r}_j$, where it forms capacitors C_{jR} and C_{jG} (Fig. 1). The surfaces of capacitor C_{jR} are the conductive sphere and the recording electrode *R,* the electrode where E_m is applied in a voltage clamp experiment. The surfaces of capacitor

C_{jG} are the conductive sphere and the second (grounded) voltage clamp electrode G and any other grounded surfaces.

We consider two experiments. In the first experiment, labeled (1), a single, mobile, charged particle with charge q_j is placed in the small conductive sphere located at $\mathbf{r}_j$ and the electrode R is set to zero potential. The charge induced on R (the charge that the voltage clamp applies to maintain R at zero potential) will be

$$q_R^{(1)} = -q_j \frac{C_{jR}}{C_{jR} + C_{jG}}. \tag{3}$$

The charge induced on the electrode can be computed by Eq. 3 for any q_j if the calibration factor $C_{jR} \Big/ \left(C_{jR} + C_{jG} \right)$ is known. We determine this factor in a separate, second experiment, labeled (2).

In the second experiment, the charge of all charged particles is removed (that is, $q_j^{(2)} = 0$), and a voltage of 1 volt is imposed on R. The capacitors C_{jR} and C_{jG} now form a voltage divider, and the resulting voltage at $\mathbf{r}_j$ is

$$U^{(2)}\left(\mathbf{r}_j\right) = \frac{C_{jR}}{C_{jR} + C_{jG}} \times \left(1 \text{ volt}\right) \tag{4}$$

Combining the results of the two experiments, we have

$$q_R^{(1)} = -\frac{1}{1 \text{ volt}} q_j U^{(2)}\left(\mathbf{r}_j\right). \tag{5}$$

This treatment can be extended to a system of many small spheres j that contain charges q_j; by superposition, we then have

$$q_R^{(1)} = -\frac{1}{1\text{ volt}}\sum_j q_j U^{(2)}\left(\mathbf{r}_j\right) \tag{6}$$

If we move the charges j from locations $\mathbf{r}_j'$ to locations $\mathbf{r}_j''$, the electrode charge will change by

$$Q = -\frac{1}{1\text{ volt}}\sum_j q_j\left[U^{(2)}\left(\mathbf{r}_j''\right) - U^{(2)}\left(\mathbf{r}_j'\right)\right] \tag{7}$$

which is the Ramo-Shockley theorem in the form of Eq. 2.

APPLICATIONS TO ION CHANNELS

Defining electrical coordinate and electrical travel

For a given dielectric geometry of the baths, membrane, and channel, Eq. 2 relates induced electrode charge with microscopic charge and the function $U(\mathbf{r})$. The geometric coordinate $\mathbf{r}$ is thereby mapped onto the "electrical coordinate" $U(\mathbf{r})/(1\text{ volt})$ and the geometric travel $\mathbf{r}_j'' - \mathbf{r}_j'$ onto the "electrical travel" of the charge j,

$$T_{el} \equiv \frac{1}{1\text{ volt}}\left[U\left(\mathbf{r}_j''\right) - U\left(\mathbf{r}_j'\right)\right]. \tag{8}$$

The potential U is found by solving the Poisson equation for the channel geometry with 1 volt of potential on the electrode R and all the linear dielectrics in place, but no charged particles of any kind (neither fixed or mobile structural charges, nor bath ions). The only charges present are the electrode charges that maintain boundary conditions like the potential of 1 volt and polarization charges induced by the electrodes on and in the dielectrics. The dielectrics that we include are linear and isotropic; their polarization settles much faster than the experimentally observable charge movements. The effects of these linear dielectrics are expressed in Eqs. 1 and 2 by the field $\mathbf{W}$ or the potential U. A

voltage-gated channel will add what might be described as a nonlinear, time-dependent, and probably location-dependent anisotropic polarizability to the membrane; charge movements underlying such complex behavior reflect the interesting gating movements of the channel protein. They are included as explicit charge movements under the sums of Eqs. 1 and 2.

