AI-based solution methods for PDEs with application to Oncological Hyperthermia

National PhD in Artificial Intelligence – XXXVII Cycle

Guglielmo Cappellini (1643022)
Advisor: Prof. M. Vendittelli
Co-Advisor: Prof. G. Trappolini

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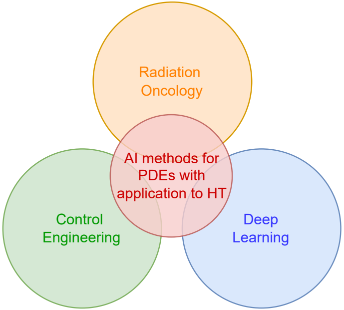
Sapienza Università di Roma

This research combines three fields: we aim at improving an Oncological treatment through the use of Control Engineering techniques with an AI-based implementation.

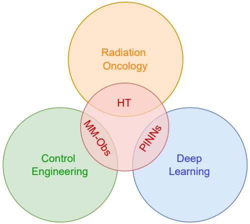


Motivation

Improving accuracy and outcomes of robot-assisted superficial **Hyperthermia (HT)** treatments;

Concept

Observing bio-heat transfer using boundary measurements and controls for real-time temperature estimation in a 1D domain with a **Multiple-model Adaptive Observer (MM-Obs)** scheme;



Approach

Each observer is implemented with **Physics-Informed Neural Networks (PINNs)** to overcome limitations of classical solvers.

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Biological Rationale [1]

Heating tumors in the 41–43 [°C] range acts as a powerful **radio-** and **chemo-sensitizer**:

- **inhibition of the repair** of DNA damage;
- **reoxygenation** increases radiosensitivity and drugs targetization;
- **direct cell killing** of radioresistant hypoxic tumor cells.

It is used especially in locally advanced tumors or local relapses, where more effective treatment strategies or their combinations are required.

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[1] Datta et al., "Local hyperthermia combined with radiotherapy and-/or chemotherapy: Recent advances and promises for the future"

Devices and Procedures
Superficial Hyperthermia

Target temperature $\simeq 43$ [°C] is achieved combining EM heating and water bolus cooling:

1. Heat is delivered via a microwave radiating **antenna**;
2. A **water bolus** placed between the applicator and the patient prevents skin burns;
3. Superficial temperature measurements are obtained using a matrix of **thermocouples**.

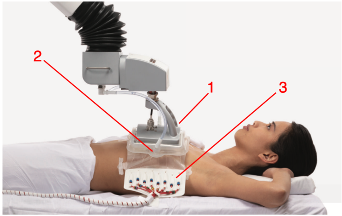
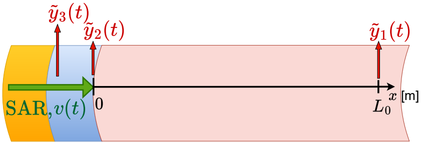


Figure: ALBA ON4000D.

We consider an **Ideal Needle** that enters perpendicularly from patient's surface.

Model

1D Pennes' Bio-Heat Equation (PBHE)[2] in homogeneous medium



$$\varrho c \partial_t T = k \partial_{xx} T - \varrho_b c_b w_b (T - T_a) + \varrho \mathrm{SAR}$$

$$\begin{cases} T(x,0) = T_0(x) & x \in [0, L_0] \\ \partial_x T\big|_{x=0} = -\frac{h}{k}\Big(v(t) - T(0,t)\Big) & t \geq 0 \\ T(L_0, t) = T_a & t \geq 0 \end{cases}$$

ϱ:	Density [kg m^{-3}]
c:	Specific heat [J kg^{-1} K^{-1}]
k:	Thermal conductivity [W m^{-1} K^{-1}]
ϱ_b:	Density of blood [kg m^{-3}]
c_b:	Specific heat of blood [J kg^{-1} K^{-1}]
T_a:	Arterial blood temperature [$^\circ$C]
SAR:	Specific Absorption Rate [W kg^{-1}]
h:	Convection coefficient [W m^{-2} K^{-1}]

w_b is the Blood perfusion rate [s^{-1}], unknown and variable in a known range for a given tissue type.

