1. Modeling flow in the shear-free device

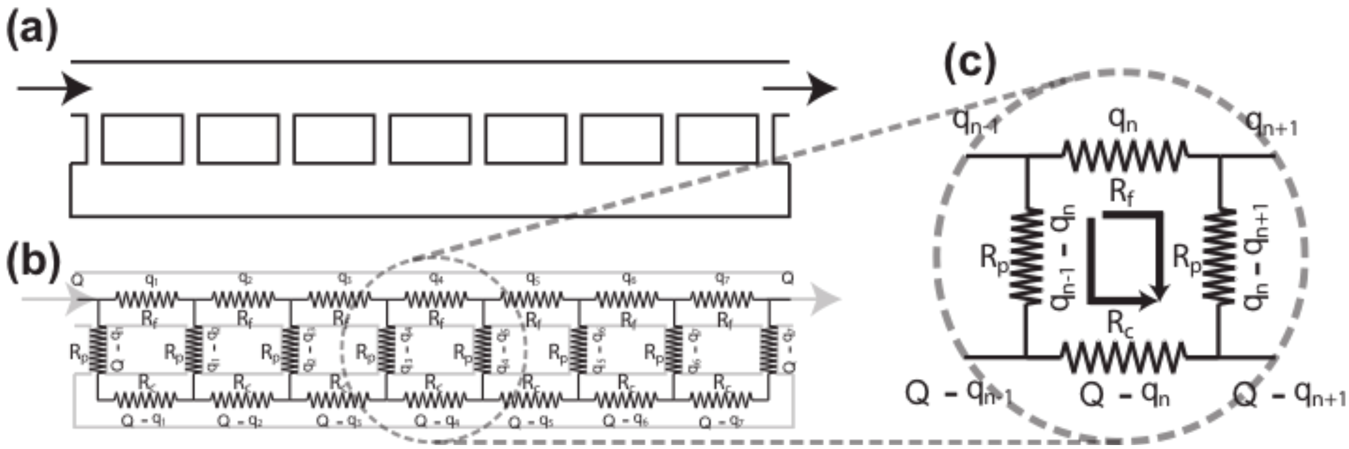


Fig. 1 (a) By taking a longitudinal cross-section of the membrane device we obtained an idealized network of flow channels connecting the flow chamber and cell chamber. (b) An equivalent circuit representation of the flow channels. (c) A unit circuit loop used to generalize the flow distribution. The flow within each branch of the loop is denoted by q, the resistance by R, and the subscript n indexed each consecutive unit of circuit loop. The pressure drops along the two flow paths indicated by the arrows are equal and form the basis of the recurrence relation below:

$$R_p\left(q_{n-1} - q_n\right) + R_c\left(Q - q_n\right) = R_f\left(q_n\right) + R_p\left(q_n - q_{n+1}\right) \qquad (1)$$

After expanding, grouping the flow rate terms with the same indices together, and rearranging terms, we obtain a 2nd order recurrence relation that describes the flow across the n^{th} unit circuit loop of the flow chamber:

$$q_n = \hat{R}_m \cdot q_{n-1} + \hat{R}_m \cdot q_{n+1} + \hat{R}_c \cdot Q \qquad (2)$$

$$\text{where} \quad \hat{R}_m = \frac{R_p}{2R_p + R_c + R_f} \quad \text{and} \quad \hat{R}_c = \frac{R_c}{2R_p + R_c + R_f} \qquad (3)$$

The two dimensionless terms in (3) can be thought of as normalized resistances of the membrane and the cell chamber, respectively.

Due to the last constant term, the 2nd order recurrence relation in (2) is inhomogeneous with constant coefficients (that are independent of n). The closed form solution to (2) will be a sum of a homogeneous and a particular solution.

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

$$\alpha = \frac{1}{2 \cdot \hat{R}_m} \quad \text{and} \quad \hat{q} = \frac{\hat{R}_c \cdot Q}{\hat{R}_m} \qquad (4)$$

Thus (2) transforms to:

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

Since R_p, R_f, and R_c 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 obtain:

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

Homogeneous Solution:

Any solution to the homogeneous equation satisfies

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

We try solution of the form

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

Substituting (8) into (7), we have:

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

which has the solution

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

We make one more transformation to simplify the calculations, let

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

After substituting into (10), we have

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

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:

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

And the full solution to (2) is

$$q_n = q_n^{(H)} + q_n^{(p)} = c_1 \cdot e^{\beta \cdot n} + c_2 \cdot e^{-\beta \cdot n} + \frac{\hat{q}}{2\left[\cosh(\beta) - 1\right]} \tag{14}$$

Applying the boundary conditions (B.C.):

