Università degli studi di Genova

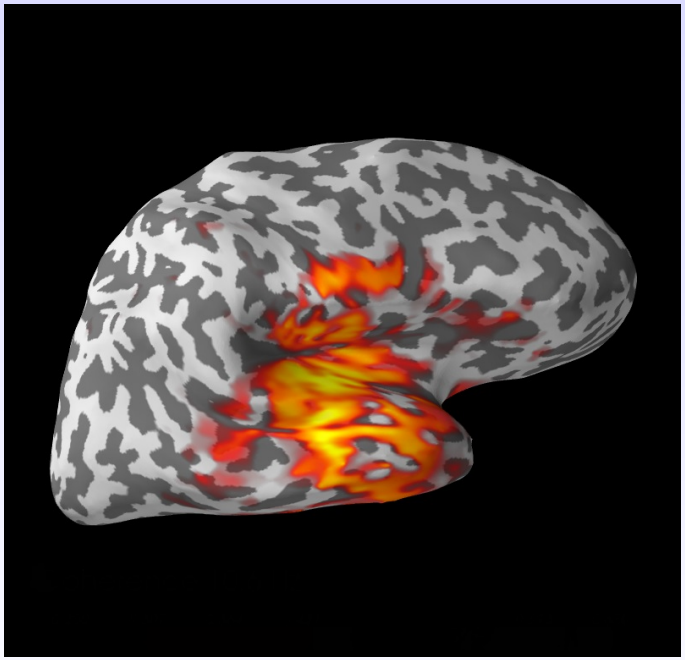
Dynamic inverse problem - XXVIII ciclo

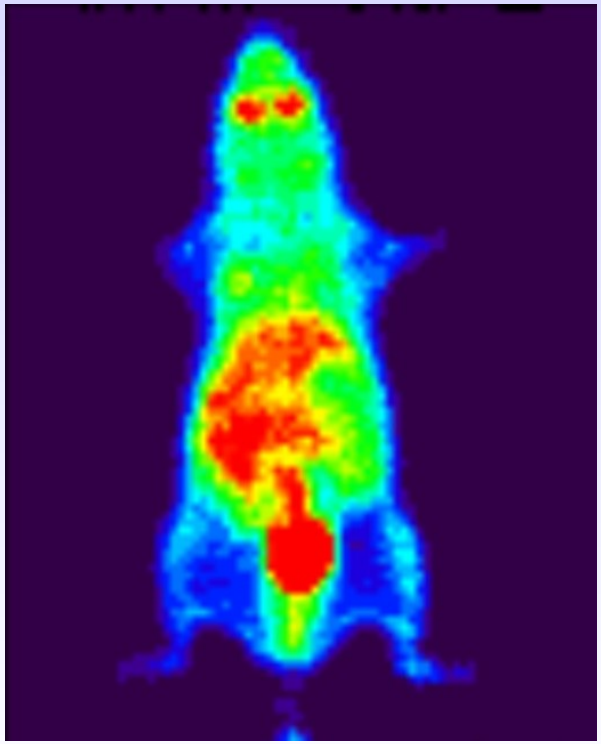
Valentina Vivaldi

Monday, 27th April 2015

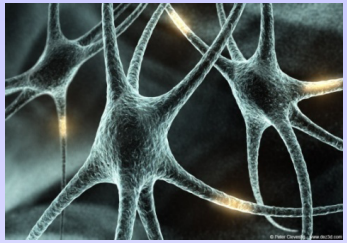
Working fields

- Neuroscience
- Medical imaging





MEG - MagnetoEncephaloGraphy



Neurons communicate via electrical currents that generate magnetic fields

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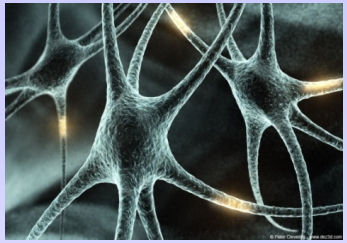

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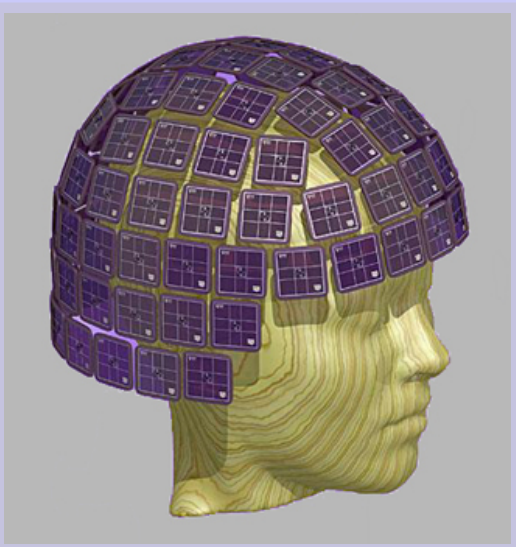
MEG Helmet



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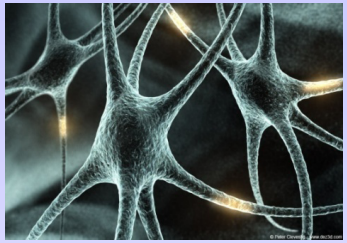

