## *Supporting Information*

# 1 Homology Model

Homology models were constructed with Modeller v9.1(1), which minimizes an objective function that accounts for dihedral angles, bond lengths and torsions, electrostatic interactions in addition to the conformation indicated by the Kv1.2 template. One hundred unique models were generated and eight, with the most favorable objective value, were chosen for further evaluation. Procheck can be used to compute a G-factor, which reflects the correspondence of the Ramachandran plot (**Figure S1**), torsion angles and covalent geometry to known protein structures. The model chosen for molecular dynamics studies had an overall G-factor of -0.3, which is within the range (>-0.5) of known high-resolution protein structures (**Figure S2**).

The model was further refined by simulating its motion in an all-atom lipid and water solvent using the NAMD simulation package(3). This enables the channel to settle into a stable conformation, taking into account physical intramolecular forces and solvent effects that affect the channel structure. For our simulations we used a recent version of the CHARMM force field(4)—CHARMM 22 for proteins(5) and CHARMM 27 for lipids(6). The initial step in simulating KCNQ1 in an all-atom environment is to insert the channel into a pre-equilibrated phosphatidylcholine (POPC) membrane, which is the main membrane constituent in a cardiac myocyte(7). This was done by aligning the protein with the membrane top and bottom as suggested experimentally, the R1 α-carbon at 13.7 Å from the membrane center(8, 9). Then lipid or water groups that overlapped or were within 0.8 Å of the protein were removed and water was inserted 10 Å above and below the protein. $Cl^-$ ions were added to compensate for an excess of positively charged residues and make the system electroneutral. The system contained 248 lipid groups and 23,939 water molecules (120,577 total atoms).

# 2 Motion of S4

In *Shaker* $K^+$ channels, experimental evidence indicates that channel opening involves translation and rotation of S4 that replaces the interaction between the outermost glutamic acid (E1) on S2 and the second arginine on S4 (R2) with interaction between E1 and the fourth arginine on S4 (R4)(10). Several experiments also suggest that in addition to rotation, S4 translates between 7 and 13 Å during channel opening(11-14). We translated S4 12 Å from the open state toward the intracellular space with an increment of 0.25 Å. The direction of translation was along the helix axis, calculated from the positions of the alpha carbons of residues 234 to 237 using vector algebra(15).

At each translation, S4 was also rotated ~2π/5 with an increment of π/100 around this axis to sample its motion (**Figure 1D**, in manuscript). A model at each position was created by creating a harmonic restraint for each of the new S4 α-carbon ($C_\alpha$) positions in Modeller, while the $C_\alpha$ in S1, S2, S5 (from the neighboring subunit) were fixed.

For these studies, we isolated the voltage sensing region of the channel, S1, S2, S3 and S4 from a single subunit and S5 from the neighboring subunit. Long extra- and intracellular loops were not expected to contribute significantly to the electrostatic energy (due to the high dielectric constant of these spaces) and were removed. Since the S4-S5 linker was not included in the simulations, the intracellular end of S4 was constrained to

stay within reach of its position in the crystal structure (15 Å, a value near to the distance that S4 was translated, 12 Å).

After each model is created, PDB type files are converted to PQR format by using PDB2PQR(16, 17) in preparation for energy calculations. At this point, the protonation state of H5 is checked to verify that its pKa is less than 7.4 (body pH). This ensures that the free charge carried by this residue remains intact. pKa determination is accomplished by using PropKa, which uses an empirical algorithm based on many known protein structures(18) and is included in PDB2PQR.

## *3 Insertion of the Protein into an Implicit Membrane*

The automated insertion of the channel into an implicit membrane requires several considerations including:

1.) the ability of water and free ions to penetrate clefts in the protein
2.) the irregular shape of the protein
3.) the transition from a low dielectric core to a higher dielectric constant in the regions where there are ester and phospholipid groups near the surfaces of the membrane.

The varying dielectric ($\varepsilon$= 78 for water, 7 for the transition region, 2 for the membrane core) is incorporated by creating 3 sets of dielectric and free charge accessibility maps, one for each region, in APBS. Maps in APBS are based on a cubic spline surface of the protein(19) (APBS srfm option spl2), with the protein interior set to $\varepsilon$=2, and solvent accessibility to 0. After the maps are created, a top and bottom surface of the protein and membrane are defined by stepping from the top of the volume of interest to the first point where free charges are excluded ($\kappa$=0). If there is no protein midway through the volume the top is assigned the defined membrane value (for dimensions see **Figure 1E**).

