An Implicit Discontinuous Galerkin Method for Modeling Intestinal Edema

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Edema in the body

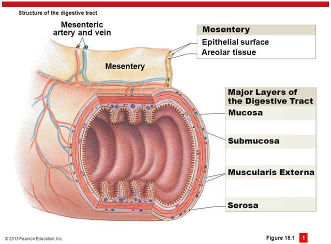
Edema: a generalized condition characterized by an excess of watery fluid collecting in body cavities or tissues

Epidermal edema (left) and cerebral edema (right)

Intestinal edema: fluid collects in the interstitium, ileus

Intestinal Physiology

Intestinal Physiology



- Young's modulus
- Shear modulus

Layer and pressure dependent values

Young's Modulus

Layer	p_{low}	p_{high}
Mucosa	1.0 kPa	0.5 kPa
Subumucosa	350 kPa	250 kPa
Musculature	40 kPa	20 kPa

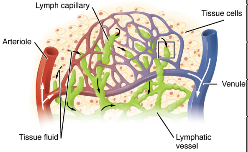
Shear Modulus

Mucosa	0.4 kPa	0.2 kPa
Subumucosa	140 kPa	100 kPa
Musculature	16 kPa	8 kPa

Vascular and Lymphatic Fluid Exchange

Vascular & Lymphatic

System, Idealized



Starling-Landis Terms	
K_F	microvascular filtration coefficient
P_V	microvascular hydrostatic pressure
σ	protein permeability of blood capillaries ($\sigma \in [0,1]$)
Π_V	microvascular oncotic pressure
Π_I	interstitial oncotic pressure
Drake-Laine Terms	
R_L	effective lymphatic resistance
P_P	lymph pumping pressure
P_L	hydrostatic pressure of lymph capillaries

Vascular : Starling-Landis $J_V(p) = K_F\left(P_V - p - \sigma(\Pi_V - \Pi_I)\right)$

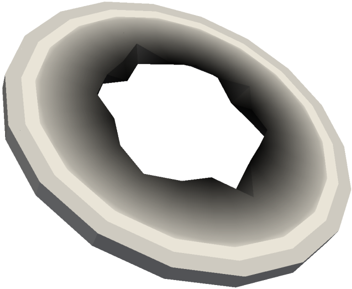
Lymphatic: Drake-Laine $J_L(p) = R_L^{-1}\left(p + P_p - P_L\right)$

Pore pressure: p

Fluid Balance Model

Capillary Distribution Function

$$C : \Omega \to [0, 1]$$



Fluid Exchange Model $\Phi(\mathbf{x}, p)$

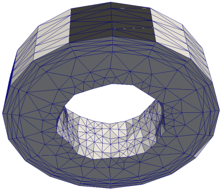
$$\Phi(\mathbf{x}, p) = \frac{\eta}{V_0} C(\mathbf{x}) \left(J_V(p) - J_L(p) \right)$$

$C(\mathbf{x})$	Piecewise linear per layer
Mucosa:	1 at lumen boundary, linearly decreasing to submucosa
Submucosa:	1×10^{-3}
Muscle:	2×10^{-3}
η	Calibrated constant scaling 10
V_0	Clinical reference volume 8400 ml

Biot's Linear Poroelasticity Equations

Displacement $\mathbf{w}$, pressure p and dilatation ε

$$
\begin{aligned}
c_1 \frac{\partial p}{\partial t} + c_0 \frac{\partial \varepsilon}{\partial t} - \kappa \Delta p &= \Phi(p), \quad \text{in} \quad \Omega \times [0, T], \\
-\nabla \cdot (\mu(p) \nabla \mathbf{w}) + c_0 \nabla p - (\mu(p) + \lambda(p)) \nabla \varepsilon &= 0, \quad \text{in} \quad \Omega \times [0, T], \\
\nabla \cdot \mathbf{w} - \varepsilon &= 0, \quad \text{in} \quad \Omega \times [0, T].
\end{aligned}
$$



Boundary conditions:

$$
\begin{aligned}
\kappa \nabla p \cdot \mathbf{n} &= 0 && \text{on } \partial\Omega \times (0, T) \\
\mathbf{w} &= \mathbf{0} && \text{on } \Gamma_{wD} \times (0, T) \\
\mu \nabla \mathbf{w} \cdot \mathbf{n} + (\mu + \lambda) \varepsilon \mathbf{n} - c_0 p \mathbf{n} &= 0 && \text{on } \Gamma_{wN} \times (0, T)
\end{aligned}
$$