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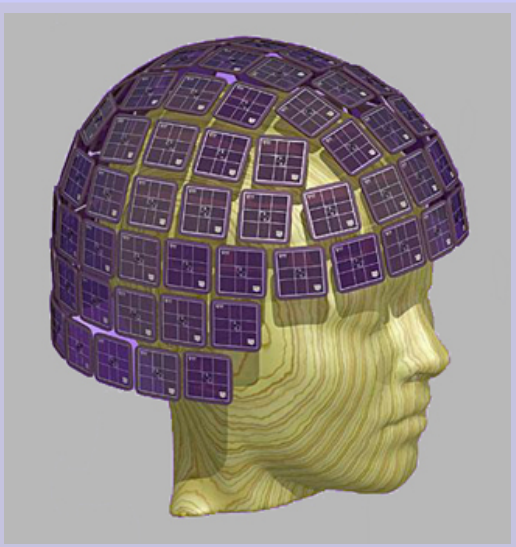
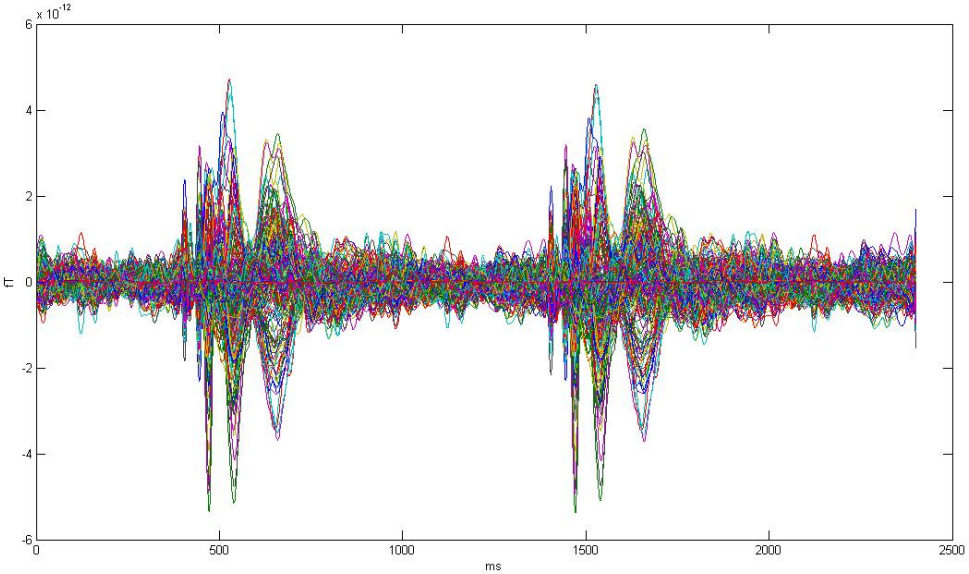


Magnetic field measured



MEG - Matematical Model

Magnetic Generation Model: BiotSavart

$$B(r) = \frac{\mu_0}{4\pi} \int_\Omega J(r^{'}) \times \frac{r - r^{'}}{|r - r^{'}|^3} \, dr^{'}$$

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$$B \Rightarrow J(r^{'}), \quad \forall r^{'} \in \Omega$$

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ILL–POSED

Assuming a multi dipolar model

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Data

- $B(r,t)\, \forall r = 1, \ldots, N_s$
  $\forall t = 1, \ldots, T$

Unknowns

- N
- q^i, $\forall i = 1, \ldots N$
- r^i, $\forall i = 1, \ldots N$

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Bayesian approach

Bayesian approach to inverse problems

If we have a random variable Y (data), a random variable X (unknown), an operator A s.t.

$$A(X) = Y$$

and if x and y are two different realisations of both X and Y , the inverse problem is to find $p(x|y)$.

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Bayes Theorem

$$p(x|y) = \frac{p(x)p(y|x)}{p(y)}$$

- $p(x)$: prior
- $p(y|x)$: likelihood
- $p(x|y)$: posterior
- $p(y)$: normalisation constant

Bayes Theorem in MEG problem

$$X = J = (R, Q, N)$$

$$Y = B$$

$$p(j_t|b_{1:t}) = \frac{p(b_{1:t}|j_t)p(j_t)}{p(b_{1:t})}$$

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Bayesian filter goal

$$p(x_t|y_{1:t}) \Rightarrow p(j_t|b_{1:t})$$

Particle Filter

Evolution-Observation filter

$$p(j_t|b_{1:t}) = \frac{p(b_t|j_t)p(j_t|b_{1:t-1})}{p(b_t|b_{1:t-1})}$$

$$p(j_{t+1}|b_{1:t}) = \int p(j_{t+1}|j_t)p(j_t|b_{1:t})\, dj_t$$

We have to choose

- $p(j_0|b_0) = p(j_0)$
- $p(j_{t+1}|j_t)$, $\forall\ t$
- $p(b_t|j_t)$, $\forall\ t$

A particle filter is an approximate solution of the Evolution-Observation filter obtained by Monte Carlo methods

Monte Carlo methods

Allow to approximate probability densities with particles and weights.