In-depth: $\tilde{y}_1(t) = T_a$;

Surface: $\tilde{y}_2(t) = T(0,t)$, $\tilde{y}_3(t) = v(t)$.

[2] Pennes, "Analysis of Tissue and Arterial Blood Temperatures in the Resting Human Forearm".

Potential and Current Limitations

HT can improve outcomes of RT and CH by a factor of 1.5. Success is critically related to the ability to reach and maintain the desired temperatures at the target.

Role of blood perfusion w_b

PRO:	Stabilization term	$\rightarrow$	Faster achievement of stationary state
CON:	Heat sink	$\rightarrow$	Cold tracks and inhomogeneous heating

No feedback. Invasive temperature probes are often avoided: cause discomfort for the patient and give only pointwise information.

Objective: a non-invasive tool to predict temperature distribution at the target, using only boundary measurements and in the presence of unknown properties.

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2 A State Observer of Pennes' Bio-Heat Equation

Application: Engineering fields in which the governing principle is known, and the actuation and sensing are non-intrusive.

Objectives: Performance improvement and optimal control, stabilization of unstable plants, trajectory tracking and generation, motion planning.

In our application, the boundary control is dedicated to the regulation of water bolus temperature $v(t)$. In-depth temperature $\tilde{y}_1(t)$ is assumed to be constant, while the boundary measurements are $\tilde{y}_2(t)$ (surface), and $\tilde{y}_3(t)$ (water bolus).

[3] Krstic and Smyshlyaev, "Adaptive control of PDEs".

Adaptive Observer Design for PDEs

Purpose: Design observers for PDEs to estimate system state from boundary measurements.

General Design Approach

1. Given the observation variable u, formulate observer dynamics $\hat{u}$ providing its estimation;
2. Define the observation error: $e_u = u - \hat{u}$;
3. Analyze the error dynamics and construct a Lyapunov functional candidate: $V(t) = \frac{1}{2}\int_0^1 e_u^2 dx$;
4. Prove exponential decay: $\|e_u(t)\|_{\mathcal{L}^2} \to 0$.

Observer Structure [4]

1D PBHE, Nominal Conditions

The observer $\hat{T}$ evolves with a copy of PBHE, translated and recasted for simplicity:

$$\partial_t \hat{T} = \sigma \partial_{xx} \hat{T} - \omega \hat{T} + \gamma \mathrm{SAR},$$

and a feedback term on the superficial boundary, where K is the Output injection gain [-]:

$$\partial_x \hat{T}(\cdot, t)\big|_{x=0} = -\frac{h}{k}(\tilde{y}_3(t) - \tilde{y}_2(t)) + \underbrace{K(\hat{T}(0,t) - \tilde{y}_2(t))}_{\text{feedback term}}.$$

The error norm $\|T(\cdot,t) - \hat{T}(\cdot,t)\|_{\mathcal{L}^2}$ converges exponentially to zero with a decay rate:

$$\Lambda \geq 2\left(\sigma\eta + \omega\right), \quad \eta = \min\{K, \pi^2/4\}.$$

[4]Cristofaro, **Cappellini**, Staffetti, Trappolini, and Vendittelli, “Adaptive Estimation of the Pennes’ Bio-Heat Equation - I: Observer Design”. *62nd IEEE CDC*, Singapore, 2023.

Sensitivity Analysis

Uncertain Perfusion w_b

In the case of uncertain w_b, consider a claimed value $\tilde{w}_b$ to be used in the definition of parameter $\tilde{\omega} = \frac{\varrho_b c_b}{\varrho c} \tilde{w}_b$:

$$\partial_t \hat{T} = \sigma \partial_{xx} \hat{T} - \tilde{\omega} \hat{T} + \gamma \mathrm{SAR}.$$

Given a maximum feasible temperature $T_{\max}$, the $\mathcal{L}^2$-norm of the error is ultimately bounded to $4c_0$, with:

$$c_0 = \frac{|\tilde{\omega} - \omega|^2 {T_{\max}}^2}{(\sigma\eta + \tilde{\omega})^2},$$

with a certain decay rate Ξ:

$$\Xi \geq (\sigma\eta + \tilde{\omega})/2, \quad \eta = \min\{K, \pi^2/4\}.$$

Multiple-model Adaptive Scheme [5]