Numerical Scheme with Discontinuous Galerkin

At time t^{n+1} find $(p_h^{n+1}, \varepsilon_h^{n+1}, \mathbf{w}_h^{n+1})$ in $M_h \times M_h \times \mathbf{V}_h$ s.t. for every $(r, q, \mathbf{v}) \in (M_h \times M_h \times \mathbf{V}_h)$

$$(c_1 \frac{p_h^{n+1} - p_h^n}{\Delta t}, r)_\Omega + (c_0 \frac{\varepsilon_h^{n+1} - \varepsilon_h^n}{\Delta t}, r)_\Omega + \kappa a_1(p_h^{n+1}, r) = (\Phi(p_h^n), r)_\Omega + \ell_1(t^{n+1}; r)$$

$$(\varepsilon_h^{n+1}, q)_\Omega + b_1(\mathbf{w}_h^{n+1}, q) = \ell_2(t^{n+1}; q)$$

$$a_2(\mathbf{w}_h^{n+1}, \mathbf{v}) - b_2(\mathbf{v}, \varepsilon_h^{n+1}) + c_0 b_1(\mathbf{v}, p_h^{n+1}) + j(\frac{\mathbf{w}_h^{n+1} - \mathbf{w}_h^n}{\Delta t}, \mathbf{v}) = \ell_3(t^{n+1}; \mathbf{v})$$

M_h, $\mathbf{V}_h$: DG broken polynomial spaces of order one.

Convergence analysis of scheme for homogeneous medium in:

Riviere, Tan, Thompson. 'Error analysis of primal discontinuous Galerkin methods for a mixed formulation of the Biot equations' CAMWA. 73(4)666-683, 2017.

DG Bilinear Forms

$$
\begin{aligned}
a_2(\mathbf{w},\mathbf{v}) &= \sum_{E\in\mathbf{T}_h} (\tilde{\mu}(p)\nabla\mathbf{w},\nabla\mathbf{v})_E - \sum_{e\in\Gamma_h\cup\Gamma_{\mathrm{wD}}} (\{\tilde{\mu}(p)\nabla\mathbf{w}\}\mathbf{n}_e,[\mathbf{v}])_e \\
&\quad + \theta_2 \sum_{e\in\Gamma_h\cup\Gamma_{\mathrm{wD}}} (\{\tilde{\mu}(p)\nabla\mathbf{v}\}\mathbf{n}_e,[\mathbf{w}])_e + \sum_{e\in\Gamma_h\cup\Gamma_{\mathrm{wD}}} \frac{\sigma_2}{h_e}\{\tilde{\mu}(p)\}([\mathbf{w}],[\mathbf{v}])_e \\
b_2(\mathbf{v},q) &= -\sum_{E\in\mathbf{T}_h} (\nabla\cdot\mathbf{v},(\tilde{\mu}(p)+\tilde{\lambda}(p))q)_E \\
&\quad + \sum_{e\in\Gamma_h\cup\Gamma_{\mathrm{wD}}} (\{\left(\tilde{\mu}(p)+\tilde{\lambda}(p)\right)q\},[\mathbf{v}]\cdot\mathbf{n}_e)_e
\end{aligned}
$$

1 Edema, Intestinal Physiology, and Fluid Balance

2 Model Equations and DG Discretization

3 Clinical Experiments and Simulations

Clinical Experiments

Abbrev.	Description
CTRL*	Sham surgical procedure (control group)
HS	An infusion of hypertonic saline
EVP**	Large infusion of normal saline, and a suture to induce elevated venous pressure
EVP-HS	A large infusion of normal saline, a suture to induce elevated venous pressure, an infusion of hypertonic saline midway

Numerical Values for Clinical Experiments					
Experiment	P_V	Π_V	K_f	P_p	σ
CTRL*	12	18.5	121	15	0.8
HS	12	20	121	15	0.8
EVP**	20	18.5	160	28	0.45
EVP-HS	20	18.5 / 20	160 / 121	28	0.45 / 0.8

*: Used to calibrate oncotic pressure Π_V (drop) due to surgical trauma
**:Used to calibrate reflection coefficient σ due to endothelial stretching

Calibrated Value - Clinical Experimental Value - Literature Value

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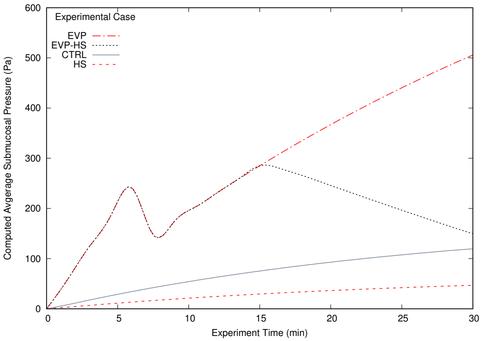
Comparison to Clinical Experiment

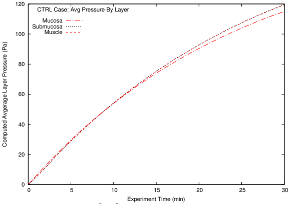
Experiment	Final Clinical Submuc. Pres. (Pa)	Comput. Avg. Submuc. Pres. (Pa)
CTRL*	Avg: 117.3	119.5
HS†	Avg:66, Range: 21 — 112	46.7
EVP*	Avg:506	505.7
EVP-HS†	Avg:133, Range:99 — 168	149.5