General idea

If we need to approximate

$$I = \int f(x)p(x|y)\,dx$$

we can sample α independent variables $\{x_i\} \sim q(x)$ and so

$$\sum_{i=1}^{\alpha} \frac{1}{\alpha} f(x_i) \frac{p(x_i|y)}{q(x_i)} \backsimeq I$$

$$\sum_{i=1}^{\alpha} \frac{1}{\alpha} \frac{p(x_i|y)}{q(x_i)} \delta(x - x_i) \backsimeq p(x|y)$$

New smoothing approach

Smoothing

Sequential approximation of the $p(j_t|b_{1:T})$ where $t = 1, \ldots T$.

$$p(j_t|d_{1:T}) = \frac{p(j_t|d_{1:t-1})p(d_{t:T}|j_t)}{p(d_{t:T}|d_{1:t-1})} \quad .$$

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Introducing

auxiliary densities $\gamma_t(j_t)$ and probability distributions $\tilde{p}(j_t|d_{t:T})$ such that

$$\tilde{p}(j_t|d_{t:T}) \propto p(d_{t:T}|j_t)\gamma_t(j_t) \quad ; \tag{1}$$

we can re–write

$$p(j_t|d_{1:T}) \propto \frac{p(j_t|d_{1:t-1})\tilde{p}(j_t|d_{t:T})}{\gamma_t(j_t)} \quad . \tag{2}$$

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Particle filtering (fwd)

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Particle filtering (bkwd)

$$p(j_t|d_{1:T}) = \frac{p(j_t|d_{1:t-1})p(d_{t:T}|j_t)}{p(d_{t:T}|d_{1:t-1})} \quad .$$

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$$p_{bkwd}(j_t|d_{1:T}) = \sum_{i=1}^{\alpha} w^i_{bkwd,t|T}\delta(j_t, \tilde{j^i_t}) \tag{3}$$

$$p(j_t|b_{1:T}) = \frac{p(j_t|b_{1:t-1})p(b_{t:T}|j_t)}{p(b_{t:T}|b_{1:t-1})}.$$

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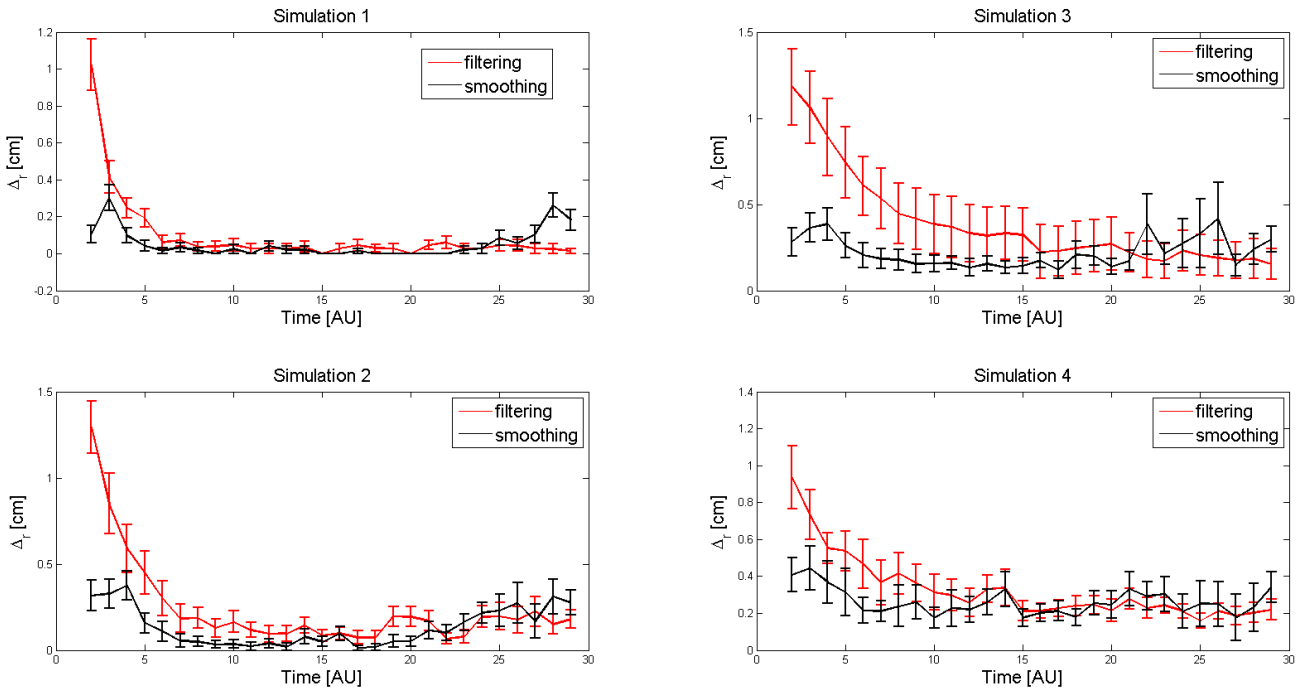
Our Smoothing

$$p(j_t|b_{1:T}) \propto \frac{p(j_t|b_{1:t-1})\tilde{p}(j_t|b_{t:T})}{\tilde{p}(j_t)} \simeq \sum_{i=1}^{\alpha} w^i_{bkwd,t|T}\delta(j_t, \tilde{j_t^i}) \quad (4)$$

$$\propto \frac{p(j_t|b_{1:t})\tilde{p}(j_t|b_{t+1:T})}{\tilde{p}_0(j_t)} \simeq \sum_{i=1}^{\alpha} w^i_{fwd,t|T}\delta(j_t, j_t^i) \quad (5)$$

