Supplementary Material:
The sliding-helix voltage sensor

Mesoscale views of a robust structure-function relationship

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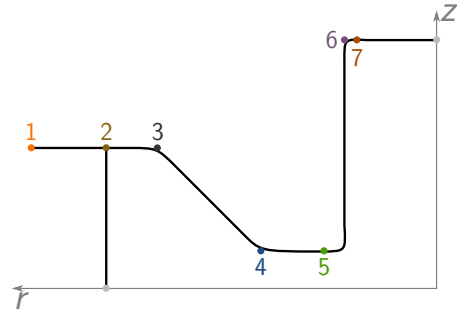
S1 Geometrical parameters of VS models

a



b

Model		1	2	3	4	5	6	7
α (1)	r	6.0	2.532	1.966	1.566	1.466	1.266	1.0
	z	1.5	1.5	1.5	0.5015	0.5015	3.7515	3.7515
3_{10} (1)	r	6.0	2.492	1.946	1.546	1.446	1.246	0.98
	z	1.5	1.5	1.5	0.602	0.602	4.602	4.602
α (2)	r	6.0	2.532	1.966	1.566	1.466	1.266	1.0
	$+z$	1.5	1.5	1.5	0.10225	0.10225	3.7515	3.7515
	$-z$	1.5	1.5	1.5	0.90075	0.90075	3.7515	3.7515
3_{10} (2)	r	6.0	2.492	1.946	1.546	1.446	1.246	0.98
	$+z$	1.5	1.5	1.5	0.253	0.253	4.602	4.602
	$-z$	1.5	1.5	1.5	0.951	0.951	4.602	4.602
α (3)	r	6.0	2.532	1.966	1.566	1.466	1.266	1.0
	z	1.5	1.5	1.5	0.90075	0.90075	4.15075	4.15075
3_{10} (3)	r	6.0	2.492	1.946	1.546	1.446	1.246	0.98
	z	1.5	1.5	1.5	0.951	0.951	4.951	4.951
α (4)	r	6.0	2.532	1.966	1.566	1.466	1.266	1.0
	$+z$	1.5	1.5	1.5	0.5015	0.5015	4.15075	4.15075
	$-z$	1.5	1.5	1.5	1.3	1.3	4.15075	4.15075
3_{10} (4)	r	6.0	2.492	1.946	1.546	1.446	1.246	0.98
	$+z$	1.5	1.5	1.5	0.602	0.602	4.951	4.951
	$-z$	1.5	1.5	1.5	1.3	1.3	4.951	4.951

Table S2: *Geometrical parameters of models.* (a) Mapping from geometrical positions in Figure 1 to indexed geometrical parameters. Inflection points and lengths are varied among different models, depending on countercharge positions, helix conformation and gating canal size. Positions in r (radial) and z (axial) coordinates are marked by a colored point and an associated number. All corners are rounded with curvature radius of 0.15 nm. Points 1,2,3,4, and 6 define the profile of the lipid and protein dielectrics, from the outermost end of the lipid domain (1) to the face of the S4 cylinder (6). Point 5 marks the radial position assigned to countercharges, point 7 the radial position of S4 charges. (b) Coordinates (in nm) of the points defining membrane and protein metrics. For models with symmetrical gating canal, r and z define both the extracellular and intracellular surfaces. For models with an asymmetric gating canal, $+z$ values are used for the extracellular surface and $-z$ for the intracellular surface. These metrics apply regardless of electrode positioning. The numbers in parentheses listed in the first column refer to the variants of gating canal geometry used in the models for Fig. 6.

S2 Charge distributions of VS models

The sliding helix in our VS models is a microscopic voltage sensor, thus subject to thermal agitation. Its behavior must be described in statistical terms. In this section, stochastic VS behavior is visualized for several models presented in the paper, both as figures for a fixed applied voltage (-100 mV; Figs. S3–S6) and in animations with voltage increasing uniformly over time from -100 to +100 mV (Animations S8–S11, respectively).

The figures show two stochastic aspects of VS behavior: (1) the mean positions of the S4 charges (marked by blue balls), and (2) the charge density distribution of S4 charge (represented by a blue cloud with a color intensity proportional to the charge density there). A high density of color marks the locations where the S4 charges dwell frequently, as opposed to their mean positions.

