Identification of the blood perfusion coefficient

D. Lesnic
University of Leeds, UK.
Email: amt5ld@maths.leeds.ac.uk
Joint work with D. Trucu
OUTLINE

• Pennes’ bio-heat conduction equation

• Inverse mathematical formulations and analyses for the identification of the blood perfusion coefficient in the dependencies \( q=q(t), q=q(x), q=q(T) \) and \( q=q(x,t) \)

• Numerical methods and results

• Conclusions
Heat Transfer in Living Tissue

Vascular Architecture and Blood Flow

- $c =$ capillaries, 5 - 15 $\mu$m dia.
- $s =$ secondary vessels, 50 - 100 $\mu$m dia.
- $P =$ primary artery and vein, 100 - 300 $\mu$m dia.
- $SAV =$ main supply artery and vein, 300 - 1000 $\mu$m dia.
1. PENNES’ BIO-HEAT CONDUCTION EQUATION

\[ \nabla^2 T - qT + S = \frac{\partial T}{\partial t}, \quad \text{in } \Omega \times (0, t_f), \]

\( T \) = is the temperature of the tissue;
\( S \) = is the heat source;
\( q = \omega_b c_b L^2 / k \) is the perfusion coefficient;
\( \omega_b \) = is the blood perfusion rate;
\( c_b \) = is the specific heat of blood;
\( L \) = is a reference length;
\( k \) = is the thermal conductivity of the tissue;
\( \Omega \) = space solution domain;
\( t_f \) = specified final time of interest.

Practical applications of mathematically modelling hyperthermia, thrombosis and vascular sclerosis.
2. MATHEMATICAL FORMULATION for $q = q(t)$
Find the temperature $T(x, t) \in C^{2,1}((0, 1) \times (0, t_f)) \cap C^{1,0}([0, 1] \times [0, t_f])$ and the time-dependent perfusion coefficient $q \in C([0, t_f]), q > 0$ satisfying

$$
\frac{\partial T}{\partial t}(x, t) = \frac{\partial^2 T}{\partial x^2}(x, t) - q(t)T(x, t), \quad (x, t) \in (0, 1) \times (0, t_f],
$$

$$
T(x, 0) = T_0(x), \quad x \in [0, 1],
$$

$$
T(0, t) = f(t), \quad T(1, t) = g(t), \quad t \in [0, t_f],
$$

where

$$
f(0) = T_0(0), \quad g(0) = T_0(1)
$$

and some measurement which can be either of the following additional information:

(a heat flux) $\quad -\frac{\partial T}{\partial x}(0, t) = h(t), \quad t \in [0, t_f],$

(an interior temperature) $\quad T(x_0, t) = T_{\text{interior}}(t), \quad t \in [0, t_f],$

(a mass or energy) $\quad \int_0^t T(x, t)dx = E(t), \quad t \in [0, t_f].$
Denoting

\[ r(t) = \exp \left( \int_0^t q(\tau) d\tau \right), \]

we employ the transformation

\[ v(x, t) = r(t) T(x, t) \]

under which the inverse problem recasts as finding the pair \((v, r)\) with \(v(x, t) \in C^{2,1}((0, 1) \times (0, t_f)) \cap C^{1,0}([0, 1] \times [0, t_f])\) and \(r \in C^1([0, t_f]), \ r' > 0, \ r(0) = 1,\) satisfying

\[
\frac{\partial v}{\partial t}(x, t) = \frac{\partial^2 v}{\partial x^2}(x, t), \quad (x, t) \in (0, 1) \times (0, t_f],
\]

\[ v(x, 0) = T_0(x), \quad x \in [0, 1], \]

\[ v(0, t) = r(t) f(t), \quad v(1, t) = r(t) g(t) \quad t \in [0, t_f], \]

\[ -\frac{\partial v}{\partial x}(0, t) = r(t) h(t), \quad t \in [0, t_f]. \]

Once \((v, t)\) is found then the solution is obtained from

\[ T(x, t) = \frac{v(x, t)}{r(t)}, \quad q(t) = \frac{r'(t)}{r(t)}. \]
3. MATHEMATICAL ANALYSIS for \( q = q(t) \)

3.1 Homogeneous Boundary Conditions

Let us define the function \( Q : [0, t_f] \rightarrow R \),

\[
Q(t) = -\frac{\pi}{h(t)} \sum_{l=1}^{\infty} l\zeta_l e^{-l^2\pi^2 t},
\]

where

\[
\zeta_l = 2 \int_{0}^{1} T_0(x) \sin(l\pi x) dx, \quad l = 1, 2, ...
\]

Then we obtain the following theorem.