Results on Simulation

Error on positions



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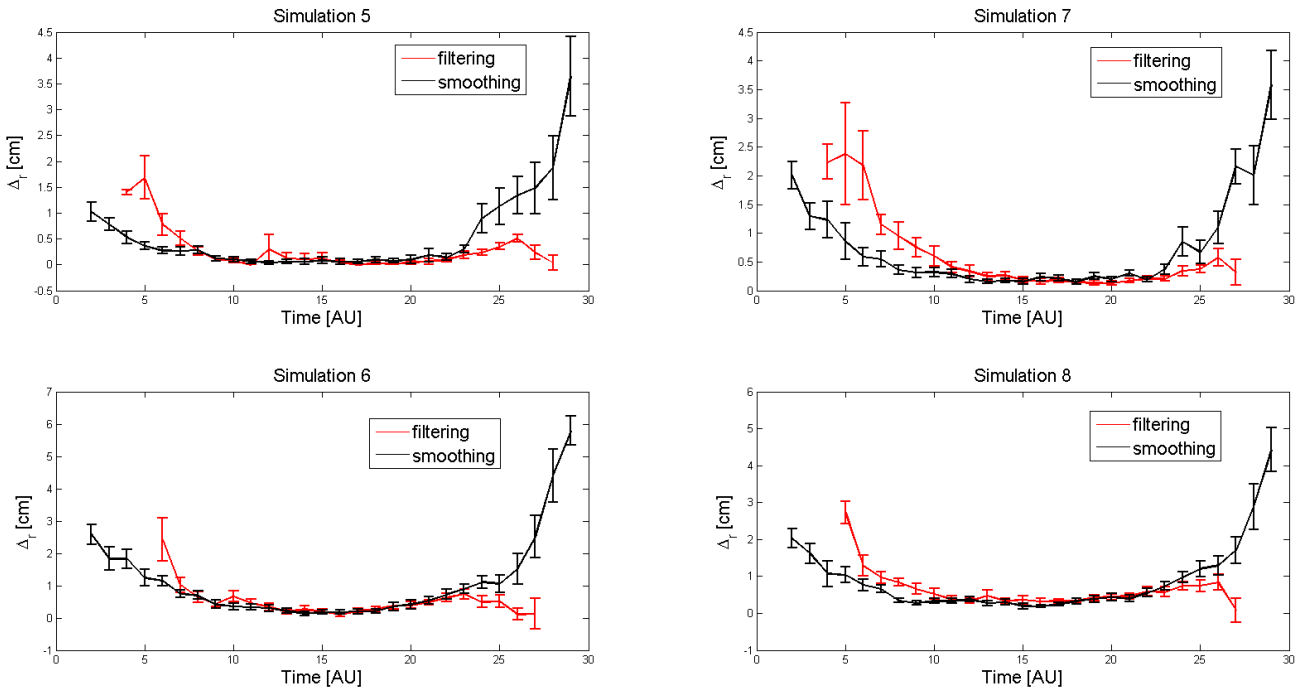


Medical Imaging

Aim of medical imaging research

Study kinetics of radioactive tracer, $[^{18}F]FDG$ in metabolism and the effect of an oral metformin based antidiabetic drug.

Physics

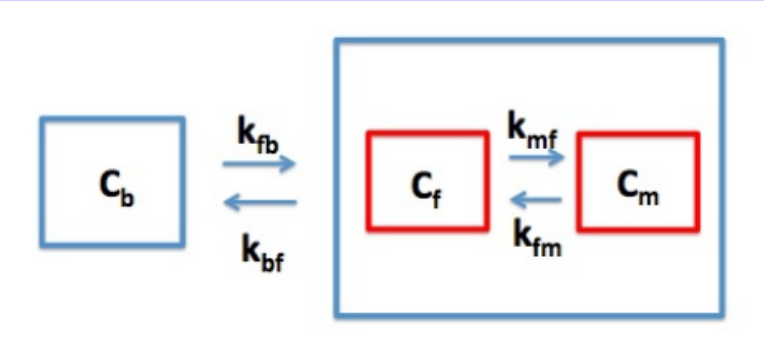
- injection of positron-emitting tracer ($[^{18}F]FDG$);
- emission of positrons ($\beta+$);
- collision with electrons ($\beta-$) causing an annihilation;
- emission of energy: two 511keV energy gamma rays at π;
- detection of gamma rays by opposing detectors;
- energy and timing discrimination are used to ensure true coincidence.

Compartmental model

physical assumption

- tracer is uniformly distributed in each compartment
- diffusive effects are neglected
- physiological processes are in a steady state
- conservation of tracer between compartments holds

Compartmental forward model



$$\dot{C}_f = -(k_{bf} + k_{mf})C_f + k_{fm}C_m + k_{fb}C_b$$

$$\dot{C}_m = k_{mf}C_f - k_{fm}C_m$$

$$M = \begin{pmatrix} -(k_{bf} + k_{mf}) & k_{fm} \\ k_{mf} & -k_{fm} \end{pmatrix} \quad W = \begin{pmatrix} C_b \\ 0 \end{pmatrix} = C_b\mathbf{e_1} \quad C = \begin{pmatrix} C_f \\ C_m \end{pmatrix}$$

$$\dot{C} = MC + k_{fb}C_b\mathbf{e_1}$$

$$C(t) = k_{fb}\int_0^t C_b(u)\exp((t-u)M)\mathbf{e_1}\,du$$

Data

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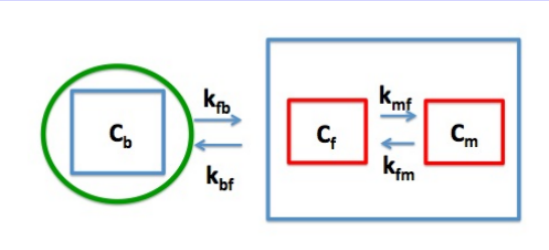
- C_b is obtained from Regions of Interest drawn over PET images of the left ventricle at many times t