Figs. 2 and 3 show calculations of electrical coordinate maps, found by solving the Poisson equation numerically on a domain in which bath solutions, lipid, and protein are represented as linear, isotropic dielectrics. The dielectric geometries shown are low-resolution representations of an open conduction pore (Fig. 2) and of a "gating pore" that allows an S4 segment to slide through the membrane (Fig. 3). The domain is cylindrical about the vertical axis, and is represented in an axial cross-section. The points **r** of each contour line are each at the same potential U; they are plotted at increments of $\Delta U = 0.05$ volt (and some at $\Delta U = 0.025$ volt). Each "electrical coordinate" $U(\mathbf{r})/(1\text{ volt})$ is a surface and not a unique location **r**; all points of the surface represented by a contour line are at the same electrical coordinate from the external voltage clamp electrode.

A map of electrical coordinates can help predict the gating charge measured in a thought experiment, for example, if a charge q were to be moved between two locations. According to Eq. 2, the gating charge would be $Q = -qT_{el}$, where T_{el} can be read from the map. Note that manipulating one or many charges this way does not affect the map; the map changes only when the geometry of the linear dielectrics changes. If many charges are moved simultaneously, their contributions to the gating charge sum algebraically. This additivity itself may appear surprising because it holds in a domain of condensed matter. The invariance of the map and the additivity of individual readings make

the “electrical travel” defined via the Ramo-Shockley theorem a useful concept.

Figs. 2 and 3A are computed in a small domain that is typical for a simulation. In actual experiments, electrodes are much farther away from the membrane, making the electrical travel across each bath much larger than the electrical travel across the membrane. This leads to an apparent paradox: in the experimental situation, movement of structural charge in the membrane itself contributes very little to the measured charge Q in Eq. 2, since the structural charge is scaled by a small electrical travel. In this case, Q is dominated by the contributions of bath ions that move in response to the movement of charges in the membrane (and thus conduct the gating current towards the electrodes). In principle, Eqs. 1 and 2 can be applied to any domain in a circuit that is bounded by surfaces where controlled potentials are applied, provided that the movements of *all* charges in the domain (for example, all ions in the bathing solutions) are included in the summation. If the domain is geometrically expanded the electrical travel of all charges is reduced, but charges newly included in the domain are appended to the summation. For a chosen domain (large or small), the Ramo-Shockley theorem *exactly* computes the current that would be measured in an experiment performed in that geometry.

In a simulation, the results that compare best to the experiments require large baths with many ions. The other extreme of modeling the bathing solutions as ideal conductors is also useful, however. Such baths extend the electrodes to the boundaries of the membrane and protein and reduce the summations in Eqs. 1 and 2 to the movements of charges within the channel/membrane. The result is an upper limit to the measured gating charge because each geometrical movement results in the maximal possible electrical travel. Such a map is shown in Fig. 3B; later we show how an upper limit of the gating

charge helps explain experimental results.

A model of the bath at higher resolution has been considered by Islas and Sigworth (2001). They described the electric field in the baths by the linearized Poisson-Boltzmann equation for a system that includes the bath ions (as their time-averaged densities) and the membrane/protein matrix without the structural charges. Their electrical coordinate was defined using this field. This approach yields a well-defined map of electrical coordinates — which is possible because the polarization of the bathing solutions is assumed to be linear — but it also contains an inconsistency. The region in which the electrical coordinate varies includes the bathing solutions, but the movements of ions contained in the bathing solutions are not considered (the sum in Eq. 2 includes only structural charges of the membrane/protein). A simulation with discrete bath ions is necessary to assess the importance of the charge they omit.