**Theorem 1.** Let \( h \in C^1([0, t_f]), T_0 \in C^1([0, 1]) \) be such that \( T_0(0) = T_0(1) = 0, T_0'(0) = -h(0) \). Then a necessary and sufficient condition for the inverse problem with homogeneous Dirichlet boundary conditions to have a unique solution is that the function \( Q \in C^1([0, t_f]) \) satisfies \( Q(0) = 1 \) and \( Q'(t) > 0 \). In this case the unique solution is given by

\[
q(t) = \frac{Q'(t)}{Q(t)}, \quad T(x, t) = \frac{1}{Q(t)} \sum_{l=1}^{\infty} \zeta_l e^{-l^2\pi^2 t} \sin(l\pi x).
\]
3.3.1 The Neumann case
If instead of the Dirichlet boundary conditions we have the Neumann boundary conditions

\[-\frac{\partial T}{\partial x}(0, t) = h(t), \quad \frac{\partial T}{\partial x}(1, t) = i(t), \quad t \in [0, t_f],\]

and the additional boundary temperature measurement

\[T(0, t) = f(t), \quad t \in [0, t_f].\]

**Theorem 4.** Let \(f \in C^1([0, t_f])\), \(h, i \in C([0, t_f])\) be positive functions and \(T_0 \in C^0([0, 1])\) with \(T_0(0) = f(0)\). Then the Volterra integral equation of the second kind

\[f(t)r(t) = \int_0^1 M(\xi, t)T_0(\xi)d\xi + \int_0^t r(\tau) [M(0, t - \tau)h(\tau) + M(-1, t - \tau)i(\tau)]d\tau, \quad t \in [0, t_f].\]

possesses a unique solution \(r \in C^1([0, t_f])\) satisfying \(r(0) = 1\). This implies the solvability of the inverse problem.
4. NUMERICAL RESULTS for $q = q(t)$

(i) Obtain $r(t)$ and $i(t) = \frac{\partial T}{\partial x}(1, t)$ by solving:

$$
\frac{1}{2} r(t) f(t) = \int_0^t r(\tau) \left[ G(0, t; 0, \tau) h(\tau) + \frac{\partial G}{\partial \xi}(0, t; 0, \tau) f(\tau) \right] d\tau \\
+ \int_0^t r(\tau) \left[ G(0, t; 1, \tau) i(\tau) - \frac{\partial G}{\partial \xi}(0, t; 1, \tau) g(\tau) \right] d\tau + \int_0^1 G(0, t; y, 0) T_0(y) dy,
$$

$$
\frac{1}{2} r(t) g(t) = \int_0^t r(\tau) \left[ G(1, t; 0, \tau) h(\tau) + \frac{\partial G}{\partial \xi}(1, t; 0, \tau) f(\tau) \right] d\tau \\
+ \int_0^t r(\tau) \left[ G(1, t; 1, \tau) i(\tau) - \frac{\partial G}{\partial \xi}(1, t; 1, \tau) g(\tau) \right] d\tau + \int_0^1 G(1, t; y, 0) T_0(y) dy,
$$

where

$$
G(x, t; \xi, \tau) = \frac{1}{\sqrt{4\pi(t - \tau)}} \exp \left( -\frac{(x - \xi)^2}{4(t - \tau)} \right).
$$
(ii) Obtain $T(x, t)$ explicitly from

\[
T(x, t) = \frac{1}{r(t)} \left\{ \int_0^t r(\tau) \left[ G(x, t; 0, \tau) h(\tau) + \frac{\partial G}{\partial \xi}(x, t; 0, \tau) f(\tau) \right] d\tau \\
+ \int_0^t r(\tau) \left[ G(x, t; 1, \tau) i(\tau) - \frac{\partial G}{\partial \xi}(x, t; 1, \tau) g(\tau) \right] d\tau + \int_0^1 G(x, t; y, 0) T_0(y) dy \right\}.
\]