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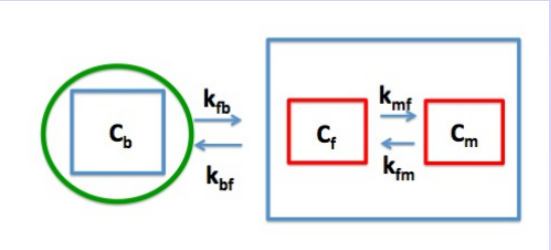
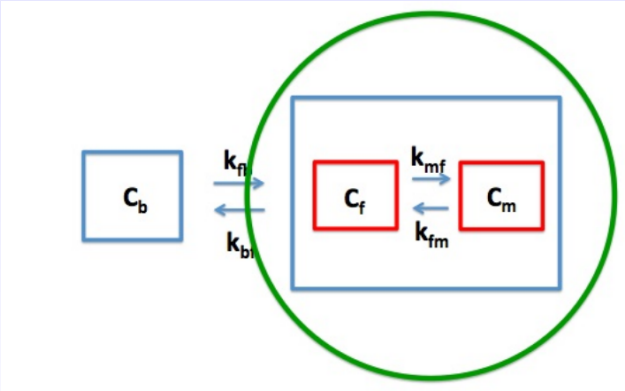


- C_{tot} is obtained from Regions of Interest drawn over PET images of the overall organ at many times t



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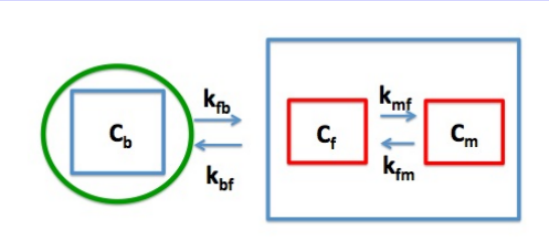

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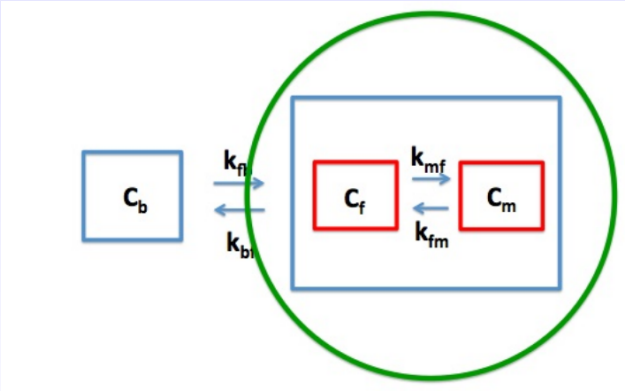

- C_{tot} is modeled as $(1-V)(C_f + C_m) + VC_b$, $V \in (0,1)$ known blood fraction that supplies the organ

The problem

measurements: C_{tot} and C_b
experimentally known: blood fraction V
data equation

$$C_{\text{tot}} = (1-V)(C_f + C_m) + VC_b$$
$$\rightarrow \tilde{C} := C_{\text{tot}} - VC_b = (1-V)(C_f + C_m)$$

forward problem solution

$$\begin{pmatrix} C_f \\ C_m \end{pmatrix} = C(t) = k_{fb} \int_0^t C_b(u) \exp((t-u)M)\mathbf{e_1}\, du$$

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inverse problem: find $\mathbf{k} := (k_{fb}, \hat{\mathbf{k}}) := (k_{fb}, k_{bf}, k_{fm}, k_{mf}) \in \mathbb{R}_+^{*4}$
from the knowledge of

$$\tilde{C} = \alpha \cdot C(t) = \alpha \cdot \mathbf{k}(1) \int_0^t C_b(u) \exp((t-u)M(\hat{\mathbf{k}}))\mathbf{e_1}\, du$$

where $\alpha = \begin{pmatrix} 1-V \\ 1-V \end{pmatrix}$

Inversion method - 1

introduce:

$$\mathcal{F}_t : \mathbb{R}_+^{*4} \to C^1(\mathbb{R}_+, \mathbb{R}) \quad \text{such that} \quad \mathcal{F}_t(\mathbf{k}) = \alpha \cdot C(\mathbf{k})(t)$$

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aim: determine $\mathbf{k}$ from experimental measurements of $\tilde{C}(t)$ such that

$$\tilde{C}(t) = \mathcal{F}_t(\mathbf{k}) \ .$$

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apply Newton algorithm:

$$\left[\frac{d\mathcal{F}_t}{dk}(k^{(0)}; h^{(0)})\right](t) = \tilde{C}(t) - \mathcal{F}(k^{(0)})(t)$$

with unknown $h^{(0)} \in \mathbb{R}_+^{*4}$, initial guess $k^{(0)} \in \mathbb{R}*_+^4$ and for all $t \in \mathbb{R}_+$

