Mathematical models of the human lungs

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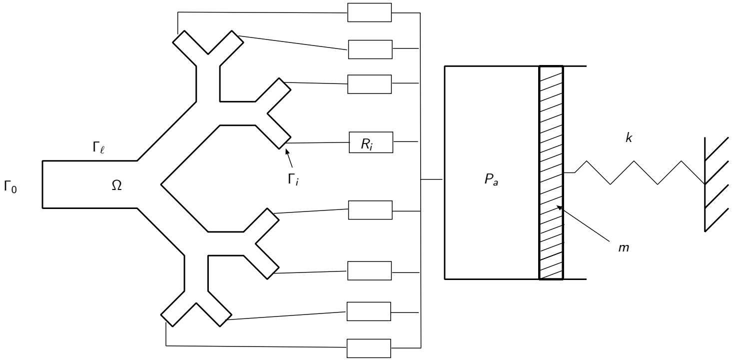
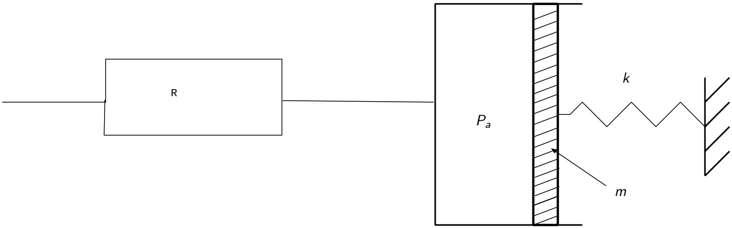
ACINIM LePoumonVousDisJe

Optimal Transport in the Human Body: Lungs and Blood
May 19 - 23, 2008


Γ_ℓ
Γ_0
Ω
R_i
Γ_i
P_a
k
m



Poiseuille's law : $0 - P_a = R \times \text{flux} = RS\dot{x}$.

Force exerted on the piston : SP_a.

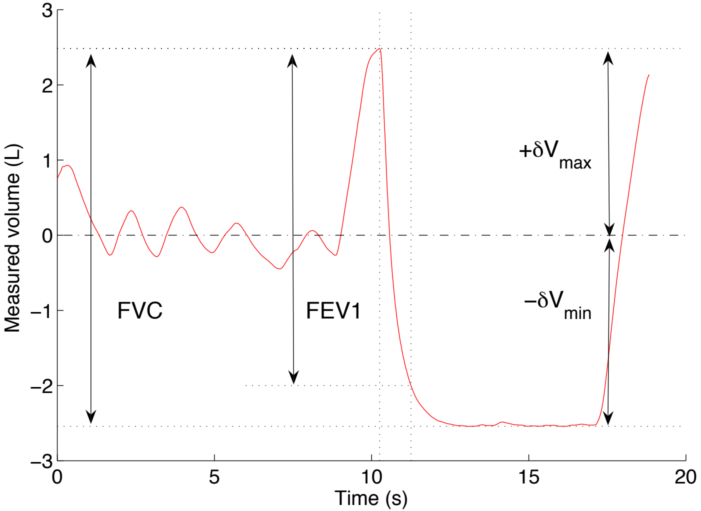
0D model (with T. Similovski, C. Strauss)

$$m\ddot{x} + (RS^2 + \mu)\dot{x} + kx = f(t).$$

A. Ben-Tal, *J. Theor. Biol.* 2006
J.R. Rodarte, K. Rehder, *Handbook of physiology*, 1986.
J.B. West, *Resp. Physiol. - The Essentials'*, 1974.
E.R. Weibel, *Morphometry of the human lung*, 1963.

$$m = 0.3\,\mathrm{kg}, \quad S = 0.011\,\mathrm{m}^2, \quad k_0 = 36.3\,\mathrm{N}\cdot\mathrm{m}^{-1},$$
$$R = 1.33 \cdot 10^5\,\mathrm{Pa}\cdot\mathrm{s}\cdot\mathrm{m}^{-3}, \quad \mu = 4.02\,\mathrm{Pa}\cdot\mathrm{s}\cdot\mathrm{m}.$$