The mean position for each charge is computed from Eq. 8 using the positions $\mathbf{r}_k$ for the charge q_k as the random variable X, using the partition function with translational and rotational degrees of freedom. Since the helix behaves as a solid body, the helix position $\mathbf{r}$ fixes the positions $\mathbf{r}_k$ for the charges q_k. That relationship allows us to define the partition function for the positions $\mathbf{r}_k$ in terms of the partition function for the helix position $\mathbf{r}$, as well as the energy functions for $\mathbf{r}_k$ in terms of the energy function for the helix position.

In other words, by applying Eq. 8 to a model with $X = \mathbf{r}_k$, the mean position $\langle \mathbf{r}_k \rangle$ for any charge can be calculated given the probability of configuration ij (P_{ij}, Eqs. 7 & 6):

$$\langle \mathbf{r}_k \rangle = \sum_{i,j} \mathbf{r}_{k,ij} P_{ij} = \frac{1}{\mathcal{Q}} \sum_{i,j} \mathbf{r}_{k,ij} e^{-\Delta W_{ij}/k_B T}, \tag{S1}$$

where ΔW_{ij} is the work to construct configuration ij from a reference configuration, and $\mathbf{r}_{k,ij}$ is the position of charge k in configuration ij.

Likewise, the distribution of charge can be computed by applying the partition and energy functions in terms of the position of charges $\mathbf{r}_k$. The charge density $\bar{z}(\mathbf{r})$ is then the sum over all charges of the probability of each charge being located at $\mathbf{r}$, multiplied by its valency, and normalized:

$$\bar{z}(\mathbf{r}) = \frac{\sum\limits_{\substack{i,j,k: \\ \mathbf{r}_{k,ij} \approx \mathbf{r}}} P_{ij} z_k}{\sum\limits_{i,j,k} P_{ij} z_k}, \tag{S2}$$

where $\mathbf{r}_{k,ij} \approx \mathbf{r}$ means that charge k in configuration ij is collocated with $\mathbf{r}$ for graphical purposes. The color representations for the animations are proportional to $\bar{z}(\mathbf{r})$ normalized to the highest charge density at that frame's potential.

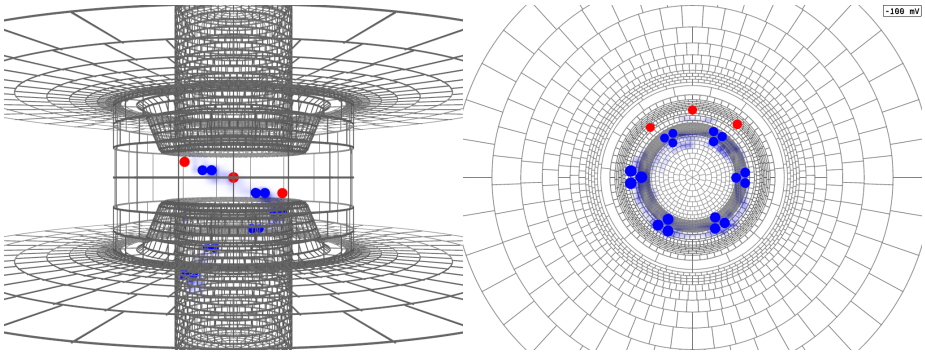


Figure S3: *Standard α-helical model: Animation S8* Position and distribution of charges for model α (1) in Table S2b with $\epsilon_p = 4$. Red symbols represent fixed negative countercharges, blue symbols represent the mean position of $+1/3$ e_0 on S4 arginines, and blue shading represents the relative probability of positive charge at a given position.

S3 Charge-voltage relations based on hypothesized energy maps

We derive analytical charge-voltage relations for two hypothesized maps of voltage-independent configurational energy W_1: (1) a map that restricts the S4 segment to exactly two possible positions associated with displaced charges Q_1 and Q_2 and equal energies ($W_1 = 0$); and (2) a map that restricts the S4 segment to a range of positions with displaced charges between Q_1 and Q_2 and provides a uniform level of energy within that range ($W_1 = 0$).

When the voltage V_m is applied at the bath electrodes, the total configurational energy for any possible S4 position with displaced charge Q is the external work W_2 as defined by Eq. 5. Because the displaced charge determines the configurational energy, no further specification (e.g. of S4 positions) is needed to fully describe the relation between displaced charge and applied voltage in these systems.

