Supporting Information for Vitarelli and Talaga, 2013

"Theoretical model for electrochemical impendance spectroscopy and local ζ-potential of unfolded proteins in nanopores"

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Derivation of Equation 1

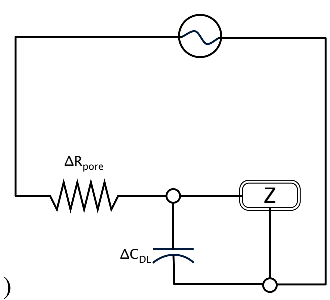
Introduction

Equation 1 was derived in brief in Vitarelli2011.[1] A similar derivation appeared in Keiser1976[2], which treated capacitive pores that are closed on one end.

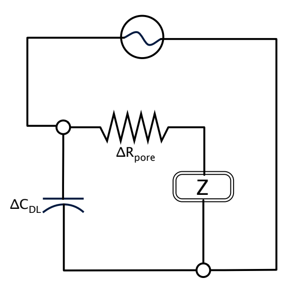
$$Z'(x) + i\,\omega\, Z(x)^2\, C'(x) - R'(x) = 0 \qquad \textbf{(1)}$$

$$\frac{\partial R}{\partial x} = R'(x) = \frac{1}{\pi\, \kappa_c\, r(x)^2}$$

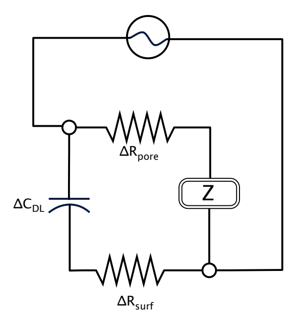
$$\frac{\partial C}{\partial x} = C'(x) = 2\,\pi\, \tilde{C}_c\, r(x)$$



1)



2)

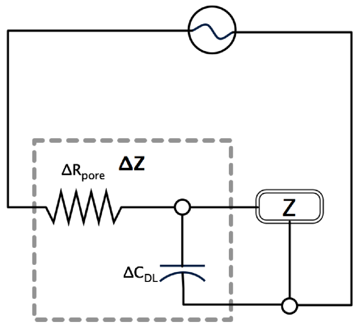


3)

Above we show three circuits that can be written to convey the recursive relationship between the differential part, dZ and the impedance Z. Circuit 1 appeared in Vitarelli2011.[1] This paper used Circuit 2. Circuit 3 is a more literal interpretation of the nanopore. Circuit 2 was used as an approximation of Circuit 3. We will now show that these three circuits give the same differential equation, Eq. 1, which forms the basis of the solution of the new equivalent circuit element, Z_{vtw}, which can be adapted for variable topology of the nanopore.

Equivalency of differential circuits

Circuit 1



Adding the discrete elements according to circuit rules gives:

$$\Delta Z + Z = \Delta R + \frac{1}{\Delta C + \frac{1}{Z}} = \Delta x\, R'(x) + \frac{1}{\frac{1}{Z(x)} + i\, \Delta x\, \omega\, C'(x)}$$

Converting to a power series in Δx

$$\Delta Z + Z(x) = Z(x) + \Delta x \left(R'(x) - i\, \omega\, Z(x)^2\, C'(x)\right) + O\left(\Delta x^2\right)$$

retaining only linear terms.

$$\Delta Z + Z(x) = Z(x) + \Delta x \left(R'(x) - i\, \omega\, Z(x)^2\, C'(x)\right)$$

$$\frac{\Delta Z}{\Delta x} = R'(x) - i\, \omega\, Z(x)^2\, C'(x)$$

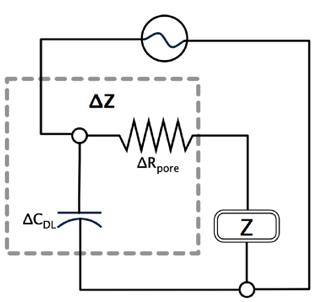
taking the limit as $\Delta \to d$

$$Z'(x) = R'(x) - i\, \omega\, Z(x)^2\, C'(x)$$

Gives Eq. 1.