These three maps are then combined such that: if a point resides on either side of the membrane the point is assigned the value of the water map, if a point is inside the transition region and beneath the membrane surface it is assigned the transition map value, and if a point is inside the membrane core and beneath the membrane surface it is assigned the core map value. To account for the penetration of water into the voltage sensing region a fourth map is created. Points indicated by this map are assigned the value of the high dielectric ($\varepsilon$=78) map. The isocontours showing the boundaries between each region are shown in **Figure 1E**.

For the membrane potential computations, described below in section 5, it is necessary to add charge to one side of the membrane. To accomplish this, we used the definition of the membrane top and added charge to any point above this surface.

## 4 Protein Energy Calculations

The electrostatic energy at a given conformation can be found by integrating the potential $\phi(\vec{r})$, found by the Linearized Poisson-Boltzmann equation (LPBE):

$$-\nabla\cdot[\varepsilon(\vec{r})\nabla\phi(\vec{r})]+\overline{\kappa}^2(\vec{r})\phi(\vec{r})=\frac{e_c}{k_BT}4\pi\rho(\vec{r})$$

where $\phi=\frac{e\Phi}{k_BT}$ is the reduced electrostatic potential and

$\Phi$ is the electrostatic potential (statvolt);

$\varepsilon$ is the inhomogeneous dielectric constant (statcoul$^2$ erg$^{-1}$ cm$^{-1}$);

$\rho$ is the density of charge within the protein (statcoul cm$^{-3}$);

$e_c$ is the electron charge (statcoul); $k_B$ is the Boltzmann constant (erg K$^{-1}$);

$T$ is the temperature (K).

and $\overline{\kappa}^2=\varepsilon_w\kappa^2$, with

$$\kappa^2=\frac{4\pi}{k_BT}\sum_\alpha q_\alpha^2\overline{\rho_\alpha}/\varepsilon_w$$

$\kappa^{-1}$ is the Debye-Hückel screening parameter (cm),

$q_\alpha$ is the charge (statcoul) and $\overline{\rho_\alpha}$ (cm$^{-3}$) is the bulk ion density of each ion type $\alpha$

and $\varepsilon_w$ is the dielectric constant of water (statcoul$^2$ erg$^{-1}$ cm$^{-1}$).

The position of the channel in the membrane determines which residues come in contact with free ions in the intra and extracellular solutions. The screening of the protein charges by these ions reduces the distance at which charged residues interact and is accounted for by $\kappa^2$ in the above equation. We assume $\kappa$ to be 0 inside the membrane as in reference(20), which implies that free ions do not reside within the membrane. The new formulation of $\kappa^2$ then becomes:

$$\kappa^2=\frac{4\pi}{k_BT}f(\vec{r})\sum_\alpha q_\alpha^2\overline{\rho_\alpha}/\varepsilon_w,$$

where $f(\vec{r})$ is 0 within the protein and membrane and 1 elsewhere.

To simulate the natural environment of the protein, a multilayer implicit membrane was constructed that is accounted for in the LPBE by $\varepsilon(\vec{r})$. The core of the membrane, which consists of the hydrophobic lipid tails, spans a region of 19 Å and is assigned a dielectric constant $\varepsilon_m$=2. Near the outer edge of the membrane, an increase in the dielectric constant is associated with the ester groups in the lipid headgroups. This transition region spans 3 Å on either side of the membrane and has a dielectric constant, $\varepsilon_i$=7. The phosphate groups that line the outer surface of the membrane correspond to a region with a very high dielectric constant, and this region is lumped with the water

region on each side of the membrane with $\varepsilon_w$=78(21). The water seen penetrating the pore in the all-atom simulation is mapped accordingly and assigned a value of $\varepsilon_w$ (**Figure 1E**, in manuscript).

The LPBE can be solved by using a multigrid method, implemented in the Adaptive Poisson Boltzmann Solver, APBS(22). Two levels of refinement are used—a coarse pass followed by a focusing step that includes only the volume of interest. For the coarse grid, the size of the box is 180x180x180 $Å^3$ which is then focused to 65x60x75 $Å^3$. Both steps utilize a mesh with 97 gridpoints in each of the x and y directions and 129 points in z. The maximum grid spacing is 0.67 Å.