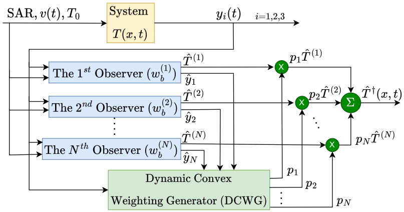
Uncertain, Bounded Perfusion w_b

Consider an ensemble of n_{obs} observers $\hat{T}^{(j)}$, each one with a different perfusion ${w_b}^{(j)}$. The overall prediction is a weighted average of each observer's prediction, based on the magnitude of the output error. The larger n_{obs} is, the smaller the ultimate error gets.

$$\dot{p}_i(t) = -\lambda \left(1 - \frac{e^{-\mu_i(t)}}{\sum_{\ell=1}^{n_{\text{obs}}} p_\ell(t) e^{-\mu_\ell(t)}} \right) p_i(t)$$

$\mu_i(t)$: Absolute output error [-]

λ: Adaptive gain [-]



[5] Hassani et al., "Further results on plant parameter identification using continuous-time multiple-model adaptive estimators"

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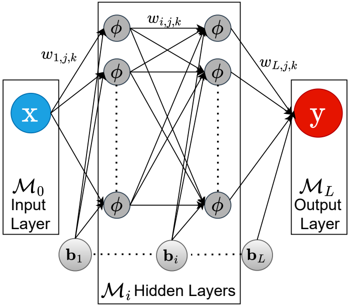
Feedforward Neural Network (FNN)

The employed architecture



Fully-connected layer:

$$\mathcal{M} = \phi(\mathbf{xw} + \mathbf{b}).$$

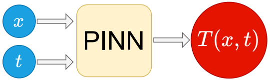
Backpropagation (BP):

Algorithm for training neural networks by computing gradients of the loss function $\mathcal{L}$ with respect to weights and biases Υ.

Physics-informed Neural Networks (PINNs) [6]

In PINNs, FNNs are leveraged as **universal function approximators** to represent solutions to complex PDE problems.

PINNs extend the concept of BP by computing derivatives of the output with respect to input coordinates, enabling direct encoding of **physical laws** described by PDEs into the learning process.



PINN for PBHE.

PRO: meshless, no training data.

[6] Raissi et al., "Physics-informed neural networks: A deep learning framework for solving forward and inverse problems involving nonlinear partial differential equations"

It is possible to think of PINNs as two interconnected networks:

FNN

- *input*: a point $\mathbf{x}$ in the problem domain;
- *output*: the approximate solution $\mathbf{y}$;
- trainable weights and biases Υ;
- output transform ζ for hard constraints.

$\Longleftrightarrow$

Residual Network

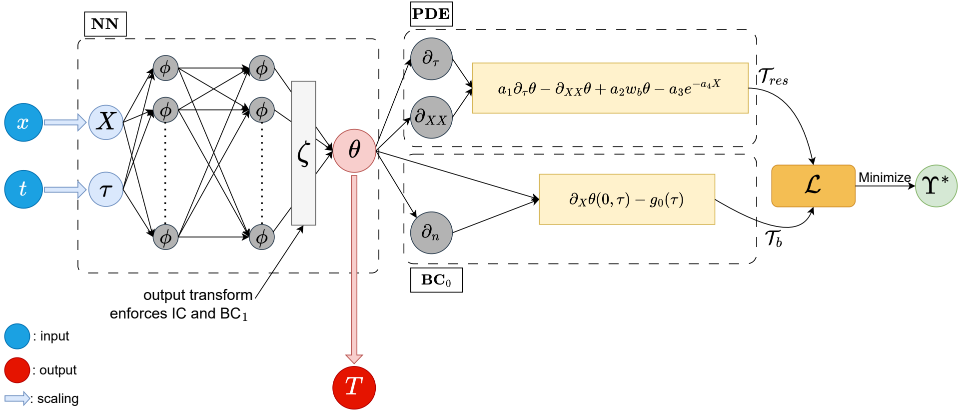
Computes the physics-informed $\mathcal{L}$ using backpropagation of $\mathbf{y}$ to enforce governing equations as soft constraints.