$$Z'(x) + i\, \omega\, Z(x)^2\, C'(x) - R'(x) = 0$$

Circuit 2



Adding the discrete elements according to circuit rules gives:

$$\Delta Z + Z = \frac{1}{\Delta C + \frac{1}{\Delta R + Z}} = \frac{1}{\frac{1}{\Delta x\, R'(x) + Z} + i\, \Delta x\, \omega\, C'(x)}$$

Converting to a power series in Δx

$$\Delta Z + Z(x) = Z(x) + \Delta x \left(R'(x) - i\,\omega\, Z(x)^2\, C'(x)\right) + O\left(\Delta x^2\right)$$

retaining only linear terms.

$$\Delta Z + Z(x) = Z(x) + \Delta x \left(R'(x) - i\,\omega\, Z(x)^2\, C'(x)\right)$$

rearranging

$$\frac{\Delta Z}{\Delta x} = R'(x) - i\,\omega\, Z(x)^2\, C'(x)$$

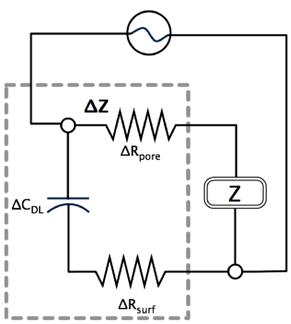
taking the limit as $\Delta \to d$

$$Z'(x) = R'(x) - i\,\omega\, Z(x)^2\, C'(x)$$

Gives Eq. 1.

$$Z'(x) + i\,\omega\, Z(x)^2\, C'(x) - R'(x) = 0$$

Circuit 3



Adding the discrete elements according to circuit rules gives:

$$\Delta Z + Z = \frac{1}{\frac{1}{\frac{1}{\Delta C} + \Delta \mathrm{Rsurf}} + \frac{1}{\Delta R + Z}} = \Delta x\, R'(x) + \frac{1}{\frac{1}{\Delta x\, R'(x) + Z} + \frac{1}{\Delta x\, \mathrm{R}\infty'(x) - \frac{i}{\Delta x\, \omega\, C'(x)}}}$$

Converting to a power series in Δx

$$\Delta Z + Z(x) = Z(x) + \Delta x \left(R'(x) - i\,\omega\, Z(x)^2\, C'(x)\right) + O\left(\Delta x^2\right)$$

retaining only linear terms.

$$\Delta Z + Z(x) = Z(x) + \Delta x \left(R'(x) - i\,\omega\, Z(x)^2\, C'(x)\right)$$

$$\frac{\Delta Z}{\Delta x} = R'(x) - i\,\omega\, Z(x)^2\, C'(x)$$

taking the limit as $\Delta \to d$

$$Z'(x) = R'(x) - i\,\omega\, Z(x)^2\, C'(x)$$

Gives Eq. 1.

$$Z'(x) + i\,\omega\, Z(x)^2\, C'(x) - R'(x) = 0$$

Comments

All three circuits produce the same differential equation defining Z. Thus, in these three cases, the connectivity of the ΔR and ΔC circuit components becomes irrelevant when the infinitessimal elements are evaluated in the continuous limit. What matters is the variability of the infinitessimal elements with the position, x, in the nanopore. Therefore Eq. 1 is to be solved.

$$Z'(x) + i\,\omega\, Z(x)^2\, C'(x) - R'(x) = 0$$

Solution to Eq. 1 for constant radius (cylindrical pore).

Eq. 1

$$Z'(x) + i\,\omega\, Z(x)^2\, C'(x) - \mathcal{R}'(x) = 0$$

Differential *R*, *C*

$$R'(x) = \left(\kappa_c\, \pi\, r(x)^2\right)^{-1} = \left(\kappa_c\, \pi\, r_0^2\right)^{-1}$$
$$C'(x) = \tilde{C}_c\, 2\, \pi\, r(x) \ = \tilde{C}_c\, 2\, \pi\, r_0$$

Constants defined to simplify notation

$$\mathcal{R} = \frac{\mathcal{L}}{\kappa_c\, \pi\, r_0^2} \quad \text{and} \quad \tau = \frac{L^2\, \tilde{C}_c}{2\, r_0\, \kappa_c}$$