The electrostatic energy of the protein inserted in this membrane is

$$W^p(q) = \frac{1}{2}\int_V \Phi^p\left(\vec{r},q\right)\rho\left(\vec{r},q\right)d^3r$$

where $q$ is the position of S4 and W is the energy in kJ/mol.

Discretizing the box in which the protein resides into a grid can result in charged atoms being split between more than one gridpoint. Upon solving, energy from the self interaction of the split charges contributes to the energy landscape. To overcome this difficulty, maps were computed for the heterogeneous dielectric (where the solvent dielectric differs from the protein) and for a homogeneous dielectric ($\varepsilon$=2). The homogeneous energy was then subtracted from the heterogeneous energy to create a solvent response map. To obtain the final energy, the coloumbic energy was added back in analytically ($\varepsilon$=2) by using Coloumb, a program that is included in the APBS package. Since the analytic solution does not split the charges, but instead considers them as point charges, it can be used as an appropriate substitute for the subtracted charges (which had contained self-interactions).

The energy of a channel in a given region of space can be reduced according to:

$$W^v = -k_B T \log \iint \exp\left(-W\left(r,\theta\right)/k_B T\right) dr d\theta$$

where $W^v$ is the effective energy for the volume, $r$ is translation and $\theta$ is rotation.

This equation returns a value close to that of the minimum energy in the region, which corresponds to the most likely state of the protein. To create our energy landscape, we used a region containing 12 conformations that spanned a translation of 1 Å and 1/25 $\pi$ radians.

While electrostatic energy provides an approximation to the free energy of the channel, the sudden changes in magnitude with small perturbations in translation and rotation prevent us from using it directly to study channel kinetics. The primary cause is a high energy barrier that must be overcome to move charged residues from the aqueous extra and intracellular environments to the transmembrane region. To compensate for these effects barriers were corrected by a factor of 0.125 to enable the energy conferred by $V_m$ to open and close the channel as required (**Figure S3**).

## 5 $V_m$ Energy Calculations

The contribution to the energy landscape from the transmembrane potential can be found with a modified Poisson-Boltzmann equation(20):

$$-\nabla \cdot [\varepsilon(\vec{r})\nabla \phi_m + (\vec{r})] + \bar{\kappa}^2(\vec{r})\phi_m(\vec{r}) = \frac{e_c \bar{\kappa}^2 V_m}{k_B T}\Theta(\vec{r}),$$

where $V_m$ is the transmembrane potential (statvolt) with respect to the extracellular space,

$\phi_m = \frac{e\Phi_m}{k_B T}$ is the reduced electrostatic potential due to $V_m$,

$\Phi_m$ is the electrostatic potential,

and $\Theta(\vec{r})$ is a Heaviside step function whose value is 1 for $\vec{r}$ within the intracellular space and 0 elsewhere.

The modified LPBE can be solved with APBS, with some slight modification to enable introduction of appropriate boundary conditions (23) (see Appendix for changes and derivation of boundary potentials). As can be seen in manuscript **Figure 2A**, the ability of water to penetrate into the voltage sensing region causes a nonlinear potential variation across the membrane.

By integrating the product of the potential with the protein charges, the contribution of $V_m$ to the total energy can be found:

$$\mathrm{W}^m(q) = \int_V \Phi^m\left(\vec{r}, q\right)\rho\left(\vec{r}, q\right) d^3 r.$$

## 6 Computing the Currents

The transition rates between points on the energy landscape can be found with the Smoluchowski equation(24, 25):

$$\frac{\partial p(x,t)}{\partial t} = \frac{\partial}{\partial x} D\left(\frac{\partial}{\partial x} p(x,t) - \beta F(x) p(x,t)\right)$$

$p(x,t)$ is the probability of finding a particle at a position x (Angstrom) at time t (ms).

$D$ ($\text{Å}^2\text{ms}^{-1}$) is the diffusion constant, $F(x)$ is the force on the particle ($\text{kJ} \cdot \text{mol}^{-1} \cdot \text{Å}^{-1}$),

and $\beta$ is $1/(k_B \cdot T)$ $(\text{kJ} \cdot \text{mol}^{-1})^{-1}$.