N.B. Nonlinear stiffness $k(x)$ used in practice


3
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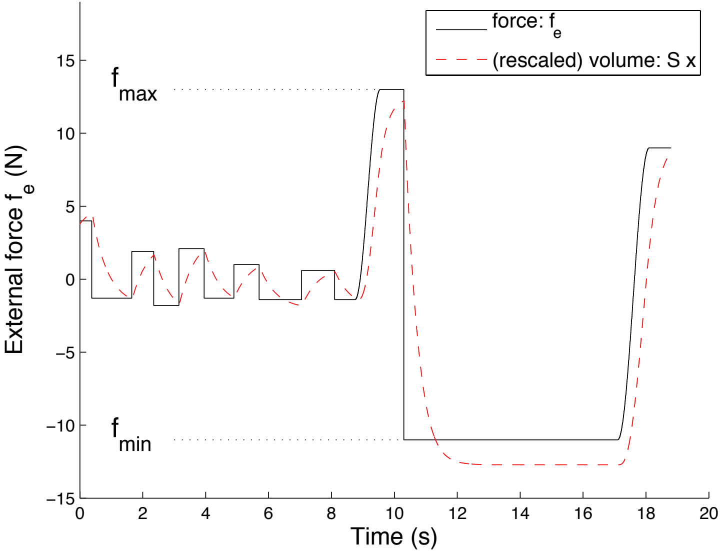
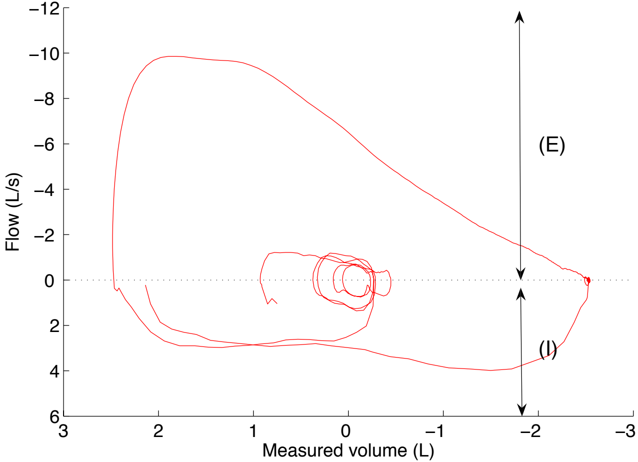
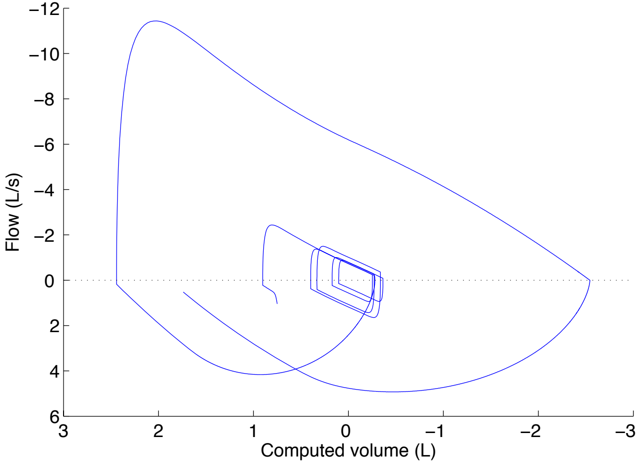
0
−1
−2
−3
0
5
10
15
20
Time (s)
Measured volume (L)
FVC
FEV1
+δV max
−δV min


force: f_e
(rescaled) volume: S x
f_{max}
f_{min}
External force f_e (N)
Time (s)
15
10
5
0
−5
−10
−15
0 2 4 6 8 10 12 14 16 18 20

Flow volume loop (exp.)



Flow volume loop (num.)



Extensions

Two compartment model : T. Similowski, J.H.T. Bates, *Two-compartment modelling of respiratory system mechanics at low frequencies : gas redistribution or tissue rheology ?*, Eur. Respir. J. (1991)

Gas transport / diffusion : A. Ben-Tal, *Simplified models for gas exchange in the human lungs*, J. Theor. Biol. (2006)

Smooth muscle (B.M, S.M, T. Similowski, C. Strauss)

Oxygen impoverishment

Non-constant resistance

Total volume variation $\delta V = Sx$: sum of δV_A (for the alveoli) and δV_B (for the bronchi) with

$$\delta V_A = (1-\theta)\, Sx, \qquad \delta V_B = \theta\, Sx.$$

θ close to 0 : the branches are rigid.
Resistance of a pipe proportional to L/D^4 :
It varies like the reciprocal of the volume (for a given shape), one has

$$R(x) = \frac{R_0}{1+\theta Sx/V_B^0}.$$

For compliant branches (neutral value $\theta_0 = V_A^0/(V_A^0+V_B^0)$), the resistance decreases significantly during inspiration.
Smooth muscle limits this decrease : apparently counter-productive.

For lower values of θ (action of the smooth muscle), the resistance is higher, but the exchange area is also likely to be larger $\longrightarrow$ improved gaz exchange.

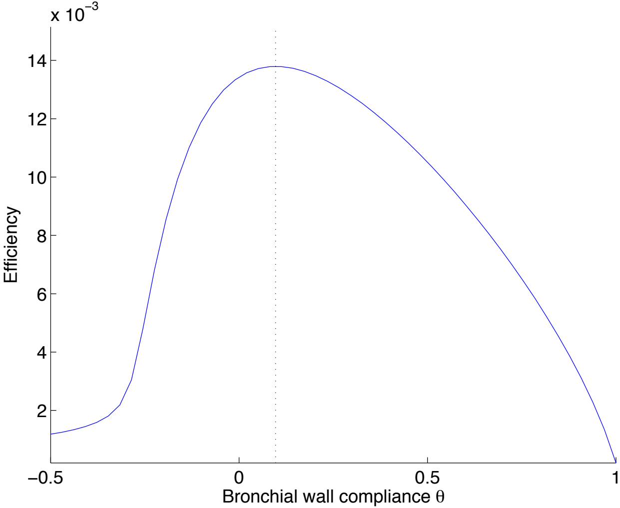
Assumption : the quantity of diffused O_2 is proportional to the total alveolar wall area, which scales like $V_A^{2/3}$:

$$q = \int_0^t \left(1 + (1-\theta) S x / V_B^0\right)^{2/3} \, dt.$$

Global system

$$\begin{cases} m\ddot{x} + \left(\dfrac{R_0\, S^2}{1+\theta S x / V_B^0} + \mu\right)\dot{x} + kx = f_e \\ \dot{q} = \left(V_A^0 + (1-\theta) S x\right)^{2/3} \end{cases}$$

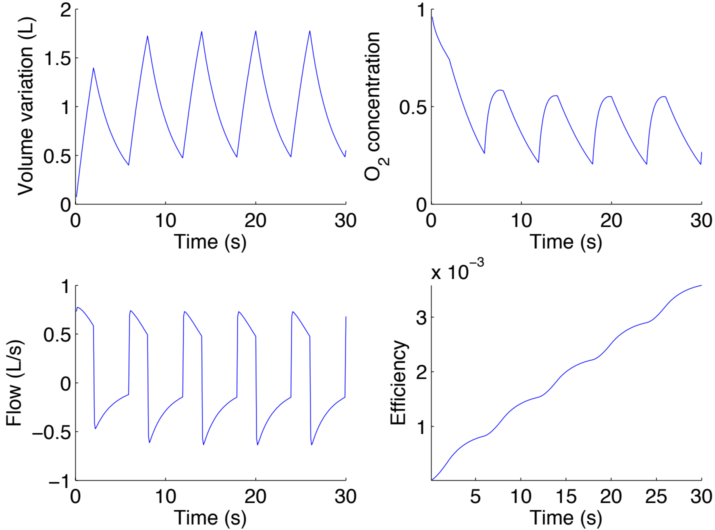
Efficiency : $q = \int_0^T \dot{q}$.
θ large $\rightarrow$ compliant branches $\rightarrow$ small resistance but also small exchange area.
θ small $\rightarrow$ rigid branches $\rightarrow$ large resistance but also larger exchange area.
Neutral value ≈ 0.4.


x 10^−3
14
12
10
8
6
4
2
Efficiency
−0.5
0
0.5
1
Bronchial wall compliance θ

O_2 IMPOVERISHMENT

Concentration c of O_2 in the alveoli is not constant :
impoverishment by diffusion through alveolar membrane
+ tidal exchange : fresh air at c_0 during inspiration
impovered air at c during expiration

$$
\left\{
\begin{array}{rcl}
\dot{x} & = & u \\
\dot{u} & = & \dfrac{1}{m}\left(f_e - \left(\dfrac{R_0\, S^2}{1+\theta S x / V_B^0} + \mu\right) u - kx\right) \\
\dot{q} & = & \Lambda \left(V_A^0 + (1-\theta) S x\right)^{2/3} c \\
\dot{c} & = & \dfrac{1}{V_A}\left(\dot{V}_A\,(c_0 - c)\,\mathbf{1}_{\mathbb{R}^+}(u) - \dot{q}\right).
\end{array}
\right.
$$


Volume variation (L)
Time (s)
O_2 concentration
Time (s)
Flow (L/s)
Time (s)
x 10^{-3}
Efficiency
Time (s)

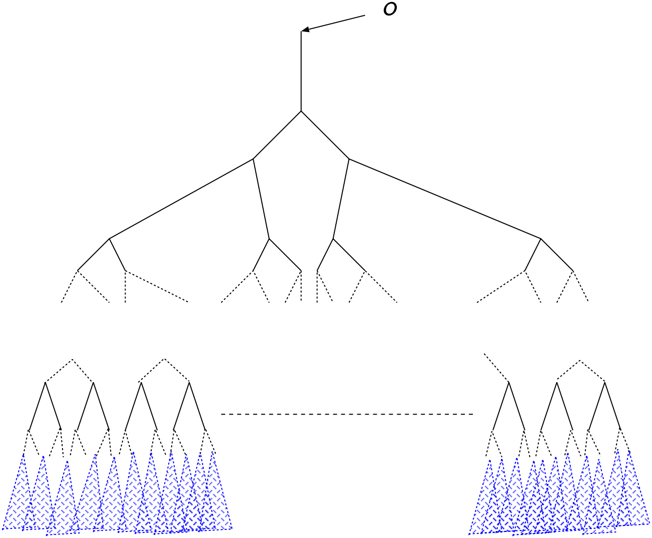
Questions : $T > 0$ is fixed, consider f_e as a control