(iii) Obtain $q(t)$ using mollification as

\[
q(t) = \frac{(J_\delta * r)'(t)}{r(t)},
\]

where

\[
J_\delta(t) = \frac{1}{\delta \sqrt{\pi}} \exp \left( -\frac{t^2}{\delta^2} \right).
\]
Test example

\[ T(x, t) = ((x - 1)^2 + 2t) \exp \left( -t - \frac{t^2}{2} \right), \quad q(t) = 1 + t. \]

Input data

\[ T(x, 0) = T_0(x) = (x - 1)^2, \quad x \in [0, 1], \]
\[ T(0, t) = f(t) = (1 + 2t) \exp \left( -t - \frac{t^2}{2} \right), \quad t \in [0, t_f = 1], \]
\[ T(1, t) = g(t) = 2t \exp \left( -t - \frac{t^2}{2} \right), \quad t \in [0, t_f = 1]. \]

Measured input data

\[ -\frac{\partial T}{\partial x}(0, t) = h(t) = 2 \exp \left( -t - \frac{t^2}{2} \right) (1 + \rho \eta(t)), \quad t \in [0, t_f = 1], \]

where \( \rho \) is the percentage of noise and \( \eta(t) \) is a random variable in \([-1, 1]\).
Figure 3. Computed and analytical values of: (a) $r(t)$, (b) $r'(t)$, and (c) $P_f(t)$, when there is 1% noise in the heat flux data (88).
2'. MATHEMATICAL FORMULATION for $q = q(x)$
Find the temperature $T(x, t) \in C^{2,1}((0, 1) \times (0, t_f)) \cap C^{1,0}([0, 1] \times [0, t_f])$ and the space-dependent perfusion coefficient $q \in C((0, 1)), q > 0$ satisfying

$$\frac{\partial T}{\partial t}(x, t) = \frac{\partial^2 T}{\partial x^2}(x, t) - q(x)T(x, t), \quad (x, t) \in (0, 1) \times (0, \infty),$$

$$T(x, 0) = T_0(x), \quad x \in [0, 1],$$

$$T(0, t) = f(t), \quad T(1, t) = g(t), \quad t \in [0, \infty),$$

and some measurement which can be either of the following additional information:

**IP1** (a heat flux) \[\frac{\partial T}{\partial x}(1, t) = i(t), \quad t \in [0, \infty),\]

**IP2** (a time-average temperature) \[E(x) = \int_0^{t_f} T(x, t) dt, \quad x \in (0, 1),\]

(a final temperature) \[e(x) = T(x, t_f) \quad x \in (0, 1).\]
3’. MATHEMATICAL ANALYSIS for $q = q(x)$

**Theorem 5.** (Isakov (1996), Ramm (2000)) (a) Let $T_0 = f = 0$, and assume that $g \neq 0$ is compactly supported and integrable. Further, assume that the bio-heat equation is satisfied at the boundary $x \in \{0, 1\}$, for $t > 0$. Then the IP1 has at most one solution $q \in L_1([0, 1])$.

(b) Let $T_0 \in C^4([0, 1])$, $T_0 > 0$ and assume that

$$f, g \in \left\{ \frac{1}{\sqrt{\pi t}} \int_0^\infty e^{-\tau^2/(4t)} \mu(\tau) d\tau \mid \mu \in C^4([0, \infty)) \right\}.$$ 

Then the IP1 has at most one solution $q \in L_\infty((0, 1))$.

