Supplementary Material

S1 COMPLIANCE-PRESSURE RELATIONSHIP OF THE EYE

According to Ethier et al. (2004), the pressure-volume relationship of the eye can be written as

$$\ln\left(\frac{P+\gamma}{P_{r,\phi}+\gamma}\right) = \frac{\alpha}{3V_{r,\phi}}\left(V - V_{r,\phi}\right) \tag{S1}$$

where $\gamma = 2Ah/R$, and $P_{r,\phi}$ and $V_{r,\phi}$ represent the values of P and V at a specific reference state. R and h represent the radius and thickness of the corneoscleral shell. A and α represent the material properties of the corneoscleral shell, defined based on the Fung constitutive relation for collagenous tissues describing stress σ in terms of strain ε according to $\sigma = A\left(e^{\alpha\varepsilon} - 1\right)$.

Expressing Equation 1 in terms of V and differentiating with respect to P yields an expression for the ocular compliance given by

$$\phi = \frac{3V_{r,\phi}}{\alpha}\frac{1}{P+\gamma} \tag{S2}$$

If we define a reference ocular compliance, ϕ_r that applies at $P = P_{r,\phi}$, then ϕ can be written in terms of ϕ_r as

$$\phi = \phi_r\left(\frac{P_{r,\phi}+\gamma}{P+\gamma}\right) \tag{S3}$$

This expression describes the ocular compliance relationship as a function of pressure and is consistent with Equation 3 of the main text.

S2 NOMENCLATURE OF KEY VARIABLES

		Time-dependent variables
Q	nl/min	Flow rate as measured by the flow sensor
Q_s	nl/min	Flow rate into the system compliance
Q_ϕ	nl/min	Flow rate into the ocular compliance
Q_r	nl/min	Flow rate through the aqueous humour outflow pathway.
P	$mmHg$	Pressure as measured by the pressure sensor, representative of intraocular pressure
P_a	$mmHg$	Applied pressure
		Pressure-dependent variables
ϕ	$nl/mmHg$	Ocular compliance
R	$mmHg/\,(\mu l/min)$	Hydrodynamic resistance of the outflow pathway
C	$nl/min/mmHg$	Conventional outflow facility ($C = 1/R$)
		Variables for each step, j
Q_j	nl/min	Steady state flow rate for step j
P_j	$mmHg$	Steady state pressure for step j
$P_{a,j}$	$mmHg$	Applied pressure for step j
$P_{\phi,j}$	$mmHg$	Pressure corresponding to the measured compliance for step j using the Discrete Volume Method
ΔP_j	$mmHg$	Difference in steady state pressure P between two steps
$\Delta P_{a,j}$	$mmHg$	Difference in applied pressure P_a between two steps
ΔV_ϕ	nl	Change in intraocular volume for a change in intraocular pressure
ϕ_j	$nl/mmHg$	Ocular compliance for step j
λ_j	-	Non-linearity parameter arising in Step Response Method.
		Variables that are constant for each eye
ϕ_s	$nl/mmHg$	System compliance
ϕ_r	$nl/mmHg$	Reference compliance at $P_{r,\phi}$
R_q	$mmHg/\,(\mu l/min)$	Combined hydrodynamic resistance of the flow sensor and capillary
R_c	$mmHg/\,(\mu l/min)$	Hydrodynamic resistance of the cannula
C_q	$nl/min/mmHg$	Hydrodynamic conductance of flow sensor and capillary
C_r	$nl/min/mmHg$	Reference facility at $P_{r,c}$
β	-	Non-linearity parameter characterising pressure dependence of outflow facility
γ	$mmHg$	Non-linearity parameter characterising deviation from Friedenwald's model
$P_{r,c}$	$mmHg$	Reference pressure for facility calculations
$P_{r,\phi}$	$mmHg$	Reference pressure for compliance calculations