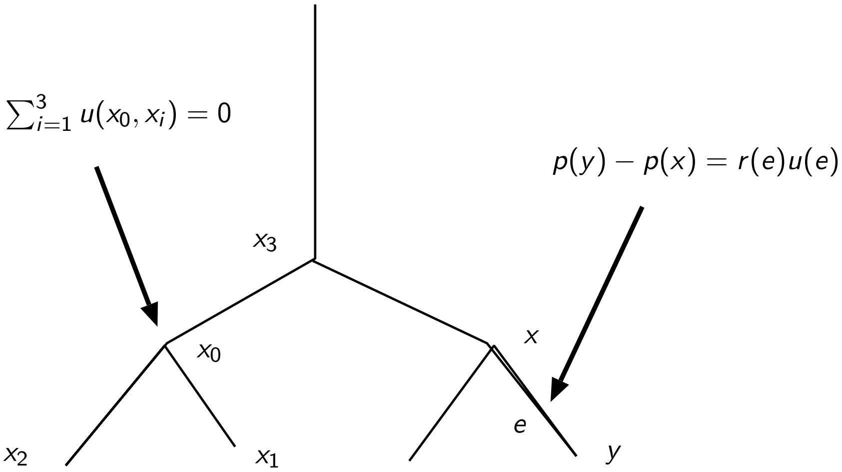
Maximize $q(T)$ with respect to f_e, under the constraint $W = \int_0^T \dot{x} f_e = W_0$ fixed.

Maximize $q(T)$ with respect to f_e, under the constraint $|f_e| \leq F_{max}$.

Is f_e (quasi-)periodic ?
Does forced expiration occur ?
How does it evolve as R is increasing ?

Infinite resistive infinite tree (with D. Salort & C. Vannier)




$\sum_{i=1}^{3} u(x_0, x_i) = 0$
$p(y) - p(x) = r(e)u(e)$
x_3
x_0
x
e
x_2
x_1
y

V set of vertices, $E \subset V \times V$ set of edges.

Resistance field $R = (r(e))_{e \in E}$, symmetric, $r(e) \in (0, +\infty)$.

Pressure $p \ : \ V \longrightarrow \mathbb{R}$

Flux $u \in \mathbb{R}^E$, $(u(y,x) = -u(x,y))$,

Divergence and gradient operators :

$$\begin{array}{rcl} \partial : \mathbb{R}^E & \longrightarrow & \mathbb{R}^V \\ u & \longmapsto & \partial u \, , \ \partial u(x) = \sum_{y \sim x} u(x,y) \end{array}$$

$$\begin{array}{rcl} \partial^\star : \mathbb{R}^V & \longrightarrow & \mathbb{R}^E \\ p & \longmapsto & \partial^\star p \, , \ \partial^\star p(e) = \partial^\star p(x,y) = p(y) - p(x) \end{array}$$

Poiseuille's Law : $u = -r^{-1}\partial^\star p$
Kirchhoff's law : $\partial u = 0$
Ventilation model :

$$\left\{ \begin{array}{lcl} u + c\,\partial^\star p & = & 0 \\ \partial u & = & \delta_0. \end{array} \right.$$

Functional spaces :

$$L^2(T) = \left\{ u \in \mathbb{R}^E \,,\; \sum_e r(e)\,|u(e)|^2 < +\infty \right\},$$

$$H^1(T) = \left\{ p \in \mathbb{R}^V \,,\; |p|_1^2 = \sum_e c(e)\,|p(y) - p(x)|^2 < +\infty \right\}$$

L^2 : weighted ℓ^2 space
H^1 Hilbert space for $\|p\|^2 = p(0)^2 + |p|_1^2$

Poiseuille's Law : $u = -r^{-1}\partial^\star p$ $\qquad$ $\mathbf{u} = -k\nabla \mathrm{p}$

Kirchhoff's law : $\partial u = 0$ $\qquad$ $\nabla \cdot \mathbf{u} = 0$

Ventilation model :

$$\left\{ \begin{array}{lcl} u + c\,\partial^\star p & = & 0 \\ \partial u & = & \delta_0. \end{array} \right. \quad \longleftrightarrow \quad \left\{ \begin{array}{lcl} \mathbf{u} + k\nabla p & = & 0 \\ \nabla \cdot \mathbf{u} & = & \delta_0 \end{array} \right. \quad \text{(Darcy)}$$

Functional spaces :

$$L^2(T) = \left\{ u \in \mathbb{R}^E \, , \, \sum_e r(e)\,|u(e)|^2 < +\infty \right\} ,$$

$$H^1(T) = \left\{ p \in \mathbb{R}^V \, , \, |p|_1^2 = \sum_e c(e)\,|p(y) - p(x)|^2 < +\infty \right\}$$

L^2 : weighted ℓ^2 space

H^1 Hilbert space for $\|p\|^2 = p(0)^2 + |p|_1^2$

T : infinite dyadic tree

H_0^1 : closure of $D(T)$ (finitely supported fields) in H^1.

Question : is H_0^1 different from H^1 ?

Or : is $\tilde{H}^{1/2} = H^1/H_0^1$ different from $\{0\}$?