We know that the entrance flow rate at $n = 1$ and the exit flow rate at $n = N$ are both equal to the input flow rate Q. We therefore have two equations for the two unknown constant c_1 and c_2 in (14), giving us the final solution:

$$q_n = Q\left[\left(\frac{R_f}{R_f + R_c}\right)\left(\frac{e^{\beta \cdot n}}{e^{\beta} + e^{\beta \cdot N}} + \frac{e^{-\beta \cdot n}}{e^{-\beta} + e^{-\beta \cdot N}}\right) + \frac{R_c}{R_f + R_c}\right] \tag{15}$$

The cell chamber flow rate at the n^{th} unit circuit, $q_c(n)$, is given by $Q - q_n$:

$$q_c(n) = Q\left(\frac{R_f}{R_f + R_c}\right)\left[1 - \left(\frac{e^{\beta \cdot n}}{e^{\beta} + e^{\beta \cdot N}} + \frac{e^{-\beta \cdot n}}{e^{-\beta} + e^{-\beta \cdot N}}\right)\right] \tag{16}$$

At last, we let

$$\begin{aligned}\omega(n) &= \frac{e^{\beta \cdot n}}{e^{\beta} + e^{\beta \cdot N}} + \frac{e^{-\beta \cdot n}}{e^{-\beta} + e^{-\beta \cdot N}} = \frac{e^{\beta \cdot (n-1)} + e^{-\beta \cdot (N-n)} + e^{-\beta \cdot (n-1)} + e^{\beta \cdot (N-n)}}{2 + e^{\beta \cdot (N-1)} + e^{-\beta \cdot (N-1)}} \\ &= \frac{\cosh[\beta(n-1)] + \cosh[\beta(N-n)]}{1 + \cosh[\beta(N-1)]}\end{aligned} \tag{17}$$

which simplifies (16) to

$$q_c(n) = Q\left(\frac{R_f}{R_f + R_c}\right)\left[1 - \omega(n)\right] \tag{18}$$

which is the solution described in the main text.

The term $R_f\,(R_f + R_c)^{-1}$ describes the reduction of flow in the cell chamber base on the ratio of flow chamber resistance to the total. The term $1 - \omega(n)$ describes the flow reduction enabled by the membrane.

2. Finding the flow rate maxima and minima in the cell compartment

The flow rate maxima and minima in the cell chamber occur when ω is at its minimum and maximum. Although the variable n takes on only integer values, the function $\omega(n)$ is defined for all n, so we may use basic calculus techniques to find the minima and maxima. We follow the usual procedure of checking the endpoint values and then looking for stationary points in the interior. It is easy to see from the final form in equation (17) that ω is 1 for both $n = 1$ and $n = N$ (a value required by the boundary conditions we imposed earlier). To check the interior points we find the derivative of $\omega(n)$ with respect to n. The result is

$$\frac{d\omega(n)}{dn} = \beta \frac{\sinh[\beta(n-1)] - \sinh[\beta(N-n)]}{1+\cosh[\beta(N-1)]} \qquad (19)$$

From equation (19) and the monotonicity of the sinh, it is easy to show that the derivative is negative for $n < \frac{1}{2}(N+1)$ and positive for $n > \frac{1}{2}(N+1)$. Hence there is a zero derivative and a minimum at $n_{\min} = \frac{1}{2}(N+1)$. If N is odd, this gives the number of the cell for which the minimum occurs. If N is even, the minimum occurs on either side of the midpoint. For N large, we don't need to worry about the distinction. The value of the minimum is obtained by substituting $n_{\min}$ into the formula (17) for ω. The result, after we simplify using the double angle formula for the cosh, is

$$\omega_{\min} = \omega(n_{\min}) = \mathrm{sech}[(\beta/2)(N-1)] \qquad (20)$$

3. An asymptotic approximation for the maximum cell chamber flow rate

For our situation, we are interested in very small values of β and very large values of N such that $\beta{\cdot}N$ is of order one. We temporarily let $z = \beta{\cdot}N$ and we seek an expansion of ω_{min} in powers of β at fixed values of z. Using (20) we write ω_{min} as

$$\omega_{\min} = \operatorname{sech}[\tfrac{1}{2}(z-\beta)]\,. \qquad (21)$$

We now use a Taylor series in β about $\beta = 0$. The result is

$$\omega_{\min} = \operatorname{sech}(\tfrac{1}{2}z)[1+\tfrac{1}{2}\tanh(\tfrac{1}{2}z)\beta + O(\beta^2)]. \qquad (22)$$

For β very small we keep only the first term, which gives

$$\omega_{\min} = \operatorname{sech}(\tfrac{1}{2}z)\,. \qquad (23)$$

For moderate values of z, we can carry the approximation further by expanding the hyperbolic secant. The first three terms are