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with unknown $h^{(0)} \in \mathbb{R}_+^{*4}$, initial guess $k^{(0)} \in \mathbb{R}*_+^4$ and for all $t \in \mathbb{R}_+$ Fréchet derivative:

$$\begin{array}{rcl} \frac{d\mathcal{F}_t}{dk} : \mathbb{R}_+^{*4} & \to & C^1(\mathbb{R}_+, \mathbb{R}), \\ \mathbf{h} & \mapsto & (t \mapsto \nabla \mathcal{F}_t(\mathbf{k}) \cdot \mathbf{h}) \end{array}$$

Inversion method -2

discretized Newton equation

$$\begin{pmatrix} \left[\nabla \mathcal{F}_{t_1}(\mathbf{k}^{(0)})\right]^T \\ \vdots \\ \left[\nabla \mathcal{F}_{t_n}(\mathbf{k}^{(0)})\right]^T \end{pmatrix} \mathbf{h}^{(0)} = \begin{pmatrix} \tilde{C}(t)(t_1) - \mathcal{F}_{t_1}(\mathbf{k}^{(0)}) \\ \vdots \\ \tilde{C}(t)(t_n) - \mathcal{F}_{t_n}(\mathbf{k}^{(0)}) \end{pmatrix}$$

i.e.

$$A^{(0)}\mathbf{h}^{(0)} = Y^{(0)}.$$

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warning: may have no solution! Regularization is needed

$$\left(rI + (A^{(0)})^T A^{(0)}\right)\mathbf{h}^{(0)} = (A^{(0)})^T Y^{(0)},$$

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discretized Newton equation

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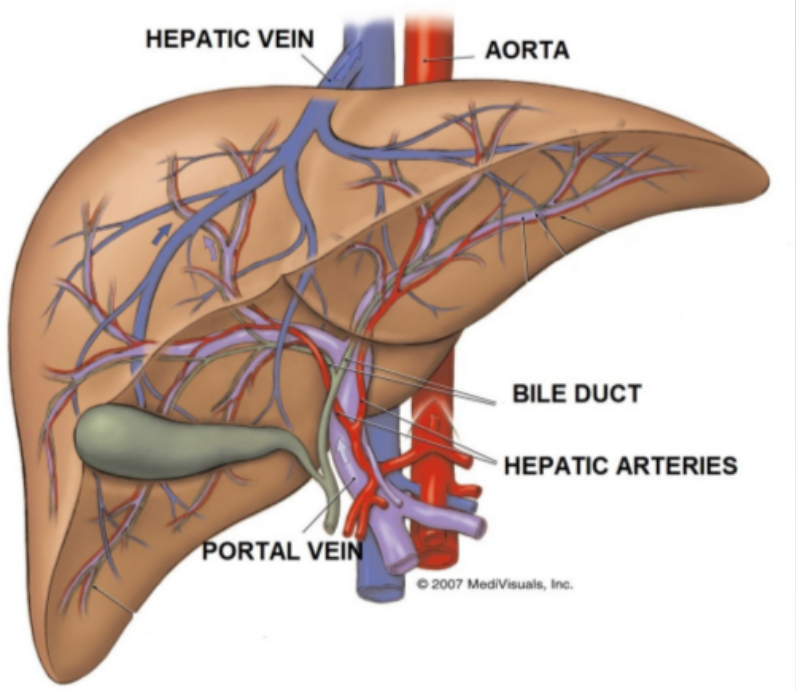
$$\left(rI + (A^{(0)})^T A^{(0)}\right)\mathbf{h}^{(0)} = (A^{(0)})^T Y^{(0)},$$