Yes $\iff$ the effective resistance is finite

For a regular geometric tree ($r_N = r_0\alpha^N = r_0/h^{3N}$) :
yes iff $h > 1/\sqrt[3]{2} \approx 0.79$.

N.B. $\sqrt[3]{2}$ is the critical value in
Mauroy, Filoche, Weibel, Sapoval, Nature '2004

The condition holds true for $h = 0.85$.

Under the assumption that the effective resistance is finite

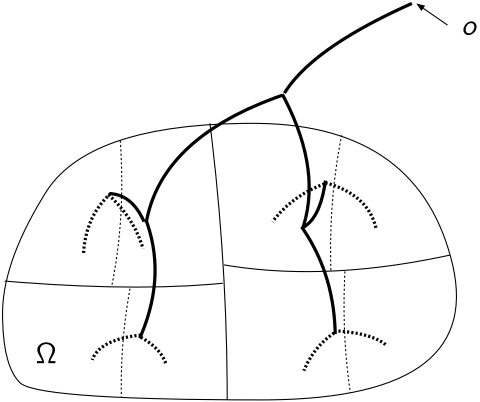
$$\left\{\begin{array}{lcll} u + c\,\partial^\star p & = & 0 & \\ \partial u & = & \delta_0 & \\ \tilde{\gamma}_0 p & = & \tilde{g} & \text{on } \Gamma \end{array}\right.$$

is well-posed, but purely abstract

How to describe $H^{1/2}$, space of pressures defined on the set of leafs

Semi abstract approach :
$H^{1/2}$ can be identified to a subset of $L^2(\Gamma)$, where Γ is the set of ends (set of paths to infinity $= \{0,1\}^{\mathbb{N}}$).

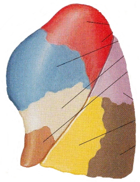
Embedding of the tree



Regularity of the "real" pressure field

Main idea : $\Gamma = \{0,1\}^{\mathbb{N}}$ is imbedded in a given domain Ω

Human lung



Modelling :

$\Omega \subset \mathbb{R}^d$

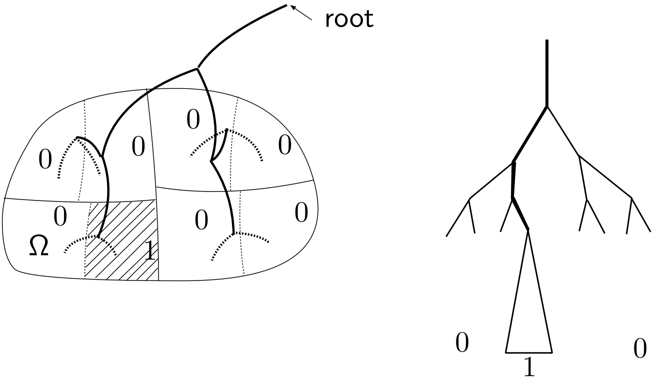
$N \geq 1$ index of the generation

A partition $(\Omega_N^j)_{j\in\{0\cdots 2^N-1\}}$ of Ω is given with the following hierarchical structure :

$\Omega_{N+1}^{2k} \cup \Omega_{N+1}^{2k+1} = \Omega_N^k$

Imbedding of the tree

One considers the set F of functions which are piecewise constant at infinity : spanned by



It defines a mapping

$$\gamma \ : \ F \subset H^1(T) \longrightarrow L^2(\Omega).$$

Prop.

If the tree is regular, and if the decomposition is balanced : $\left|\Omega_j^n\right| = 2^{-n}$

γ *can be extended by density to a continuous mapping*

$$\gamma \ : \ H^1(T) \longrightarrow L^2(\Omega).$$

Regularity of the continuous pressure field

By using Besov-type characterization of H^s :

Prop.

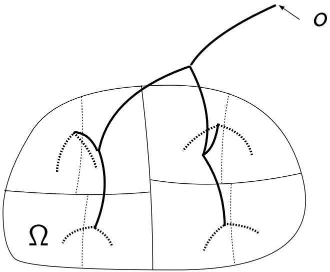
Regular tree, geometric increase of pipe resistances
$\gamma(H^1) = H^s(\Omega)$ *with*

$$s = d\left(\frac{1}{2} - \frac{ln(\alpha)}{2ln2}\right).$$

Regularity for the human lung :
reduction coefficient : $h \simeq 0.85$
geometric resistances : $\alpha = \dfrac{1}{h^3} \simeq 1.63$
It yields $s \simeq 0.45$: pressure field in $H^s(\Omega)$.

It leads to the following "elliptic" problem
$g \in H^{0.45}(\Omega)$ prescribed pressure field within the paremchyma Ω

$$\begin{cases} \text{Find} \quad p \in H^1(T) \text{ s.t.} \quad p(o) = 0, \\ -\partial c \partial^\star p = 0 \quad \text{in} \quad T \setminus \{o\}, \\ \gamma(p) = g. \end{cases}$$



Fluxes : $\Phi(\Omega_N^k)$ obtained from p, for any subdomain Ω_N^k.