Interpreting gating charges

When applied to gating charge experiments, the Ramo-Shockley theorem expresses gating charge as the product of the physical charge and the well-defined electrical travel of the physical charge, summed over all mobile charges present in the domain. To apply Ramo-Shockley, we consider, as a specific example, an experiment by Seoh *et al*. (1996) that produced an unforeseen result. Seoh *et al*. created mutants in which a charged residue of a membrane-spanning segment in a K channel monomer was replaced by a neutral residue. They found that deleting a positive charge of the S4 segment eliminated up to $7e_0$ of measured gating charge (e_0 is the proton charge). Because of the tetrameric structure of the protein, one might expect that at most $4e_0$ of gating charge would be eliminated in such mutants. In the Seoh *et al*. experiment, the removed physical charges

are known, but their movement is not. It is not clear a priori if the movement of these atomic charges (in the native protein) could contribute a disproportionately large amount to the gating charge recorded by the external electrodes.

Eq. 2 allows one to narrow the interpretation of these results. For instance, one might think that even if the charges move between the same starting and ending points, the measured charge would depend on the local electric field in which the physical charges travel. If this were true, charges traveling across a region of high local field strength might contribute disproportionately to the measured gating charge, or their deletion might reduce gating charge disproportionately. Eq. 2 states, however, that neither structural charges nor polarization charges can exert such an amplifying effect on the relation between atomic and measured charge movements; if the mobile charges move between the same points $\mathbf{r}_j'$ and $\mathbf{r}_j''$, the electrical travel $\left[U\left(\mathbf{r}_j''\right)-U\left(\mathbf{r}_j'\right)\right]/\left[1\text{ volt}\right]$ does not change because the particle charges and charges induced by particle charges do not contribute to $U\left(\mathbf{r}\right)$.

The gating process is, of course, not independent of the local electric field present where and when the charges move. In particular, changes in the local electric field can change the electrical travel that the mobile charges actually undergo when perturbed by an applied voltage, although they do not change the map defining electrical coordinates. For example, deletion of some of the mobile structural charges of an S4 helix that moves as a solid body likely reduces the total electric force acting on the helix. Consequently, the geometric travel of the mutated helix, and of the undeleted S4 charges on it, might be reduced. The positions $\mathbf{r}_j'$ and/or $\mathbf{r}_j''$ would change, reducing the measured gating charge.

Within the constraints set by the Ramo-Shockley theorem, the experiment of Seoh *et al*. can be interpreted in two ways: (1) that deletion of charges q_k restricts in some way the electrical travel of the other mobile charges q_j (changing $\mathbf{r}_j'$ and/or $\mathbf{r}_j''$) or (2) that the mutant channels have a different dielectric geometry from the native channel, changing $U(\mathbf{r})$. Of course, the experiment might both restrict electric travel and change the dielectric geometry.

Ramo-Shockley and energy

Electrophysiologists have long used effective parameters to assign energy contributions to physical processes inferred from experiments. For example, Hodgkin and Huxley (1952) hypothesized that charged particles moving in the membrane electric field do the work $W = ze_0E_m$ on the membrane component that creates the voltage dependence of the Na^+ and K^+ conductances. Here, E_m is the membrane potential, z the effective valency of the particle, and e_0 the proton charge. Similarly, Woodhull (1973) described the voltage-dependent block of Na^+ current by protons assuming that the "potential energy" of the blocking proton included a contribution $W = e_0\delta E_m$, where δ is the "fraction of membrane potential acting at the site." However, caution must be taken if measured gating charges (or effective charges described by parameters like z or δ) are used to infer the energetics of the underlying physical process.

When a gating current flows between the external electrodes of a voltage clamp, external work is exchanged with the circuitry of the voltage clamp. The amount of work is easily computed because it is the work that moves the gating charge between the constant potentials of the two electrodes. However, the Ramo-Shockley theorem cannot be

used to identify the external work with a change in energy of the particles (for example, inside the channel protein) whose movement produces the gating current. *The Ramo-Shockley theorem connects external current and internal charge movement, but not the associated energies*. The theorem is based on the superposition principle, which applies to the electrostatic field and potential, but not energy (Griffiths, 1999, p. 96). Therefore, the external work can *not* be assigned to individual charges q_j using the electrical travel in Eq. 2 as a distribution key.