Substitute simplified versions of differential capacitance and resistance

$$R'(x) == \frac{\mathcal{R}}{\mathcal{L}}$$
$$C'(x) == \frac{\tau}{\mathcal{L}\mathcal{R}}$$

The constant radius version of Eq. 1 can be written as:

$$\frac{i\tau\omega\, Z(x)^2}{\mathcal{L}\mathcal{R}} - \frac{\mathcal{R}}{\mathcal{L}} + Z'(x) = 0$$

Or in a slightly simpler form:

$$\mathcal{L}\,\mathcal{R}\, Z'(x) + i\tau\omega\, Z(x)^2 - \mathcal{R}^2 = 0$$

Eq. 1 has a single arbitrary constant to be determined from the boundary condition Z[0]. A general solution to Eq. 1 is

$$Z(x) = \mathcal{R}\tanh\!\left(\sqrt{i\tau\omega}\ x / \mathcal{L} + \tanh^{-1}\!\left(\sqrt{i\tau\omega}\ Z_0\ / \mathcal{R}\right)\right) \Big/ \sqrt{i\tau\omega}$$

with Z0 representing the boundary condition impedance. When Z_0 approaches $\pm\sqrt{\mp\infty}$ the $\tan^{-1}$term approaches $\mp\frac{i\pi}{2}$. this has the effect of converting Tanh to Coth giving

$$Z(x) = \mathcal{R}\coth\!\left(\sqrt{i\tau\omega}\ x / \mathcal{L}\right) \Big/ \sqrt{i\tau\omega}$$

This solution is consistent with a pore that is closed on one end. As $Z_0 \to 0$ the solution is consistent with an open pore. The $\tanh^{-1}$ term approaches zero giving

$$Z(x) = \mathcal{R}\tanh\left(\sqrt{i\tau\omega}\; x / \mathcal{L}\right) \Big/ \sqrt{i\tau\omega}$$

Substitute $x \to \mathcal{L}$

$$Z(\mathcal{L}) = \mathcal{R}\tanh\left(\sqrt{i\tau\omega}\right) \Big/ \sqrt{i\tau\omega}$$

Recursion formula approach to solving the network equivalent circuit.

The recursion approach uses the same network circuit, but solves the circuit through a different formalism. We will still consider the total impedance to be the circuit rules addition of a network of $\mathcal{N}$ pairs of resistors and capacitors. We obtain a recursion relationship for the k^{th}element.

$$\mathcal{Z}_k = \mathcal{R}_k + \frac{1}{\frac{1}{\mathcal{Z}_{k-1}} + i\,\omega\,C_k}$$

subject to the initialization condition $\mathcal{Z}_0$ which is equivalent to the boundary condition for the differential equation approach. The discrete elements $\mathcal{R}_k$and C_k are the position-dependent resistances and capacitances with $x == k\,\frac{\mathcal{L}}{\mathcal{N}}$

$$\mathcal{R}_k = \mathcal{R}'(k\,\mathcal{L} / \mathcal{N})\,\mathcal{L} / \mathcal{N}$$

$$C_k = C'(k\,\mathcal{L} / \mathcal{N})\,\mathcal{L} / \mathcal{N}$$

Where $\mathcal{R}'(x)$ and $C'(x)$ are the differential capacitances as defined for Eq. 1. For the constant radius nanopore (cylindrical geometry) the discrete elements $\mathcal{R}_k$and C_k become:

$$\mathcal{R}_k = \mathcal{L} \Big/ \left(\mathcal{N}\pi\, r_0^2\,\kappa_c\right) = \mathcal{R}_{\text{cyl}} \Big/ \mathcal{N}$$

$$C_k = 2\,\pi\, r_0\,\mathcal{L}\,\tilde{C}_c / \mathcal{N} = C_{\text{cyl}} \Big/ \mathcal{N} = \tau_{\text{cyl}} \Big/ \left(\mathcal{N}\,\mathcal{R}_{\text{cyl}}\right)$$