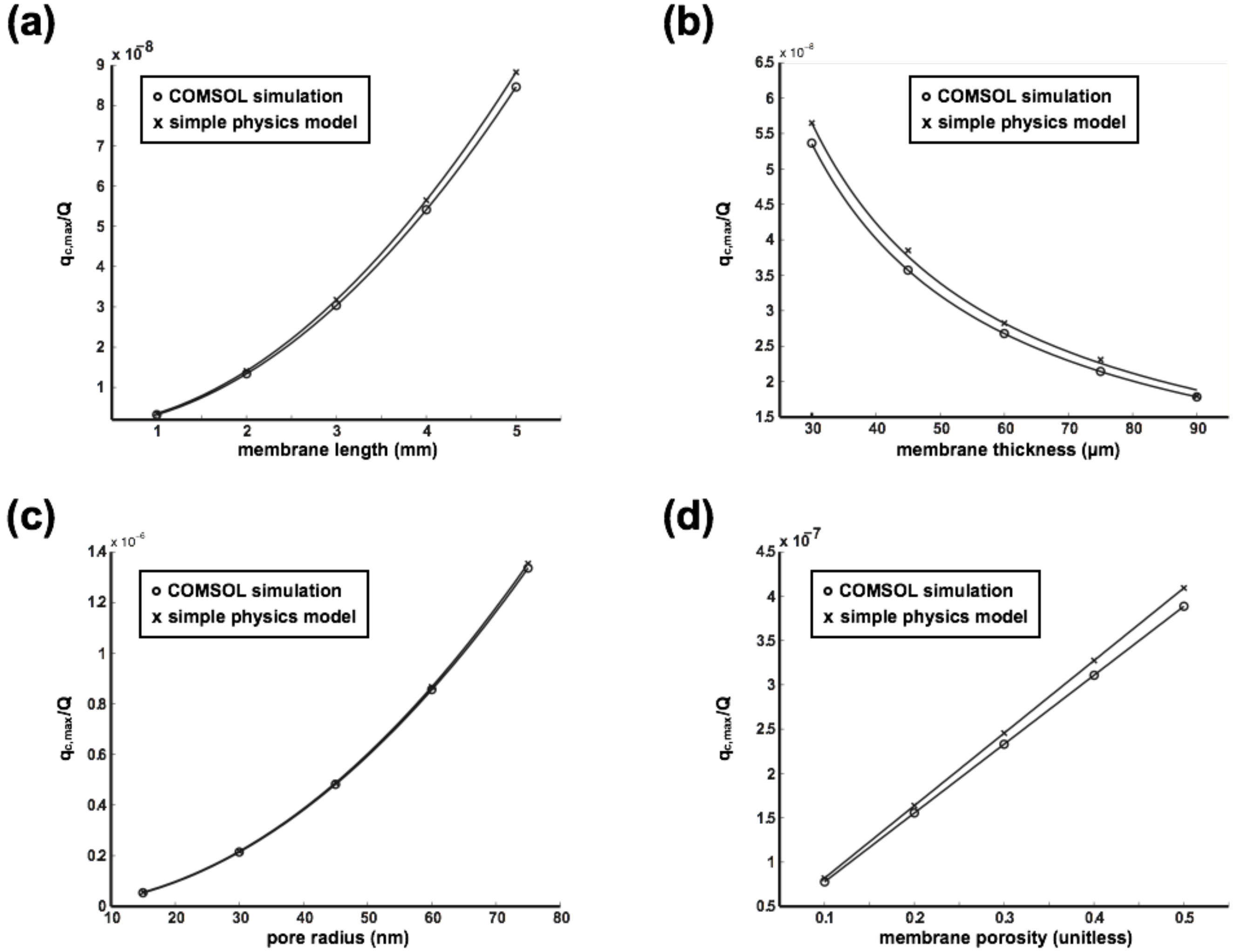
$$\omega_{\min} = \operatorname{sech}(\tfrac{1}{2}z) = 1 - \frac{z^2}{8} + \frac{5z^4}{384} + O(z^6).$$

For $z = 0.5$, for example, the third term is less than 0.1% of the first term. For z-values in that range, we may approximate ω_{min} and the maximum q_c as

$$\omega_{\min} = 1 - \frac{(\beta N)^2}{8}, \;\; \text{and} \;\; q_c = Q\frac{R_f}{R_f + R_c}\left[\frac{1}{8}(\beta N)^2\right], \qquad (24)$$

which is the approximation given in the main text.

ESI Fig. 1



ESI Fig. 1 Comparison of flow reduction predicted by the analytical solutions and COMSOL simulations. The comparisons were made while varying different membrane parameters: (a) membrane length, (b) membrane thickness, (c) average pore radius in the membrane, and (d) membrane porosity. The cell chamber flow rate maxima $q_{c,max}$ were normalized by the input flow rate Q in the flow compartment to indicate flow reduction. The analytical solutions and COMSOL simulations both showed close agreement and predicted that flow reduction in the cell chamber is quadratically-dependent on membrane length (a) and pore radius (c), inversely proportional to membrane thickness (b), and linearly proportional to porosity (d).