The complexity of the system makes the interpretation of external work difficult in other ways. A voltage clamp experiment involves the thermodynamically coupled electrodes, bathing solutions, lipid membrane, and channel. The experiment occurs in an open system in which charge, energy, and matter can flow from one part of the system to another (for example, from the bathing solution into the channel protein). The change in internal energy in an open and dissipative system like a channel is not well-defined until the reversible and irreversible flows of heat and all other flows of energy and matter into and out of the system are known.

Calculating current in simulations of ion channels

Eq. 1 allows calculation of currents when charged particles in a simulation move between positions, for instance in simulations of gating current or of ionic current flowing through the pore of an ion channel. Eq. 1 estimates current much more efficiently than counting ions crossing a surface (Chung *et al.*, 1998), because it provides a sample of the instantaneous current at each time step of the simulation, whereas counting of crossings produces relatively few current pulses and does not capture displacement current nor its contribution to the noise. Similarly, Eq. 2 allows one to track charge effi-

ciently.

The sampling of current is an important application of the Ramo-Shockley theorem in electronic device simulations at the particle level (Gruzinskis *et al.,* 1991; Babiker *et al.,* 1998). This method is just now finding its way into simulations of ion channels (U. Ravaioli (University of Illinois, Urbana-Champaign), personal communication; M. Saraniti (Illinois Institute of Technology), personal communication).

CONCLUSION

The Ramo-Shockley theorem allows one to relate, in a general way, microscopic movements of physical charges in ion channels to macroscopic currents recorded in a voltage clamp.

ACKNOWLEDGEMENTS

We thank Drs. Marco Saraniti and Karl Magleby for useful discussions. This work is based upon work supported under an NSF Graduate Research Fellowship (to A.P.) and grants from DARPA (SimBioSys BAA01-07) and NIH/NIGMS (R01 GM 067241) (to B.E.).

References

Aggarwal, S.K. and R. MacKinnon 1996. Contribution of the S4 segment to gating charge in the *Shaker* K^+ channel. Neuron 16:1169-1177.

Babiker, S., A. Asenov, N. Cameron, S. P. Beaumont, and J. R. Barker. 1998. Complete Monte Carlo RF analysis of "real" short-channel compound FET's. IEEE Transactions on Electron Devices. 45:1644-1652.

Bezanilla, F. 2002. Voltage sensor movements. J. Gen. Physiol. 120:465-473.

Chung, S.H., M. Hoyles, T.W. Allen and S. Kuyucak. 1998. Study of ionic currents across a model membrane channel using Brownian dynamics. Biophys. J. 75:793-809.

Feynman, R. P., R. B. Leighton and M. Sands. 1963. The Feynman Lectures on Physics: Mainly Electromagnetism and Matter. Addison-Wesley Publishing Co., New York, USA.

Griffiths, D.J. 1999. Introduction to electrodynamics. 3rd ed. Prentice Hall, Upper Saddle River, New Jersey, USA.

Gruzinskis, V., S. Kersulis, and A. Reklaitis. 1991. An efficient Monte Carlo particle technique for two-dimensional transistor modelling. Semicond. Sci. Technol. 6:602-606.

Hille, B. (2001). Ion channels of excitable membranes. 3rd ed. Sinauer Associates, Inc., Sunderland, Massachusetts, USA.

Hodgkin, A. L. and A. F. Huxley. 1952. A quantitative description of membrane current and its application to conduction and excitation in nerve. J. Physiol. 117:500-544.

Hodgkin, A. L., A. F. Huxley, and B. Katz. 1952. Measurement of current-voltage relations in the membrane of the giant axon of *Loligo*. J. Physiol. 116:424-448.

Jackson, J. D. 1999. Classical Electrodynamics. 3rd ed. John Wiley and Sons, Inc. New York, USA.

Jiang, Y., A. Lee, J. Chen, V. Ruta, M. Cadene, B. T. Chait and R. MacKinnon. 2003. X-ray structure of a voltage-dependent K^+ channel. Nature (London) 423: 33-41.