iteration step

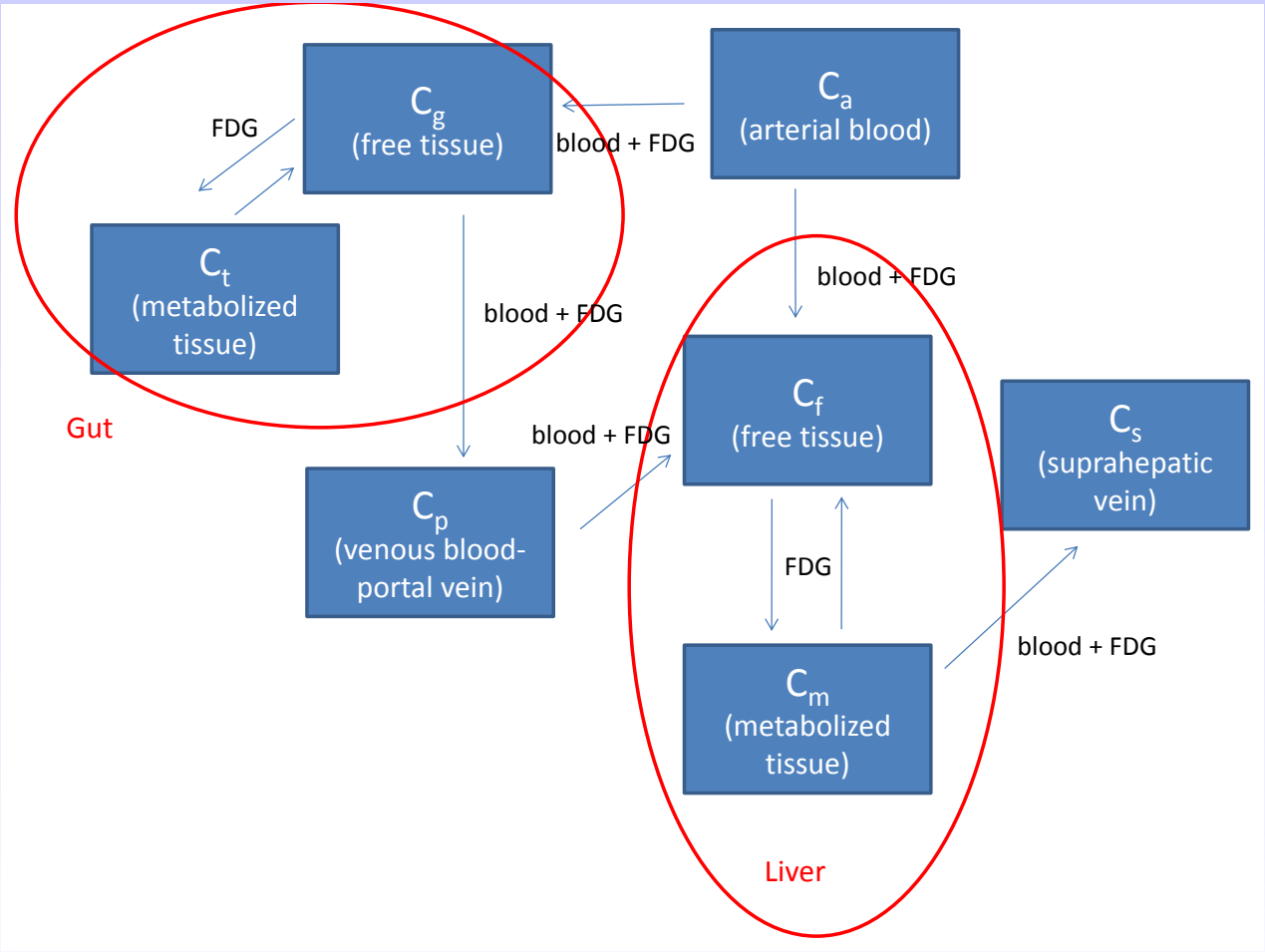
$$\mathbf{k}^{(1)} = \mathbf{k}^{(0)} + \mathbf{h}^{(0)}$$