The Smolochowski equation has two terms: 1) a diffusive term that causes particles to disperse from a region in which they are concentrated, and 2) an advective term that accounts for the force on the particles introduced by the energy landscape. If $F = -\nabla W$, which means that the force on the particle depends on the gradient of the potential (a conservative field), the adjoint Smoluchowski equation can be used and solved with finite differences(26):

$$\frac{\partial p(x,t)}{\partial t} = \frac{\partial}{\partial x} D(x) e^{-\beta W(x)} p \frac{\partial}{\partial x}\left(e^{\beta W(x)} p\right).$$

Noise variance analysis and studies in the presence of rubidium indicate that the channel can transition into a state-independent flickery blocked state, which would be reflected on the single channel recordings(27-29). In the model, channels can transition from any state to the blocked state, and the transition rates back and forth from the blocked state are independent of the state of the channel (**Figure 2C**, in manuscript).

Single channel activity can be simulated by using the scheme in manuscript figure **Figure 2C** and employing a Monte-Carlo simulation. A single channel has four voltage-sensing subunits, and each subunit is initialized to a position on the energy landscape. For a given timestep, *dt*, the channel can make a transition from its current point to an adjacent point only if a random number (between 0 and 1, found with the Mersenne-Twister algorithm(30)) is less than the product of *dt* and the transition rate (found by the Smoluchowski equation). Then, if all 4 subunits are in the activated region of the energy landscape, the full channel can make a cooperative transition into the open state $O_1$. Once the channel has made this transition, the subunits are locked in the activated region of the energy landscape. From the first open state the channel can then transition to open states that are further from the closed state ($O_2$-$O_5$). The presence of these states is inferred from a delay before the onset of inactivation and an increase in the time constant of deactivation that is proportional to the length of a depolarizing pulse(31, 32). The inactivated state is therefore only accessible when the channel reaches the final open state ($O_5$).

## 7 Pseudo ECG

A recently published model of the canine epicardial myocyte (33) was used for action potential simulations. A one dimensional fiber of 160 model cells connected by gap junctions was used to represent the planar wavefront that travels from endocardium to epicardium during normal ventricular excitation. Experimentally observed transmural differences in APD in control (34) were reproduced by incorporating regions of endocardial, M and epicardial cells with heterogeneity in $I_{Ks}$ (35), $I_{NaL}$ (36) and $I_{to1}$ (37). Distribution of cell types and ion channel densities are shown in the table below.

| Cell type | Endocardial | M | Epicardial |
|---|---|---|---|
| Cell Numbers | 1-20 | 21-80 | 81-160 |
| $\bar{G}_{Ks}$ (mS/µF) | 1*epi | 0.5*epi | 1*epi |
| $\bar{G}_{NaL}$ (mS/µF) | 0.01495 | 0.0221 | 0.0130 |
| $\bar{G}_{to1}$ (mS/µF) | 0.3375 | 2.49 | 2.6182 |

To allow computationally tractable single cell and strand simulations, ion concentrations were initialized using steady state data from simulations using a previously published model of $I_{Ks}$ (33). Single cell and strand results are reported for the fourth paced beat following concentration initialization. Single cell action potentials and adaptation are shown for a single epicardial cell simulation. Pseudo-ECG results are shown for the fourth beat at CL = 1 s.

The pseudo ECG is calculated as in reference (38) by

$$\Phi_e(x', y', z') = \frac{a^2 \sigma_i}{4\sigma_e} \int -\nabla V_m \cdot \nabla \frac{1}{r} dx$$
$$r = \left[ (x - x')^2 + (y - y')^2 + (z - z')^2 \right]^{1/2} \quad (0.1)$$

where $\nabla V_m$ is the spatial gradient of $V_m$, $a$ is the radius of the fiber, $\sigma_i$ is the intracellular conductivity, $\sigma_e$ is the extracellular conductivity, and $r$ is the distance from a source point $(x, y, z)$ to a field point $(x', y', z')$. $\Phi_e$ is computed at 2.0 cm away from the epicardium along the fiber axis.

# 8 Oocyte Experiments

Whole-cell currents were recorded by two-electrode voltage clamp using a Dagan CA-1B amplifier (Dagan, Minneapolis, MN). Records were low-pass filtered at 100 Hz or 1 kHz with the amplifier's built-in Bessel filter and digitized at 500 Hz or 5 kHz, respectively. The electrodes were filled with 3 M KCl solution. Oocytes were bathed in ND96 or high $K^+$ solution as indicated in Fig 3. The ND96 solution contained (mM) 96 NaCl, 4 KCl, 1.8 MgC12, 0.1 CaC12, 5 Hepes; pH 7.6. To measure voltage-dependent activation, currents were elicited by testing voltage pulses from -40 to 20 mV in 10 mV increments. Holding potential was –80 mV. Leak current was subtracted digitally.