Islas, L.D. and F.J. Sigworth. 2001. Electrostatics and the gating of *Shaker* potassium channels. J. Gen. Physiol. 117:69-89.

Kim, H., H. S. Min, T. W. Tang, and Y. J. Park. 1991. An extended proof of the Ramo-Shockley theorem. Solid-State Electronics. 34:1251-1253.

Pellegrini, B. 1986. Electric charge motion, induced current, energy balance, and noise.

Phys. Rev. B. 34:5921-5924.

Purcell, E. M. 1985. Electricity and Magnetism. McGraw Hill, New York, USA.

Ramo, S. 1939. Currents induced by electron motion. Proc. IRE. 27:584-585.

Schneider, M. and W.K. Chandler 1973. Voltage-dependent charge movement in skeletal muscle: a possible step in excitation-contraction coupling. Nature (London) 242:244-246.

Seoh, S.-A., D. Sigg, D. M. Papazian, and F. Bezanilla. 1996. Voltage-sensing residues in the S2 and S4 segments of the Shaker K^+ channel. Neuron. 16:1159-1167.

Shockley, W. 1938. Currents to conductors induced by a moving point charge. J. Appl. Phys. 9:635-636.

Stühmer W.F., F. Conti, H. Suzuki, X. Wang, M. Noda, N. Yahagi, H. Kubo and S. Numa 1989. Structural parts involved in activation and inactivation of the sodium channel. Nature (London) 339:597-603.

Woodhull, A. M. 1973. Ionic blockage of sodium channels in nerve. J. Gen. Physiol. 61:687-708.

Yoder, P. D., K. Gärtner, and W. Fichtner. 1996. A generalized Ramo-Shockley theorem for classical to quantum transport at arbitrary frequencies. *J. Appl. Phys.* 79:1951-1954.

Yoder, P. D., K. Gärtner, U. Krumbein, and W. Fichtner. 1997. Optimized terminal current calculation for Monte Carlo device simulation. IEEE Transactions on Computer-Aided Design of Integrated Circuits and Systems. 16:1082-1087.

Figure Captions

Figure 1. Equivalent circuits for the two thought experiments used to derive the Ramo-Shockley theorem (see text).

Figure 2. Mapping geometric coordinates to electrical coordinates. A conductive pore provides an aqueous bridge through the membrane (qualitatively similar to the open pore of a K channel (Jiang et al., 2003)). The domain (*panel A*, drawn to scale) is a generalized cylinder (maximal radius 5 nm, length 13 nm) and is shown in an axial cross-section; the highlighted part in A is shown at larger scale in *panel B*. Electrodes bound the two hemispherical baths. The top (external) electrode is grounded, whereas the bottom (internal) electrode is maintained at 1 volt. Isopotential lines are shown at 50 mV intervals (*solid lines*); some intermediate isopotentials corresponding to 25 mV intervals are also included (*dashed lines*). The isopotential lines also mark surfaces of constant "electrical coordinate" (with respect to the grounded electrode), corresponding to intervals of 0.05 (or 0.025). The dielectrics are described by dielectric coefficients of 80 (bath solutions and pore, *unshaded*) and 2 (lipid and channel, *shaded in gray*). A linearly varying potential is imposed at the lateral boundary of the membrane (*dark gray lines)*.

Figure 3. Mapping geometric coordinates to electrical coordinates. An S4 helix segment spans the membrane through a "gating pore" (as envisioned by Bezanilla (2002)). The domain either includes bath solutions between the membrane and electrodes (*panel A*, c.f.

Fig. 2), or the electrodes cover membrane and protein like a thin metal foil (*panel B*). Isopotential lines are shown at 50 mV intervals (*solid lines*); some intermediate isopotentials corresponding to 25 mV intervals are also included (*dashed lines*). The dielectrics are described by dielectric coefficients of 80 (bath solutions, *unshaded*) and 2 (lipid and channel, *shaded in gray*).