Liver application

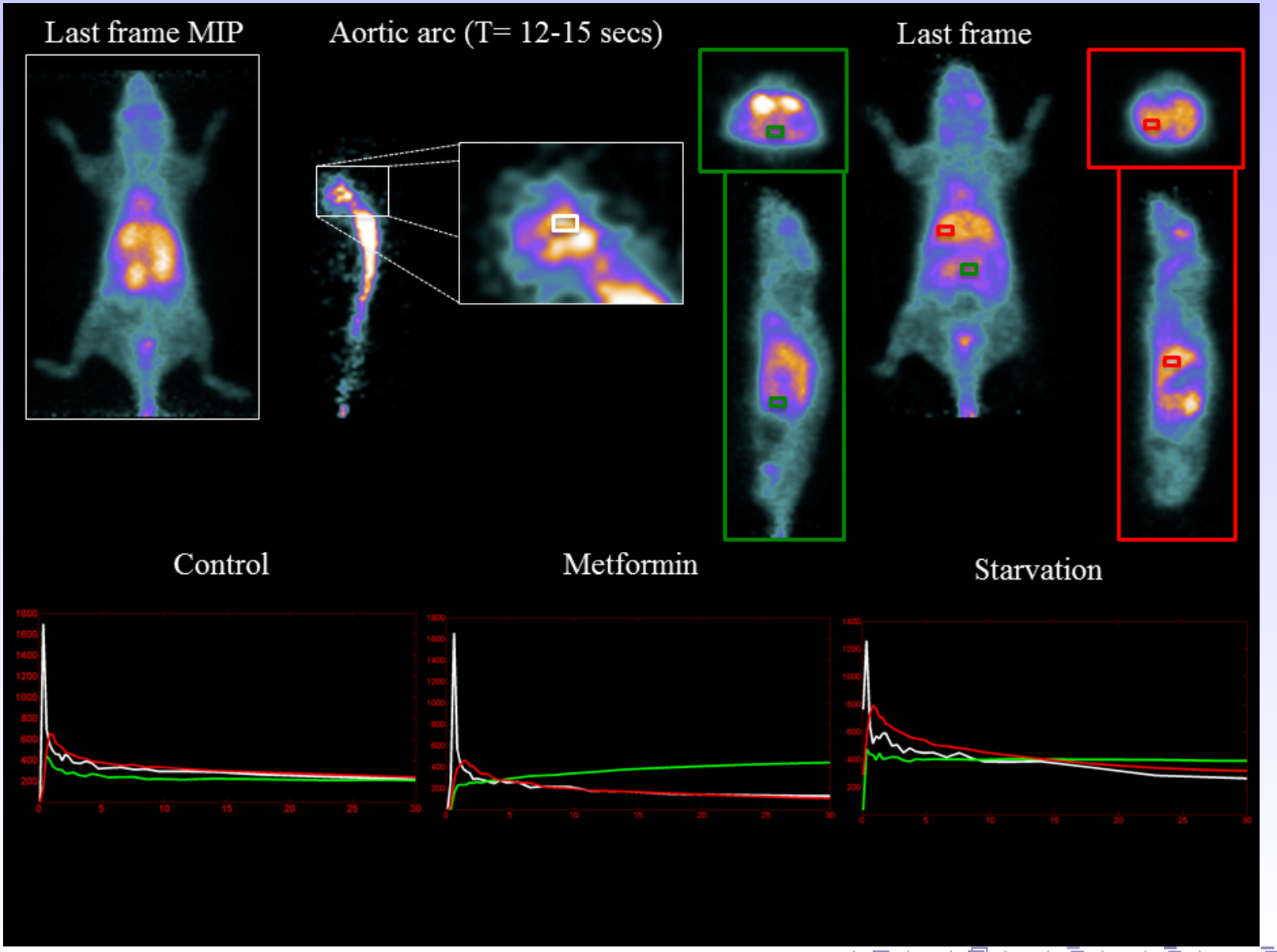
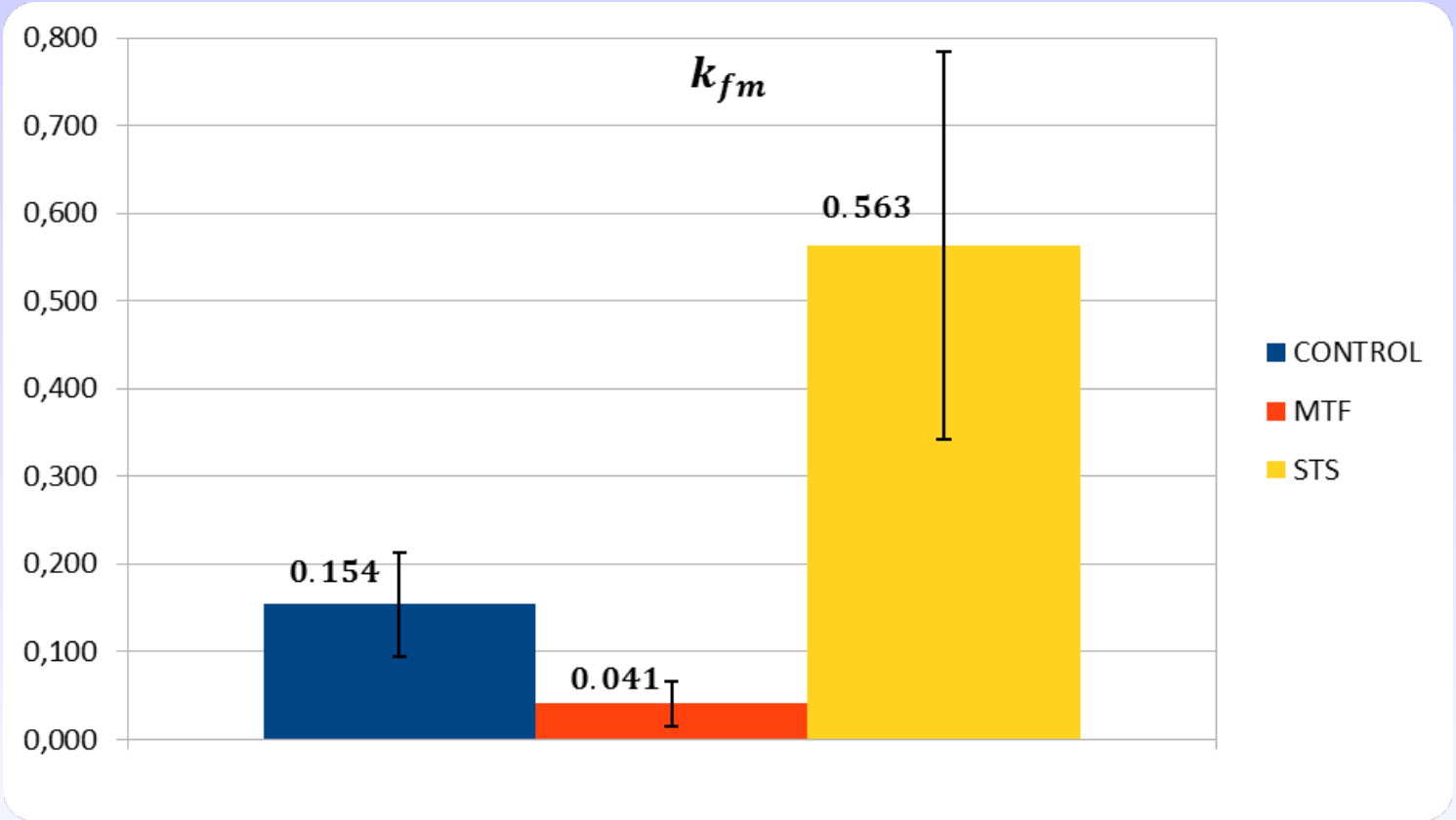


- liver both stores and releases glucose
- the need to store or release glucose is signaled by insulin
- two possible therapies against insulin malfunction
  1. look for drugs that mimic insulin
  2. look for drugs that regulate glucose release from liver: metformin

Liver+Gut [SG, Vivaldi, Delbary et al *Eur J Nucl Med Mol Imag* (in press)]



Data


Last frame MIP
Aortic arc (T= 12-15 secs)
Last frame
Control
Metformin
Starvation

Results [SG, Vivaldi, Delbary et al *Eur J Nucl Med Mol Imag* (in press)]