where

$$\mathcal{R}_{\text{cyl}} \equiv \mathcal{L} \Big/ \left(\pi\, r_0^2\,\kappa_c\right) \quad C_{\text{cyl}} \equiv 2\,\pi\, r_0\,\mathcal{L}\,\tilde{C}_c \quad \tau_{\text{cyl}} = C_{\text{cyl}}\,\mathcal{R}_{\text{cyl}} = 2\,\mathcal{L}^2\,\tilde{C}_c / (r_0\,\kappa_c)$$

yielding the following continued fraction recursion relationship for a constant radius nanopore:

$$\mathcal{Z}_k = \frac{\mathcal{R}_{\text{cyl}}}{\mathcal{N}} + \frac{1}{\frac{1}{\mathcal{Z}_{k-1}} + \frac{i\,\omega\,\tau_{\text{cyl}}}{\mathcal{R}_{\text{cyl}}\,\mathcal{N}}}$$

For a constant radius the finite continued fraction with $\mathcal{Z}_0 == 0$ and $\mathcal{N}$ terms has solution.

$$\mathcal{Z}(\mathcal{N}) = 2\,i\,\mathcal{N}\,\mathcal{R}_{\text{cyl}}\left(\tau_{\text{cyl}}\,\omega - \sqrt{\tau_{\text{cyl}}\,\omega\left(\tau_{\text{cyl}}\,\omega - 4\,i\,\mathcal{N}^2\right)}\left(1 + 2\left(\left(\frac{\tau_{\text{cyl}}\,\omega - 2\,i\,\mathcal{N}^2 + \sqrt{\tau_{\text{cyl}}\,\omega\left(\tau_{\text{cyl}}\,\omega - 4\,i\,\mathcal{N}^2\right)}}{\tau_{\text{cyl}}\,\omega - 2\,i\,\mathcal{N}^2 - \sqrt{\tau_{\text{cyl}}\,\omega\left(\tau_{\text{cyl}}\,\omega - 4\,i\,\mathcal{N}^2\right)}}\right)^{\mathcal{N}} - 1\right)^{-1}\right)\right)^{-1}$$

Taking the limit as $\mathcal{N} \to \infty$ yields

$$\mathcal{Z}(\omega) = \mathcal{R}_{\text{cyl}}\tanh\left(\sqrt{i\,\tau_{\text{cyl}}\,\omega}\right) \Big/ \sqrt{i\,\tau_{\text{cyl}}\,\omega}$$

Sequences used

```
haSyn      MDVFMKGLSKAKEGVVAAAEKTKQGVAEAAGKTKEGVLYVGSKTKEGVVHGVATVAEKTK
maSyn      MDVFMKGLSKAKEGVVAAAEKTKQGVAEAAGKTKEGVLYVGSKTKEGVVHGVTTVAEKTK
hbSyn      MDVFM-GLSMAKEGVVAAAEKTKQGVTEAAEKTKEGVLYVGSKTREGVVQGVASVAEKTK
           ***** *** ****************:*** *************:****:**::******

haSyn      EQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEG-----APQEGILED
maSyn      EQVTNVGGAVVTGVTAVAQKTVEGAGNIAAATGFVKKDQMGKGEEG-----YPQEGILED
hbSyn      EQASHLGGAVFSG-----------AGNIAAATGLVKREEFPTDLKPEEVAQEAAEEPLIE
           **.:.:****.:*           **.******:**:::: .  :         *  * :

haSyn      MPVDPDNEAYEMPSEEGYQDYEPEA
maSyn      MPVDPGSEAYEMPSEEGYQDYEPEA
hbSyn      PLMEPEGESYEDPPQEEYQEYEPEA
             ::*  *:** * :* **:*****
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Sequences and sequence alignments for human and mouse α-synuclein and human β-synuclein as used to illustrate sequence sensitivity of nanopore EIS to sequence: **haSyn** = human α-synuclein, **maSyn** = mouse α-synuclein, **hbSyn** = human β-synuclein.

References cited in supporting information.

1 M. J. Vitarelli, S. Prakash, and D. S. Talaga, Anal. Chem. 83, 533 (2011).

2 H. Kaiser, K.D. Beccu, M.A. Gutjahr, Electrochim. Acta 21, 539 (1976).