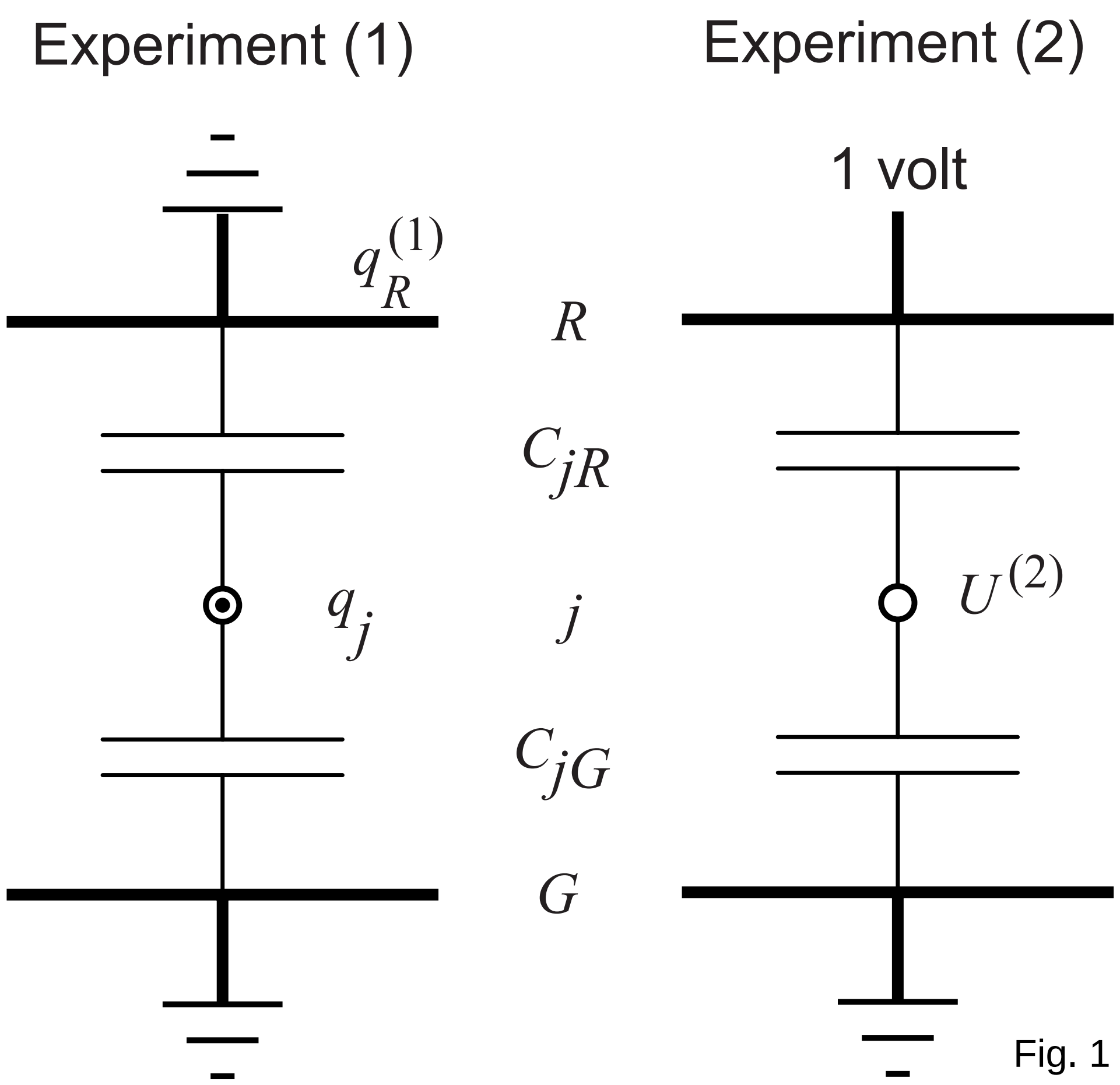

Fig. 1