Bistable system

For the bistable system (1), the partition function is the sum

$$\mathcal{Q} = \exp\left(\frac{Q_1 V_\mathrm{m}}{k_B T}\right) + \exp\left(\frac{Q_2 V_\mathrm{m}}{k_B T}\right). \tag{S3}$$

The expected charge-voltage relation is

$$\langle Q \rangle = \frac{Q_1 \exp\left(\frac{Q_1 V_\mathrm{m}}{k_B T}\right) + Q_2 \exp\left(\frac{Q_2 V_\mathrm{m}}{k_B T}\right)}{\mathcal{Q}}. \tag{S4}$$

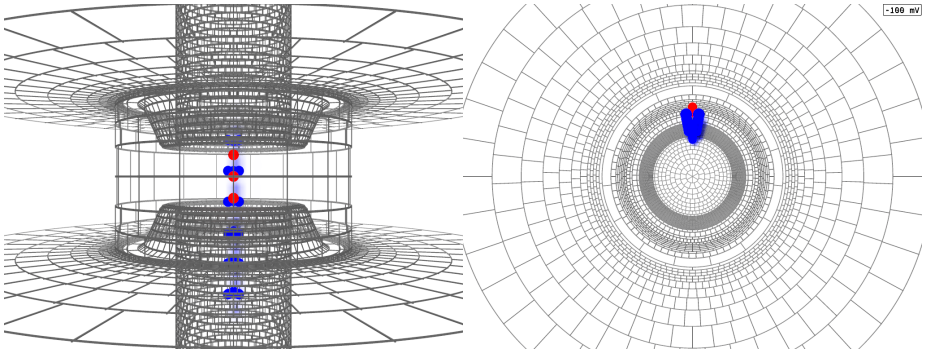


Figure S4: *Standard* 3_{10}*-helical model: Animation S9* Position and distribution of charges for model 3_{10} (1) in Table S2b with $\epsilon_p = 4$. See the description of Fig. S3 for further details.

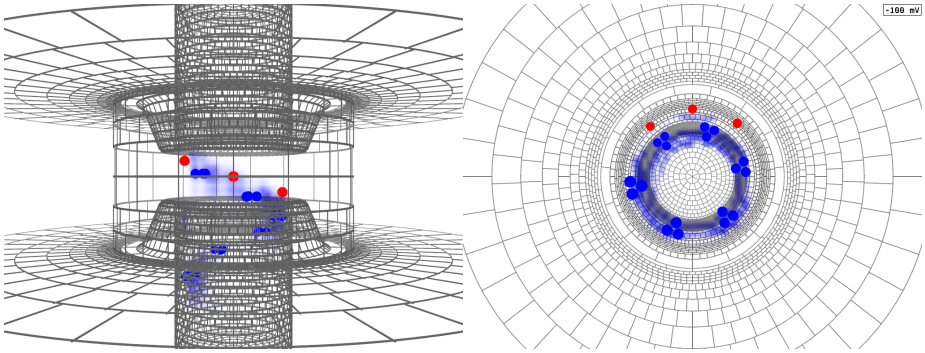


Figure S5: α*-helical model with* $\epsilon_p = 16$*: Animation S10* Position and distribution of charges for model α (1) in Table S2b with $\epsilon_p = 16$. See the description of Fig. S3 for further details. This is the model used in Fig. 5.

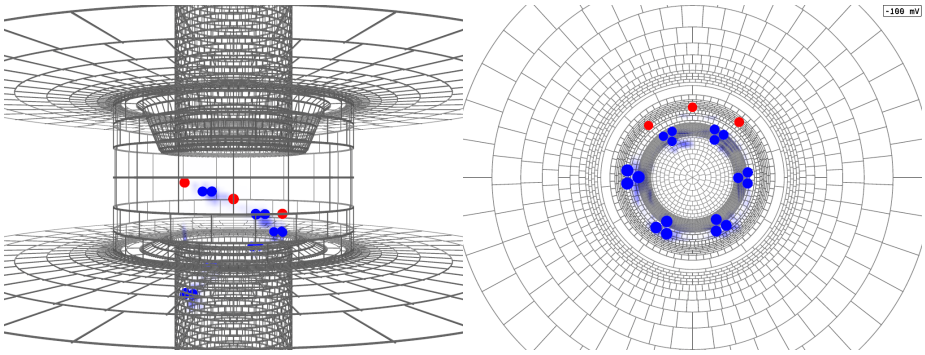


Figure S6: *α-helical model with asymmetric gating canal: Animation S11* Position and distribution of charges for model α (4) in Table S2b with $\epsilon_p = 4$. See the description of Fig. S3 for further details. This is the model used in Fig. 6, outline 4.