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# Appendix I

## *Transition Rates*

### KCNQ1 Rates

$I_{KCNQ1} = \overline{G_{KCNQ1}} \cdot O_{KCNQ1} \cdot (V_m - E_{Ks})$

**Where maximum conductance, $\overline{G_{KCNQ1}}$ , is:**

$$\overline{G_{KCNQ1}} = 2.4 \cdot 10^{-3} \cdot \left( 1 + \frac{0.6}{1 + \left( \frac{3.8 \cdot 10^{-5}}{[Ca^{2+}]_i} \right)^{1.4}} \right)$$

← **Accounts for dependence of conductance on intracellular calcium concentration $[Ca^{2+}]_i$[16].**

**and open probability, O:**

$O_{KCNQ1} = O_1 + O_2 + O_3 + O_4 + O_5$

$$E_{Ks} = \frac{R \cdot T}{F} \cdot \log \frac{[K^+]_o + P_{Na/K} \cdot [Na^+]_i}{[K^+]_i + P_{Na/K} \cdot [Na^+]_i}$$

**All rates in $ms^{-1}$**

$\theta = 3.19 \cdot 10^{-1}$

$\eta = 3.09 \cdot 10^{-2} \cdot \exp(-2.08 \cdot 10^{-1} \cdot \frac{V_m \cdot F}{R \cdot T})$

$\psi = 2.54 \cdot 10^{-2} \cdot \exp(6.46 \cdot 10^{-2} \cdot \frac{V_m \cdot F}{R \cdot T})$

$\omega = 1.78 \cdot 10^{-2} \cdot \exp(-5.32 \cdot 10^{-1} \cdot \frac{V_m \cdot F}{R \cdot T})$

$\lambda = 2.32 \cdot 10^{-2} \cdot \exp(1.21 \cdot 10^{-1} \cdot \frac{V_m \cdot F}{R \cdot T})$

$\mu = 6.19 \cdot 10^{-2} \cdot \exp(-9.46 \cdot 10^{-2} \cdot \frac{V_m \cdot F}{R \cdot T}$

$x_\psi = 8.74 \cdot 10^{-1}$

$x_\omega = 3.29 \cdot 10^{-1}$

$\psi_y = \psi \cdot x_\psi^{y-1}$

$\omega_y = \omega \cdot x_\omega^{y-1}$

$D = 27.0$ Å$^2 ms^{-1}$ **for translation and rotation and radius of S4 is 5 Å**

## Flickery Block

$\rho = 0.72$

$\sigma = 2.0$

## Mutation Effects

$x_\omega = 8.23 \cdot 10^{-1}$

For E160A,

$\overline{G_{KCNQ1}}$ is divided by 5.

For E160Q,

$\overline{G_{KCNQ1}}$ is equal to $\overline{G_{Ks}}$

For E160K,

$\overline{G_{KCNQ1}}$ is 0.

## KCNE1 Effects

$x_\omega = 8.23 \cdot 10^{-1}$

$$\eta = 8.24 \cdot 10^{-2} \cdot \exp(-5.20 \cdot 10^{-1} \cdot \frac{V_m \cdot F}{R \cdot T})$$

$$\overline{G_{KCNQ1}} = 0.017 \cdot \left( 1 + \frac{0.6}{1 + \left( \frac{3.8 \cdot 10^{-5}}{\left[ Ca^{2+} \right]_i} \right)^{1.4}} \right)$$

$D = 0.75 \ \text{Å}^2 ms^{-1}$

*1.1*

# Appendix II

## Derivation of the Boundary Potentials

For each region of the membrane the potential obeys (20),

$$\phi_1''(z) = \kappa^2 \phi_1(z)$$
$$\phi_2''(z) = \phi_3''(z) = \phi_4''(z) = 0$$
$$\phi_5''(z) = \kappa^2 (\phi_5(z) - V_m)$$

Region 1 is the extracellular space, 2 the transition between extracellular region and the core, 3 the core region, 4 the transition between the core and intracellular region, and 5 the intracellular region.