†: Predictive computation, no calibration. ∗ Calibration to experimental average

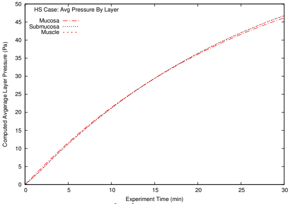


Average Submucosal Pressure

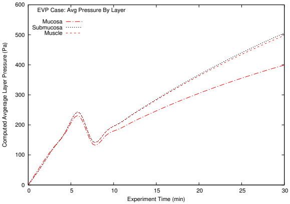
Average Pressure, All Layers



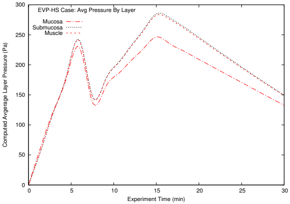
(a) CTRL



(b) HS

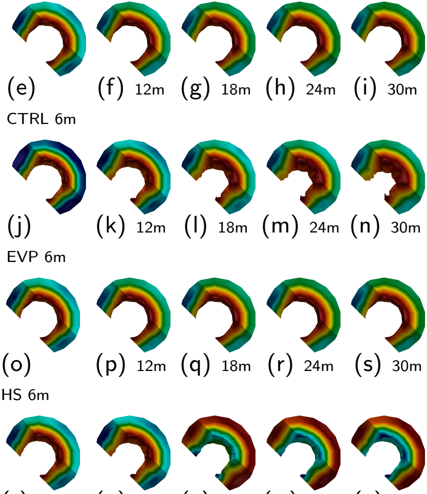


(c) EVP



(d) EVP-HS

Relative Pressure, All Experiments



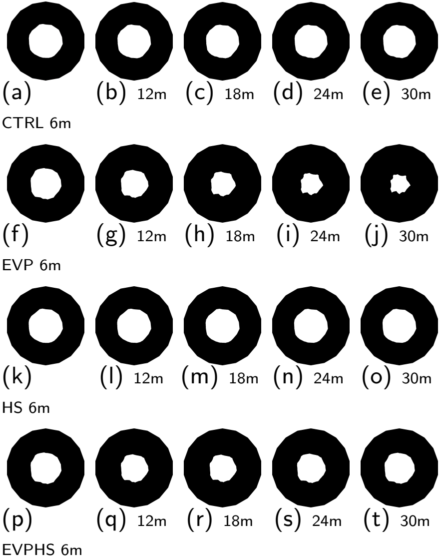
(e) CTRL 6m (f) 12m (g) 18m (h) 24m (i) 30m

(j) EVP 6m (k) 12m (l) 18m (m) 24m (n) 30m

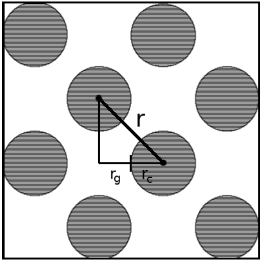
(o) HS 6m (p) 12m (q) 18m (r) 24m (s) 30m

(t) EVPHS 6m (u) 12m (v) 18m (w) 24m (x) 30m

Lumen Radius dilatation, All Simulations



Intestinal Motility and Resuscitation



ϕ (porosity) estimated from clinical data: 22-24%

$$dr_g \approx \frac{r_g}{2\phi}\frac{dV_b}{V_b}\ ^*$$

$$\hat{r} \approx \sqrt{2\left(r_c + r_g\right)^2 + 2\left(r_c + r_g\right)\frac{r_g}{\phi}\frac{dV_b}{V_b} + \frac{1}{2}\frac{r_g^2}{\phi^2}\left(\frac{dV_b}{V_b}\right)^2}$$

Desigation	r_g lower (nm)	r_g upper (nm)
Healthy	2	30
EVP	15.432	242.7
EVP-HS	4.718	72.99

Optimal Communication Distance: 12-20 nm (Savtchenko, 2007).
Reduced communication outside this range.

$r = \sqrt{2(r_g + r_c)^2}$ Pre-edema

$\hat{r} = \sqrt{2(\hat{r}_g + \hat{r}_c)^2}$ Post-edema

$\hat{r} = \sqrt{2(r_c + r_g + dr_g)^2}$ Cell impermeability

$*$ Smooth muscle compressibility $\ll$ bulk tissue compressibility
V_b: Bulk volume, tracked in simulation

Goal: estimate $\hat{r}_c = r_g + dr_g$

Conclusions

- Mathematical and numerical model for intestinal edema
- Validated by in-vitro experiments
- Hypertonic saline resuscitation helps control the formation of acute edema in presence of high venous pressure
- Funding acknowledgments: NSF