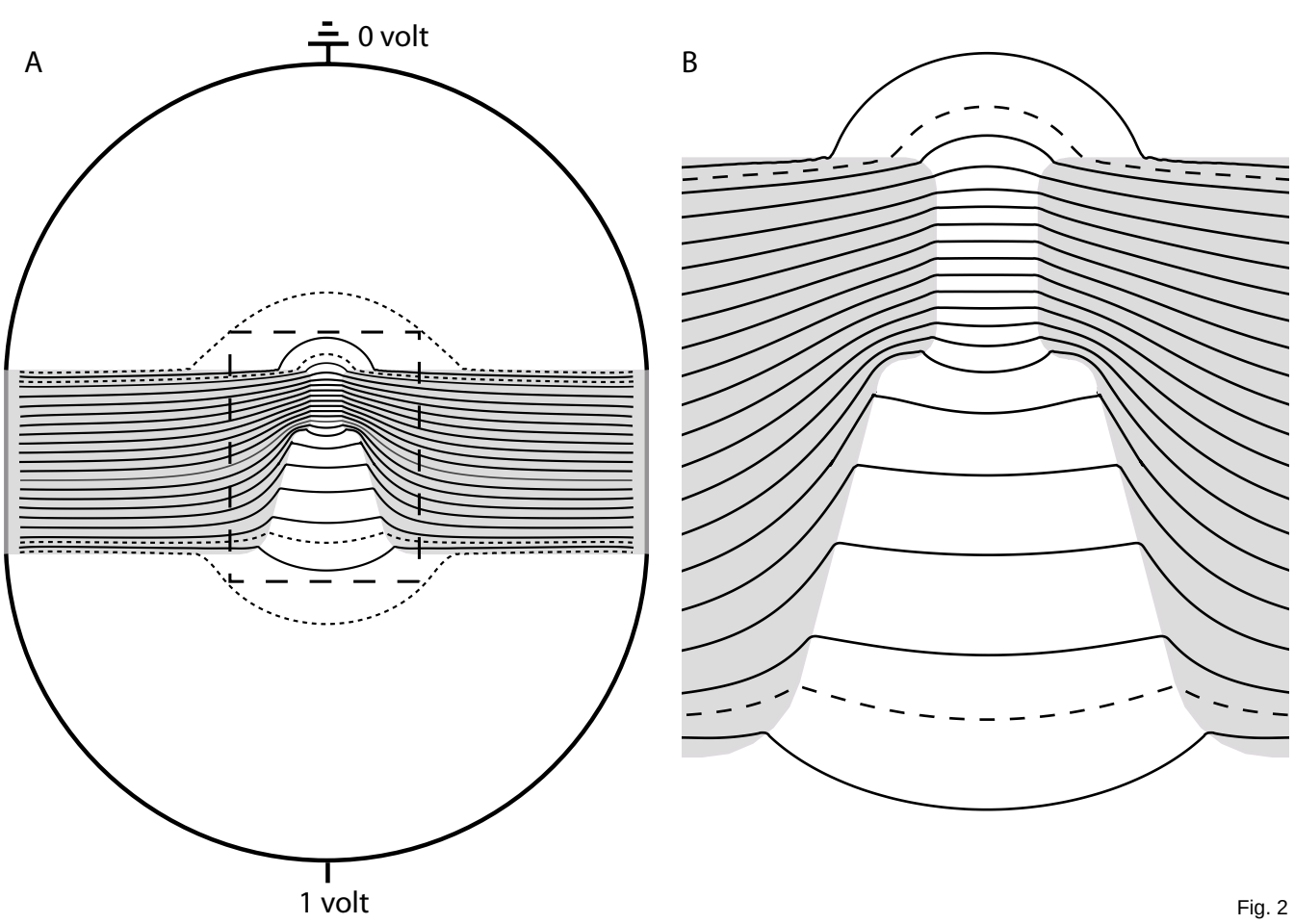

Fig. 2