For the applied voltage $V_\mathrm{m} = 0$, $\langle Q \rangle = (Q_1 + Q_2)/2$, and the slope at this midpoint of the charge-voltage relation is

$$\frac{\partial \langle Q \rangle}{\partial V_\mathrm{m}} = \frac{(Q_2 - Q_1)^2}{4 k_B T}. \tag{S5}$$

The asymptotic displaced charges Q_1 and Q_2 are approached exponentially as the applied voltage of the respective polarity is made exceedingly large.

Continuous system

For the continuous system (2), the partition function is the integral

$$\mathcal{Q} = \frac{1}{Q_2 - Q_1} \int_{Q_1}^{Q_2} \exp\left(\frac{Q V_\mathrm{m}}{k_B T}\right) dQ. \tag{S6}$$

The expected charge-voltage relation is

$$\langle Q \rangle = \frac{\frac{1}{Q_2 - Q_1} \int_{Q_1}^{Q_2} Q \exp\left(\frac{Q V_\mathrm{m}}{k_B T}\right) dQ}{\mathcal{Q}}, \tag{S7}$$

Executing the integrations yields

$$\langle Q \rangle = \frac{Q_2 \exp\left(\frac{Q_2 V_\mathrm{m}}{k_B T}\right) - Q_1 \exp\left(\frac{Q_1 V_\mathrm{m}}{k_B T}\right)}{\exp\left(\frac{Q_2 V_\mathrm{m}}{k_B T}\right) - \exp\left(\frac{Q_1 V_\mathrm{m}}{k_B T}\right)} - \frac{k_B T}{V_\mathrm{m}}. \tag{S8}$$

Using power series expansion of the exponentials in the vicinity of $V_\mathrm{m} \approx 0$, one finds for the charge $Q(V_\mathrm{m} = 0) = (Q_2 - Q_1)/2$, and for the derivative with

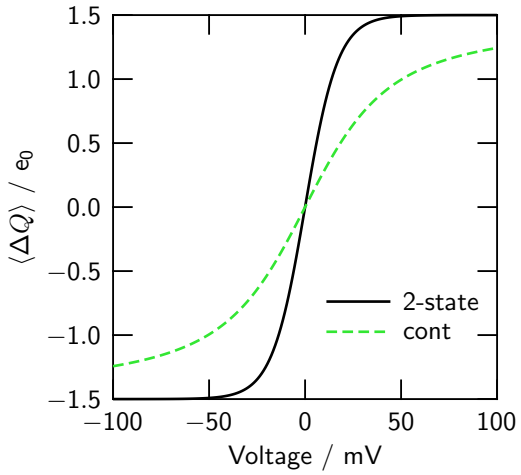


Figure S7: *Analytical charge-voltage relations for the 2-state and continuous S4 models.* Extreme charge displacements are set to $Q_1 = -1.5e_0$ and $Q_2 = +1.5e_0$ for both models.

respect to applied voltage at this point

$$\frac{\partial\langle Q\rangle}{\partial V_{\mathrm{m}}} = \frac{(Q_2 - Q_1)^2}{12k_BT}. \tag{S9}$$

This derivative is exactly 1/3 that of the bistable system (Eq. S5).

The difference between the charge-voltage relation and the asymptotic charges vanishes hyperbolically with exceedingly large voltage because of the term $-k_BT/V_m$ in equation S8, in contrast with the exponential approach predicted for the bistable system (Eq. S4).

Comparison of the analytical models

The relations between displaced charge and voltage (Eqs. S4 and S8) are shown for a total charge displacement of 3 elementary charges in Fig. S7. Note the differences in midpoint slopes and in asymptotic behaviors.