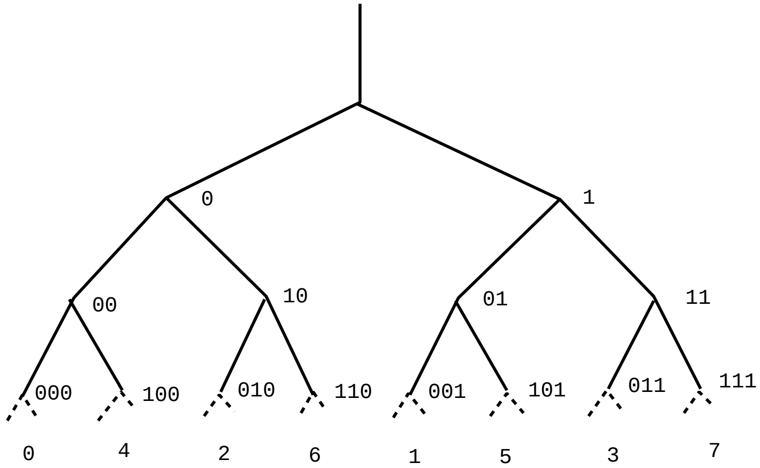
Algebraic framework

Goal : set up a framework which accounts for the notion of proximity (between leafs) with respect to the tree.

By-product : explicit formula for the mapping

$$\text{fluxes at the ends} \longmapsto \text{pressure field}$$

Extension of a previous work (with C. Grandmont and N. Meunier)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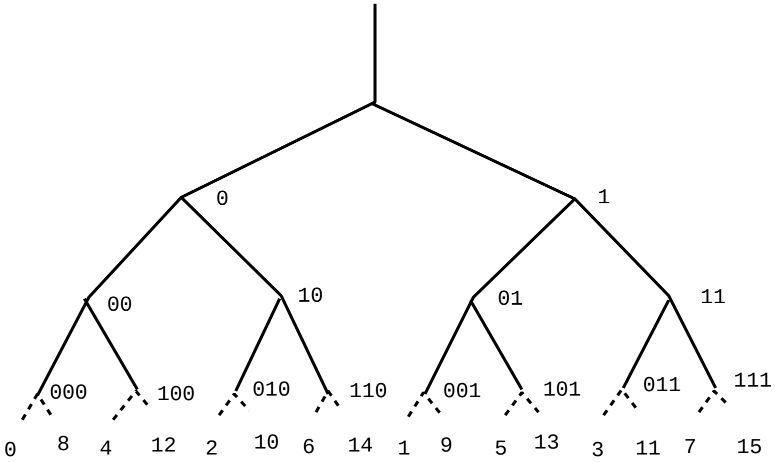
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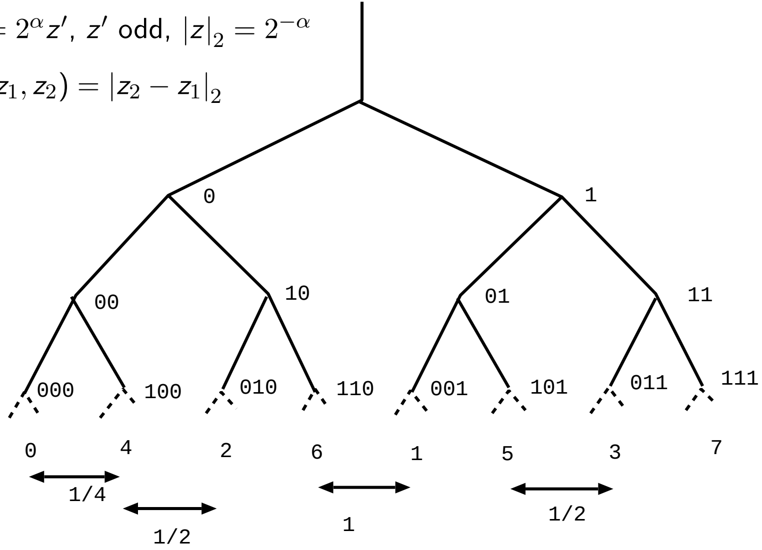
If $z = 2^{\alpha} z'$, z' odd, $|z|_2 = 2^{-\alpha}$

$\mathrm{dist}(z_1, z_2) = |z_2 - z_1|_2$



$$\Gamma_N = \{0, 1, \ldots, 2^N - 1\} \subset \mathbb{Z}$$

equipped with ultra metric-distance

$$z = 2^\alpha y\,,\ 2 \nmid y\,,\ |z|_2 = 2^{-\alpha}\,,\ \mathrm{dist}(z_1, z_2) = |z_2 - z_1|_2\,.$$