S3 DETERMINING P_Φ FOR THE DISCRETE VOLUME METHOD

Ocular compliance changes as a function of pressure. Hence, ocular compliance measured over a pressure step by the Discrete Volume Method, $\Delta V_\phi/\Delta P$, corresponds to the true value of the ocular compliance at some pressure between P_{j-1} and P_j, which we term $P_{\phi,j}$. According to the mean value theorem, $\Delta V_\phi/\Delta P$ is equivalent to dV_ϕ/dP evaluated at $P_{\phi,j}$:

$$\phi\bigg|_{P_{\phi,j}} = \frac{dV_\phi}{dP}\bigg|_{P_{\phi,j}} \tag{S4}$$

Using Equation S3 to evaluate ϕ at $P_{\phi,j}$ and by applying the integral over the j^{th} pressure step from P_j at $t=0$ to P_{j-1} at $t=T$, where $\Delta P_j = P_j - P_{j-1}$, we can write

$$\begin{aligned}
\phi_r\left(\frac{P_{r,\phi}+\gamma}{P_{\phi,j}+\gamma}\right) &= \frac{1}{\Delta P_j}\int_0^T Q_\phi\, dt \\
&= \frac{1}{\Delta P_j}\int_0^T \phi\frac{dP}{dt}\, dt \\
&= \frac{1}{\Delta P_j}\int_{P_{j-1}}^{P_j} \phi\, dP \\
&= \frac{1}{\Delta P_j}\int_{P_{j-1}}^{P_j} \phi_r\left(\frac{P_{r,\phi}+\gamma}{P+\gamma}\right) dP \\
&= \frac{\phi_r\left(P_{r,\phi}+\gamma\right)}{\Delta P_j}\ln\left(\frac{P_j+\gamma}{P_{j-1}+\gamma}\right)
\end{aligned} \tag{S5}$$

Cancelling $\phi_r\left(P_{r,\phi}+\gamma\right)$ from both sides yields

$$\frac{1}{P_{\phi,j}+\gamma} = \frac{1}{\Delta P_j}\ln\left(\frac{P_j+\gamma}{P_{j-1}+\gamma}\right) \tag{S6}$$

Hence

$$P_{\phi,j} = \frac{\Delta P_j}{\ln\left(1+\frac{\Delta P_j}{P_{j-1}+\gamma}\right)} - \gamma \tag{S7}$$

Using the Laurent series expansion $1/\ln(1+x) = 1/x + 1/2 - x/12 + \mathcal{O}\left(x^2\right)$ allows us to write an solution for $P_{\phi,j}$

$$P_{\phi,j} = P_j - \frac{\Delta P_j}{2}\left(1+\frac{1}{6}\left(\frac{\Delta P_j}{P_{j-1}+\gamma}\right)+\mathcal{O}\left(\frac{\Delta P_j}{P_{j-1}+\gamma}\right)^2\right) \tag{S8}$$

This reveals that to leading order, $P_{\phi,j}$ is simply the midpoint between P_{j-1} and P_j.

S4 ANALYSIS FOR THE STEP RESPONSE METHOD

In this section, we derive an analytical solution to the step response of a system with pressure-dependent resistance and compliance. We start with the simple lumped parameter model shown in Fig 1b, with R_c neglected andcompliances ϕ and ϕ_s in parallel . This yields the equation:

$$\frac{dP}{dt} + \frac{(C + C_q)P - C_q P_a}{\phi + \phi_s} = 0 \tag{S9}$$

where the compliance dependence on pressure is described by

$$\phi + \phi_s = \phi_r \left(\frac{P_{r,\phi} + \gamma}{P + \gamma} \right) + \phi_s \tag{S10}$$

The facility pressure dependence is given by

$$C = C_r \left(\frac{P}{P_{r,c}} \right)^{\beta} \tag{S11}$$

In the experiments, the applied pressure is adjusted in a series of steps and held constant until the pressure in the eye asymptotes to a steady value. For an arbitrary step starting at $t = 0$ the initial condition is defined as P_{j-1}, which is the steady state pressure of the previous step. The steady state asymptote for the j^{th} step is found by setting the derivative in Equation S9 to zero which yields

$$P_j = \left(\frac{C_q}{C_j + C_q} \right) P_{a,j} \tag{S12}$$

where C_j is the facility at $P = P_j$. Because of the non-linearity due to the pressure dependence in both the compliance and facility, we seek a solution to Equation S9 using asymptotic analysis, where we assume that the size of the imposed pressure step, $\Delta P_j = P_j - P_{j-1}$, is small relative to the pressure at the end of the step, P_j.

