



By taking a cross-section of the shear-free device through the long axis of the rectangular membrane and viewed from the side, we obtained an idealized schematics of the flow channels detailed in (A). The flow compartment is shown at the top, with the nanopores in the membrane idealized as a series of parallel channels connecting to the cell compartment below. (B) An equivalent circuit representation of the flow channels. (C) A unit circuit loop used to generalize the flow distribution. The flow within each branch of the loop is denote by q_i , and the resistance of each branch by R . The pressure (or voltage) drops along the two flow paths indicated by the arrows are equal and forms the basis of the recurrence relation below:

$$R_1(q_{n-1} - q_n) + R_3(Q - q_n) = R_2(q_{n-1} - q_n) + R_1(q_n - q_{n+1}) \quad (1)$$

expand, group the flow terms with the same indice together, and rearrange, we obtained a 2^{n2} order recursive relation that describes the flow across the n_{th} segment/repeat of the flow compartment:

$$q_n = R_m \cdot q_{n-1} + R_m \cdot q_{n+1} + R_c \cdot Q \quad (2)$$

$$\text{where } R_m = \left(\frac{R_1}{2R_1 + R_2 + R_3} \right) \quad \text{and} \quad R_c = \left(\frac{R_3}{2R_1 + R_2 + R_3} \right) \quad (3)$$

We can think of the dimensionless R_m and R_c as the normalized resistance of the membrane and the cell compartment, respectively.

The 2^{nd} order recurrence relation in (2) is inhomogeneous (with the constant term $R_c \cdot Q$), but linear with constant coefficients (that are independent of n).

The corresponding closed-form solution is a sum of a homogeneous and a particular solution.

Before solving (2), we performed the following scaling transformation to simplify subsequent calculations:

$$\alpha = \frac{1}{2 \cdot R_m} = \frac{2R_1 + R_2 + R_3}{2R_1} \quad \hat{q} = \frac{R_c \cdot Q}{R_m} = \frac{R_3 \cdot Q}{R_1} \quad (4)$$

and yielded

$$q_{n+1} - 2\alpha \cdot q_n + q_{n-1} = -\hat{q} \quad (5)$$

since R_1 , R_2 , and R_3 are all positive, $\alpha > 1$.

Particular solution:

The inhomogeneous term does not depend on n , so we seek out a particular solution that is constant. Substituting $q_n = q^{(P)}$ into (5), we obtained

$$q^{(P)} = \frac{\hat{q}}{2(\alpha - 1)} \quad (6)$$

Homogeneous equation and solution:

Any solution $q_n^{(H)}$ of the homogeneous equation satisfies

$$q_{n+1}^{(H)} - 2\alpha \cdot q_n^{(H)} + q_{n-1}^{(H)} = 0 \quad (7)$$

We try a solution of the form

$$q_n = \mu^n \quad (8)$$

Substituting μ into (7), we have

$$\mu^2 - 2\alpha \cdot \mu + 1 = 0 \quad (9)$$

Which has the solution

$$\mu = \alpha \pm \sqrt{\alpha^2 - 1} \quad (10)$$

We make one more transformation to simplify the calculations, let

$$\alpha = \cosh(\beta) \quad (11)$$

and substitute into (10), we have

$$\mu = \cosh(\beta) \pm \sinh(\beta) = e^{\beta}, e^{-\beta} \quad (12)$$

The transformation in (11) is well-defined because for $\alpha > 1$, there is always a unique positive value of β that satisfies (11).

The homogeneous solution is thus

$$q_n^{(H)} = c_1 \cdot e^{\beta \cdot n} + c_2 \cdot e^{-\beta \cdot n} \quad (13)$$

and the full solution to (2) is

$$q_n = q_n^{(H)} + q_n^{(P)} = c_1 \cdot e^{\beta \cdot n} + c_2 \cdot e^{-\beta \cdot n} + \frac{\hat{q}}{2(\cosh(\beta) - 1)} \quad (14)$$

The flow that we are most interested in is the flow in the cell compartment, given by $Q - q_n$. The smaller the term $Q - q_n$, the more effective is our shear-free device in reducing the shear stress seen by the cells.

NOTE: R can be estimated using the Hagen-Poiseuille equation that relates the flow resistance to the microchannel and the nanopore dimensions. Namely,

$\Delta p = R \cdot q$, where p is the pressure. $R = 12\mu \frac{L}{w \cdot h^3}$ for rectangular channel and $R = 8\mu \frac{L}{\pi \cdot r^4}$ for cylindrical channel, where μ is the fluid dynamic

viscosity, L is the channel length, w and h are the channel width and height, respectively, and r is the pore radius.

Alternatively, we can summarize the flow through each n^{th} repeat of the flow compartment in matrix form:

$$\underbrace{\begin{bmatrix} 1 & -R_m & 0 & 0 & \dots & 0 & 0 & 0 & 0 \\ -R_m & 1 & -R_m & 0 & \dots & 0 & 0 & 0 & 0 \\ 0 & -R_m & 1 & -R_m & \dots & 0 & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \dots & -R_m & 1 & -R_m & 0 \\ 0 & 0 & 0 & 0 & \dots & 0 & -R_m & 1 & -R_m \\ 0 & 0 & 0 & 0 & \dots & 0 & 0 & -R_m & 1 \end{bmatrix}}_A \underbrace{\begin{bmatrix} q_1 \\ q_2 \\ q_3 \\ \vdots \\ q_{n-2} \\ q_{n-1} \\ q_n \end{bmatrix}}_B = Q \underbrace{\begin{bmatrix} R_m + R_c \\ R_c \\ R_c \\ \vdots \\ R_c \\ R_c \\ R_m + R_c \end{bmatrix}}_I$$

5 where each q_n is readily solved by the product $A^{-1} \cdot I$. The matrix A and its inverse A^{-1} can be generated readily in MATLAB, albeit at a higher computational cost given as n gets larger.