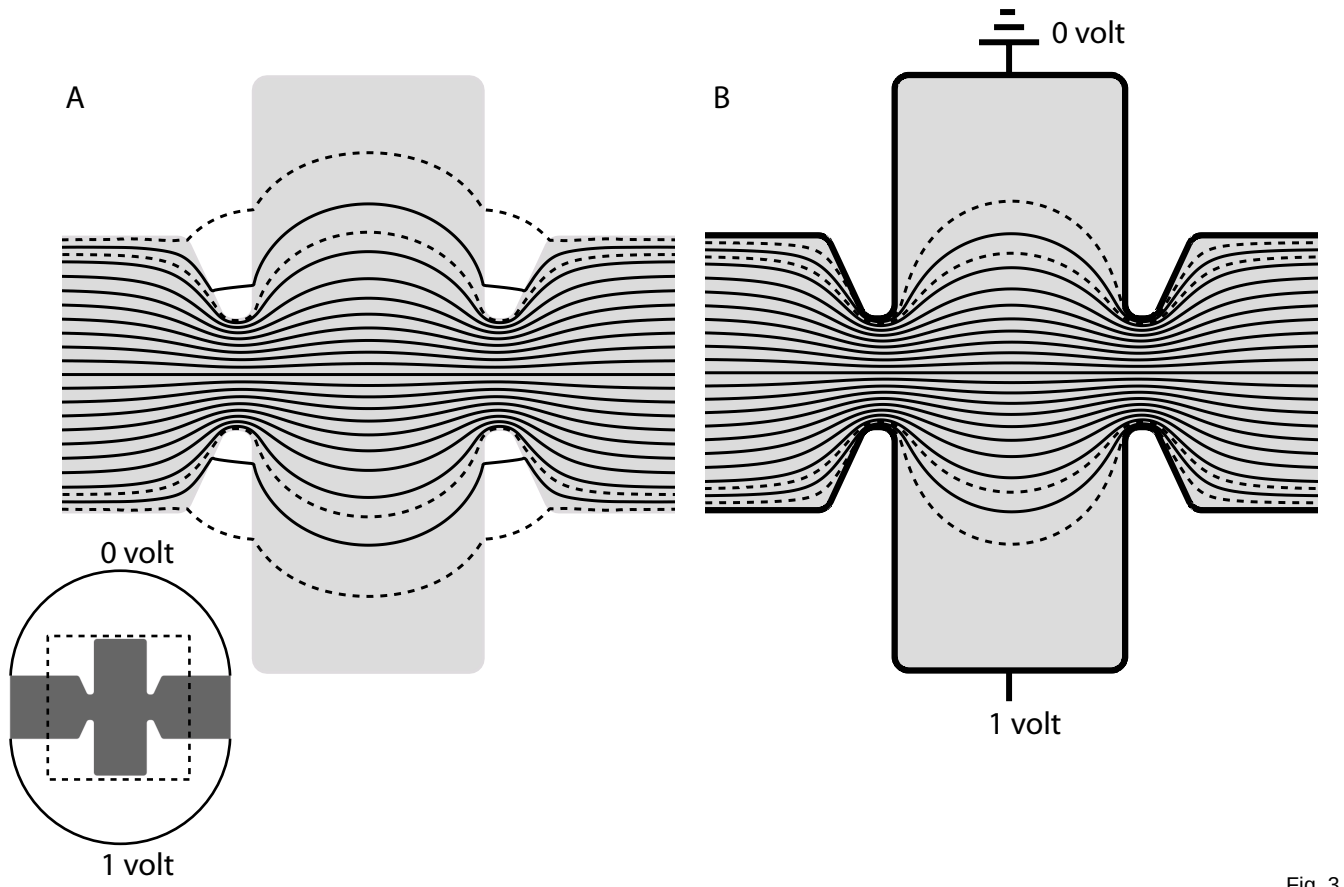

Fig. 3