One has

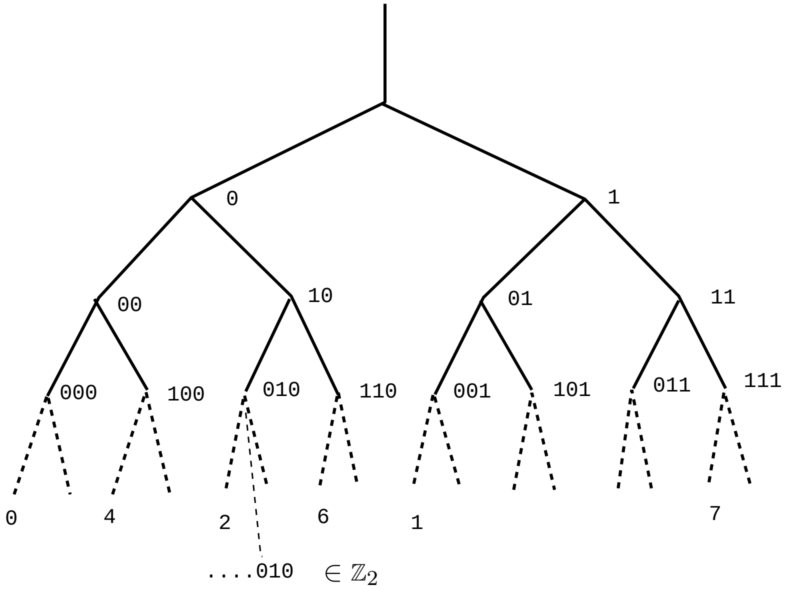
$$\overline{\bigcup_{N \in \mathbb{N}} \Gamma_N} = \mathbb{Z}_2 \quad \text{set of dyadic integers}$$

More properly :

$$\Gamma_n = \mathbb{Z}/2^n\mathbb{Z}\,,\ \varphi_{nm}\ :\ z \in \Gamma_m \longmapsto \tilde{z} \in \Gamma_n \quad (\tilde{z} \equiv z \mod 2^n) \quad n \leq m.$$

Γ is the projective limit of the Γ_n's :

$$\Gamma = \lim_{\longleftarrow} \Gamma_n = \left\{ (a_n) \in \prod_{n \in \mathbb{N}} \Gamma_n\,,\ \varphi_{nm}(a_m) = a_n \quad \forall n \leq m \right\}$$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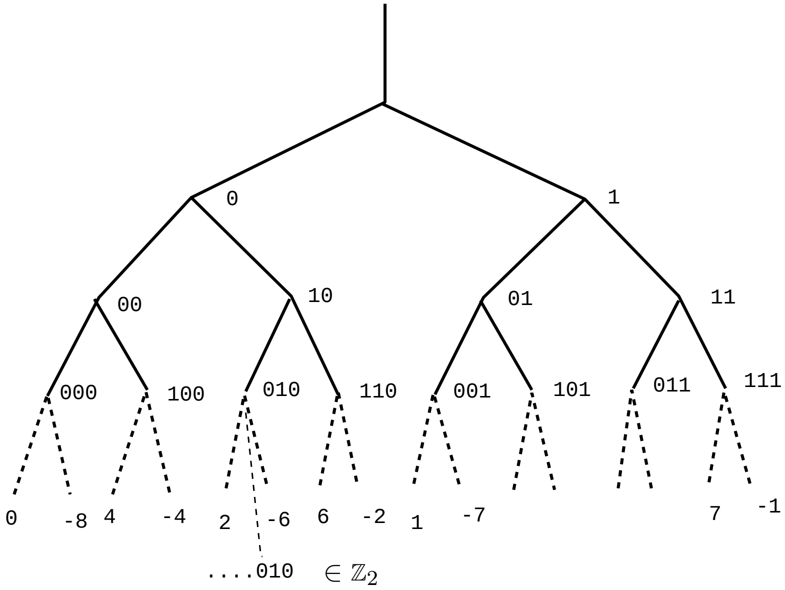
....010 $\in \mathbb{Z}_2$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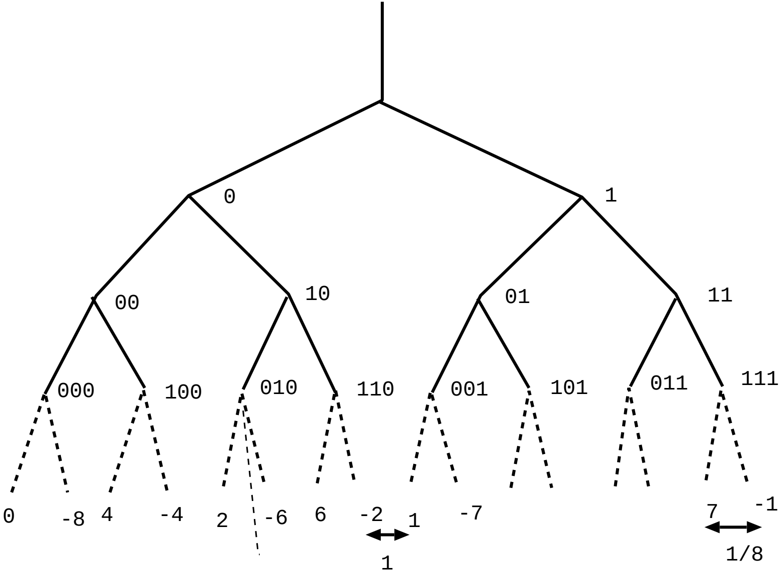
-1
....010 $\in \mathbb{Z}_2$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-2
1
-7
7
-1
1
1/8