**Theorem 6.** (Prilepko and Kostin (1993)) Let $T_0 = f = g = 0$ and $E \in W_2^2(0, 1)$, $E > 0$. Then the IP2 has at most one solution $q \in L_\infty((0, 1))$, $q \geq 0$, $T \in W_2^{2, 1}((0, 1) \times (0, t_f))$. 
4'. NUMERICAL RESULTS for $q = q(x)$

(i) Discretise the bio-heat conduction equation using the finite-difference method.

(ii) Minimize (using the NAG routine E04FCF) the functional

$$F_1(q) := \lambda \|q'\|^2_{L^2((0,1))} + \left\{ \begin{array}{ll}
\| \frac{\partial T}{\partial x}(q; (1, t)) - \tilde{i}(t) \|^2_{L^2((0,\infty))} & \text{for } IP1, \\
\| \int_{0}^{t_f} T(q; (x, t)) dt - \tilde{E}(x) \|^2_{L^2((0,1))} & \text{for } IP2,
\end{array} \right.$$ 

where $\lambda > 0$ is a regularization parameter to be prescribed according to the discrepancy principle, i.e. choose the largest $\lambda > 0$ for which

$$F(\lambda) := \sqrt{F_1(q) - \lambda \|q'\|^2_{L^2((0,1))}} \leq \left\{ \begin{array}{ll}
\| \tilde{i} - \tilde{i} \|^2_{L^2((0,\infty))} & \text{for } IP1, \\
\| E - \tilde{E} \|^2_{L^2((0,1))} & \text{for } IP2.
\end{array} \right.$$
Test example for IP1:

\[ q(x) = 1 + x^2, \quad x \in [0, 1]. \]

Input data

\[
T(x, 0) = T_0(x) = 0, \quad x \in [0, 1],
\]

\[
T(0, t) = f(t) = 0, \quad t \in (0, \infty),
\]

\[
T(1, t) = g(t) = \begin{cases} 
0 & \text{for } t = 0, \\
\frac{e^{1/(t^2-t)}}{1 + t} & \text{for } t \in (0, 1), \\
0 & \text{for } t \geq 1,
\end{cases}
\]

which satisfies the conditions of Theorem 5(a) for the uniqueness of solution of IP1.

Measured data

\[
\frac{\partial T}{\partial x}(1, t) = \tilde{i}(t) = i(t)(1 + \rho \eta(t)), \quad t \in (0, \infty),
\]

where \( \rho \) is the percentage of noise and \( \eta(t) \) is a random variable in \([-1, 1]\) and \( i(t) \) is obtained by solving the direct problem with a different mesh size than the iterative inverse solver.
Figure 1: (a) Logarithm of the objective functional $F_1$, as a function of the number of iterations, (b) the numerically obtained $P_f(x)$, (c) the discrepancy principle for exact data, $\alpha = 0$, and (d) the discrepancy principle for $\alpha = 1\%$ noisy data.
MATHEMATICAL FORMULATION for q=q(T)

Find temperature \( T(x,t) \) in the temperature perfusion coefficient \( \alpha \) satisfying

\[
\frac{\partial T}{\partial t}(x,t) = \alpha \left( \frac{\partial^2 T}{\partial x^2}(x,t) - q(x,t) T(x,t) + S(x,t) \right), \quad (x,t) \in (0,1) \times (0,t_f),
\]

\( T(x,0) = 0 \quad x \in [0,1], \)

\( \frac{\partial T}{\partial x}(0,t) = 0, \quad \frac{\partial T}{\partial x}(1,t) = 0 \quad t \in [0,t_f), \)

and the additional temperature on namely

\( T(x,0) = g(x), \quad t \in [0,t_f). \)
MATHEMATICAL ANALYSIS for $q=q(T)$

Theorem (Pilant and Runde (1986)) Let us consider data

$\omega \in C^{1+1}[0,t_f], \quad \omega(0)=0, \quad \omega'(t)<0, \quad t \in [0,t_f]$

$g \in C^{1+1}[0,t_f], \quad g(0)=0, \quad g'(0)=S(0,0), \quad g'(t)>0, \quad t \in [0,t_f]$

$S \in C^{0+1}[0,t_f], \quad S(x,t)>0, \quad (x,t) \in (0,1) \times (0,t_f)$.