We assume: 1) that the potentials far away from the membrane on the extra and intracellular sides (at z=+∞,-∞) are 0 and $V_m$, respectively, and 2) that the potential at the interface between the solution and the membrane is continuous.

$$\phi_1(-\infty) = 0$$
$$\phi_5(+\infty) = V_m$$

$$\phi_1(0) = \phi_2(0)$$
$$\phi_2(L_{\text{int}}) = \phi_3(L_{\text{int}})$$
$$\phi_3(L_m - L_{\text{int}}) = \phi_4(L_m - L_{\text{int}})$$
$$\phi_4(L_m) = \phi_5(L_m)$$

$$\varepsilon_w \phi_1'(0) = \varepsilon_i \phi_2'(0)$$
$$\varepsilon_i \phi_2'(L_{\text{int}}) = \varepsilon_m \phi_3'(L_{\text{int}})$$
$$\varepsilon_m \phi_3'(L_m - L_{\text{int}}) = \varepsilon_i \phi_4'(L_m - L_{\text{int}})$$
$$\varepsilon_i \phi_4'(L_m) = \varepsilon_w \phi_5'(L_m)$$

$$\phi_1 = C_1 \exp(\kappa z) \;\Rightarrow\; \phi_1' = \kappa C_1 \exp(\kappa z)$$
$$\phi_2 = C_2 + C_3 z \;\Rightarrow\; \phi_2' = C_3$$
$$\phi_3 = C_4 + C_5 z \;\Rightarrow\; \phi_3' = C_5$$
$$\phi_4 = C_6 + C_7 z \;\Rightarrow\; \phi_4' = C_7$$
$$\phi_5 = C_8 \exp(-\kappa z) - V_m \;\Rightarrow\; \phi_5' = -\kappa C_8 \exp(-\kappa z)$$

Then the following system of equations can be set up to find the constants $C_1$ to $C_8$.

$$\begin{bmatrix} 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & L_{int} & -1 & -L_{int} & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & L_m - L_{int} & -1 & L_{int} - L_m & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & L_m & -\exp(-\kappa L_m) \\ 0 & 0 & \varepsilon_i & 0 & -\varepsilon_m & 0 & 0 & 0 \\ \varepsilon_w \kappa & 0 & -\varepsilon_i & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \varepsilon_m & 0 & -\varepsilon_i & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \varepsilon_i & \varepsilon_w \kappa \exp(-\kappa L_m) \end{bmatrix} \begin{bmatrix} C_1 \\ C_2 \\ C_3 \\ C_4 \\ C_5 \\ C_6 \\ C_7 \\ C_8 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ V_m \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

After solving, $\phi_1(z)$ to $\phi_5(z)$ are-

$$\mathrm{A} = \frac{\mathrm{V_m} \varepsilon_i \varepsilon_m}{2\varepsilon_i \varepsilon_m - 2\varepsilon_i \varepsilon_w \kappa L_{\mathrm{int}} + 2\varepsilon_m \varepsilon_w \kappa L_{\mathrm{int}} + \varepsilon_i \varepsilon_w \kappa L_m}$$
$$\phi_1(z) = A \exp(\kappa z)$$
$$\phi_2(z) = A\left(1 + \frac{\varepsilon_w \kappa}{\varepsilon_i} z\right)$$
$$\phi_3(z) = A\left(1 + \frac{\varepsilon_w \kappa L_{\mathrm{int}}}{\varepsilon_i} - \frac{\varepsilon_w \kappa L_{\mathrm{int}}}{\varepsilon_m}\right) + \frac{A \varepsilon_w \kappa z}{\varepsilon_m}$$
$$\phi_4(z) = \frac{A\Big(\varepsilon_m \varepsilon_w \kappa \left(2L_{\mathrm{int}} - L_m\right) + \varepsilon_i \left(\varepsilon_m + \varepsilon_w \kappa \left(-2L_{\mathrm{int}} + L_m\right)\right)\Big)}{\varepsilon_i \varepsilon_m} + \frac{A \varepsilon_w \kappa z}{\varepsilon_i}$$
$$\phi_5(z) = -A \exp\big(\kappa (L_m - z)\big) + V_m.$$

Which reduces to the previously published equations(20) when $L_{\mathrm{int}}$ is set to 0.