We define the non-dimensional pressure p^* during step j according to

$$p^* = \frac{P_j - P}{\Delta P_j} \tag{S13}$$

which is equivalent to

$$P = P_j(1 - \varepsilon p^*) \tag{S14}$$

where

$$\varepsilon = \frac{\Delta P_j}{P_j} \ll 1 \tag{S15}$$

Substituting Equations S14 into Equation S9

$$-\varepsilon P_j \frac{dp^*}{dt} + \frac{(C + C_q)P_j(1 - \varepsilon p^*) - C_q P_{a,j}}{\phi + \phi_s} = 0$$

The pressure dependent facility (see Equation S11) can be written using a series expansion around $\varepsilon = 0$, to $\mathcal{O}(\varepsilon^2)$:

$$C = C_j\left(1 - \varepsilon\beta p^* + \frac{1}{2}\varepsilon^2\beta(\beta-1){p^*}^2\right) \tag{S16}$$

Substituting Equations S12 and S16 the differential equation becomes

$$\frac{dp^*}{dt} + \frac{\big((1+\beta)C_j + C_q\big)p^* - \frac{1}{2}\varepsilon\beta(\beta+1)C_j{p^*}^2}{\phi+\phi_s} = 0 \tag{S17}$$

Similarly the reciprocal of the pressure dependent total compliance can be written to $\mathcal{O}(\varepsilon)$:

$$\frac{1}{\phi+\phi_s} = \frac{1}{\phi_j+\phi_s}\left[1 - \frac{\varepsilon P_j\phi_j p^*}{(P_j+\gamma)(\phi_j+\phi_s)}\right]$$

where $\phi_j = \phi_r\left(\frac{P_{r,\phi}+\gamma}{P_j+\gamma}\right)$ is the ocular compliance at step j. Substituting this expression into S17 and collecting powers of ε, we obtain to $\mathcal{O}(\varepsilon)$

$$\frac{dp^*}{dt} + \frac{p^*}{\tau_j} - \frac{\varepsilon a_j{p^*}^2}{\tau_j} = 0 \tag{S18}$$

where

$$\frac{1}{\tau_j} = \frac{C_q + (1+\beta)C_j}{\phi_j+\phi_s}$$

and

$$a_j = \frac{\frac{1}{2}\beta(\beta+1)C_j}{C_q+(1+\beta)C_j} + \frac{P_j\phi_j}{(P_j+\gamma)(\phi_j+\phi_s)}$$

Equation S18 has the exact solution due to Bernoulli

$$p^*(t) = \frac{1}{k_j e^{\frac{t}{\tau}} + \varepsilon a_j}$$

where k_j is an arbitrary integration constant.

Using the initial condition $p^*(0) = 1$, yields $k_j = 1 - \varepsilon a_j$, hence:

$$p^*(t) = \frac{1}{(1-\varepsilon a_j)e^{\frac{t}{\tau_j}} + \varepsilon a_j} \tag{S19}$$

Substituting into Equation S13 and letting $\lambda_j = \varepsilon a_j$ we obtain the equation for $P(t)$

$$P\left(t\right) = P_j\left(1 - \frac{\Delta P_j}{P_j}\frac{1}{(1-\lambda_j)e^{t/\tau_j}+\lambda_j}\right) \tag{S20}$$

where using the definition of ε (Equation S15)

$$\lambda_j = \frac{\Delta P_j}{P_j}\left(\frac{1}{\phi_s + \phi_j}\right)\left[\left(\frac{\beta(\beta+1)C_j\tau_j}{2}\right) + \left(\frac{P_j\phi_j}{P_j+\gamma}\right)\right] \tag{S21}$$

and

$$\tau_j = \frac{\phi_j + \phi_s}{C_q + (1+\beta)C_j} \tag{S22}$$

Due to the dependence of λ_j on γ, an iterative process must be applied. The initial estimate of τ_j for this process can be calculated by omitting terms of $\mathcal{O}(\varepsilon)$, which is equivalent to setting $\lambda_j = 0$.