Assume that there exists a $C>0$ such that $\|g'(.)-\psi_t(0,.)\|_1 \leq C$, where $\psi$ is the solution of the problem

$$
\frac{\partial \psi}{\partial t}(x,t) - \frac{\partial^2 \psi}{\partial x^2}(x,t) = S(x,t), \quad (x,t) \in (0,1) \times (0,t_f)
$$

$\psi(x,0)=0, \quad x \in [0,1]$

$$
\frac{\partial \psi}{\partial x}(0,t)=\omega(t), \quad \frac{\partial \psi}{\partial x}(1,t)=0, \quad t \in (0,t_f).
$$

Then the inverse problem has a unique solution

$(T(x,t), f(T)) \in C^{2+1,1+1}([0,1] \times [0,t_f]) \times C^{0+1}(-\infty, \infty)$. 
NUMERICAL RESULTS for $q=q(T)$

Numerical based the FD/Mir's order Tikhonov regularization piecewise approximations $q=q(T)$ over a uniform discretization in the interval $[0,t_f]$ assuming $1(t) \leq T(q)=g(t)$ for all $t \in [0,1] \times [0,t_f]$.

Test Example

$T(x,t) = (x-1)^2(\ell-1)$, $q(T)=T^2+1$.

$\frac{\partial T}{\partial x} (q(t)=\alpha(t)=2(\ell-1))$, $T(q(t)=g(t)= \ell-1+noise$

$S(x,t)=\ell(x-1)^2-2(\ell-1)^2+(x-1)^2(\ell-1)[(x-1)^4(\ell-1)^2+1]$
Numerical and analytical solutions for $P_f(T)$, when $p=0$, $p=1\%$ and $p=3\%$ noise is in the data.
MATHEMATICAL FORMULATION for $q=q(x,t)$

Find a space and independent diffusion coefficient $q(x,t) \in \mathcal{L}_2((0,1) \times (0,\infty))$ such that

$$ \frac{\partial T}{\partial t}(x,t) = \frac{\partial^2 T}{\partial x^2}(x,t) - q(x,t)T(x,t), \ (x,t) \in (0,1) \times (0,\infty) $$

$$ T(x,0) = T_0(x), \ x \in [0,1], $$

$$ T(0,t) = f_0(t), \ f(1,t) = f_1(t), \ t \in [0,\infty), $$

and the additional data $u(x,t)$ from $u(x,t) = G(x,t) + \text{noise}(x,t) \in (0,1) \times (0,\infty).$
MATHEMATICAL ANALYSIS for \( q=q(x,t) \)

**Theorem 8.** If the measure of the level set \( G(x,t)=0 \) is zero, then the inverse problem has a unique solution given by

\[
q(x,t) = \ldots
\]

NUMERICAL RESULTS for \( q=q(x,t) \)

To stabilise the results and make the above formula applicable, we employ a first- and second-order regularizations for approximating the time and space partial derivatives, respectively, by recasting them as Fredholm ill-posed integral equations of the first kind, and with the choice of the regularization parameter based on the L-curve criterion.

**Test example.**
(a) Analytical and (b) numerical contour plots for $P_f(x,t)$, when there is $\rho=1\%$ noise in the data.
CONCLUSIONS

• Inverse problems which require the determination of the time-, space-, temperature-, or both space-and-time dependent perfusion coefficient and temperature satisfying the bio-heat conduction equation subject to an initial condition, Dirichlet/Neumann boundary conditions and additional heat/flux boundary/interior temperature measurements have been investigated.

• Sufficient conditions on the input data were given such that the inverse problem have at most one solution.

• Numerical results obtained using the boundary element method/ finite difference method combined with mollification or Tikhonov regularization procedure have been presented and discussed. Choice of the regularization parameter based on the discrepancy or L-curve criterion.

• Future work will investigate the retrieval of a space- and temperature-dependent perfusion coefficient $q=q(x,T)$ entering the bio-heat conduction equation

$$\frac{\partial T}{\partial t} = \nabla \cdot (\kappa \nabla T)$$