Notion of integral over $\mathbb{Z}_2$, based on

$$\int_{\mathbb{Z}_2} \mathbb{1}_{a+2^n\mathbb{Z}_2} = 2^{-n}$$

Fluxes : $\mu \in \mathcal{M}(\mathbb{Z}_2)$: $\mu(a + 2^n\mathbb{Z}_2)$ is known

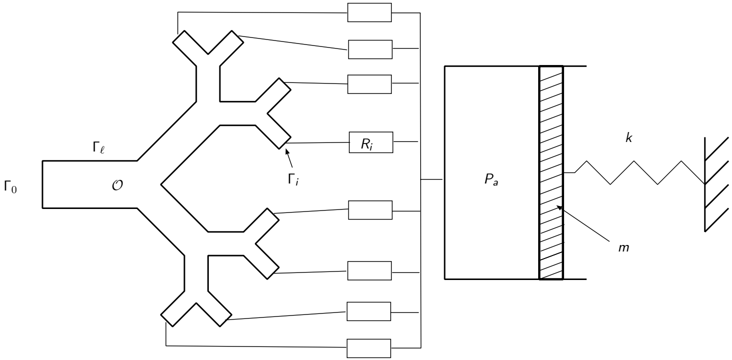
$$p(x) = \mathcal{R}\mu(x) = \int_{\mathbb{Z}_2} \frac{\mu(y)}{|x-y|^{\log_2(\alpha)}} dy = G \star \mu(x).$$

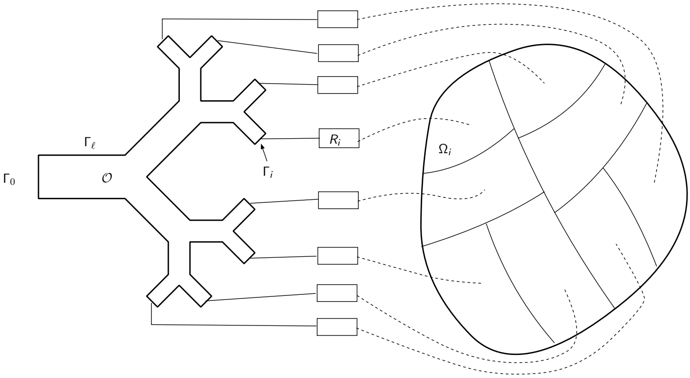
where G is a Green-like Kernel (like $1/|x-y|^{d-2}$ in $\mathbb{R}^d$).

N.B. : for $R < \infty$, $\log_2(\alpha) \in (-\infty, 1)$

In particular $\log_2(\alpha) \approx 0.7$ for $\alpha = 0.85$

"Equivalent" dimension $d = 2.7$


Γ_ℓ
Γ_0
$\mathcal{O}$
R_i
Γ_i
P_a
k
m


Γ_ℓ
Γ_0
$\mathcal{O}$
R_i
Γ_i
Ω_i

d : displacement field in the paremchyma
$P = \sum P_i \mathbb{1}_{\Omega_i}$ outlet pressures (on Γ_i)
$\Pi = \sum \Pi_i \mathbb{1}_{\Omega_i}$ pressure field in the paremchyma

$$P_i - \Pi_i = \mathcal{R}_i \nabla \cdot \partial_t \mathbf{d}$$

$$\rho\, \partial_{tt}\mathbf{d} - k\, \nabla \cdot \left(\nabla \mathbf{d} + \nabla^T \mathbf{d} \right) + \nabla \Pi = 0 \quad \text{in } \Omega$$

$$\mathbf{d} \quad \text{prescribed on } \partial\Omega.$$

$$\begin{aligned} \frac{\partial \mathbf{u}}{\partial t} + (\mathbf{u}\cdot\nabla)\mathbf{u} - \mu\triangle\mathbf{u} + \nabla \mathrm{p} &= 0 \text{ in } \mathcal{O} \\ \nabla\cdot\mathbf{u} &= 0 \text{ in } \mathcal{O}. \end{aligned}$$

$$\left\{ \begin{array}{rcll} \mu\nabla\mathbf{u}\cdot\mathbf{n} - \mathrm{p}\mathbf{n} &=& 0 & \text{on } \Gamma_0 \\ \mu\nabla\mathbf{u}\cdot\mathbf{n} - \mathrm{p}\mathbf{n} &=& -P_i\mathbf{n} & \text{on } \Gamma_i \end{array} \right.$$

$$\int_{\Gamma_i} \mathbf{u}\cdot\mathbf{n} = \int_{\Omega_i} \nabla \cdot \partial_t \mathbf{d}$$