Training: Υ of the FNN are adjusted to minimize the $\mathcal{L}$ computed by the residual network on a set of sampling points $\mathcal{T}$.

Parameters: Optimized during training (additional data required), or treated as inputs, extending the problem domain.

Neural Bio-heat System (NBHS)

A PINN trained to solve PBHE



PINNs Implementation of PBHE

To ensure robustness of the network, inputs and output must be scaled to $\mathcal{O}(1)$:

$$X = \frac{x}{L_0}\,[-], \quad \tau = \frac{t}{t^*}\,[-], \quad \theta = \frac{T - T_{\min}}{T_{\max} - T_{\min}}\,[-].$$

The PBHE is transformed as:

$$a_1 \partial_\tau \theta = \partial_{XX}\theta - w_b a_2 \theta + a_3 e^{-a_4 X}$$

IC, BC_0, and BC_1 are:

$$\begin{cases} \theta(X,0) = \theta_0(X) & X \in [0,1] \\ \partial_X \theta\big|_{X=0} = g_0(\tau) & \tau \geq 0 \\ \theta(1,\tau) = 0 & \tau \geq 0 \end{cases}$$

IC and BC_1 are enforced as hard constraints:

$$\zeta = \mathbf{y} \cdot \tau \cdot (1 - X) + \theta_0(X);$$

PDE residual and BC_0 are optimized as soft constraints:

$$\mathcal{L}(\Upsilon, \mathcal{T}) = \mathrm{w}_{\mathrm{res}}\, \mathcal{L}_{\mathrm{res}}(\Upsilon, \mathcal{T}_{\mathrm{res}}) + \mathrm{w}_{\mathrm{bc}}\, \mathcal{L}_{\mathrm{bc}}(\Upsilon, \mathcal{T}_{\mathrm{bc}}).$$

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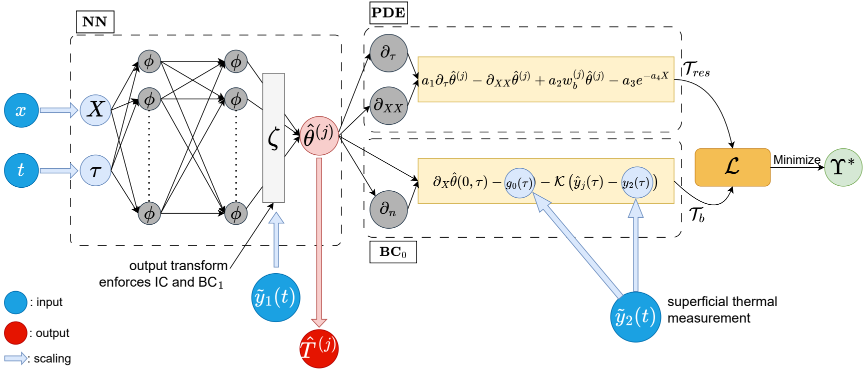
4 Adaptive Estimation for Hyperthermia

Neural Bio-heat Observer (NBHO) [7]

PINNs Implementation of the Observer

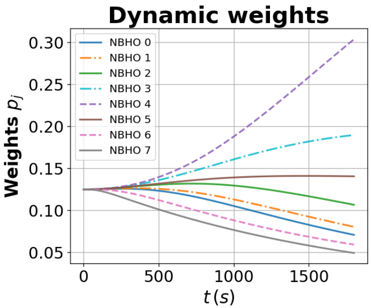


[7] **Cappellini**, Trappolini, Staffetti, Cristofaro, and Vendittelli, “Adaptive Estimation of the Pennes’ Bio-Heat Equation - II: A NN-Based Implementation for Real-Time Applications”. *62nd IEEE CDC*, Singapore, 2023.

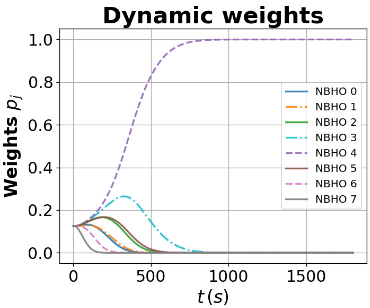
Results

PINNs-based Adaptive Estimation for Hyperthermia

The solution is predicted in few [ms], allowing for convergence to the best observer.



Replicating MATLAB.



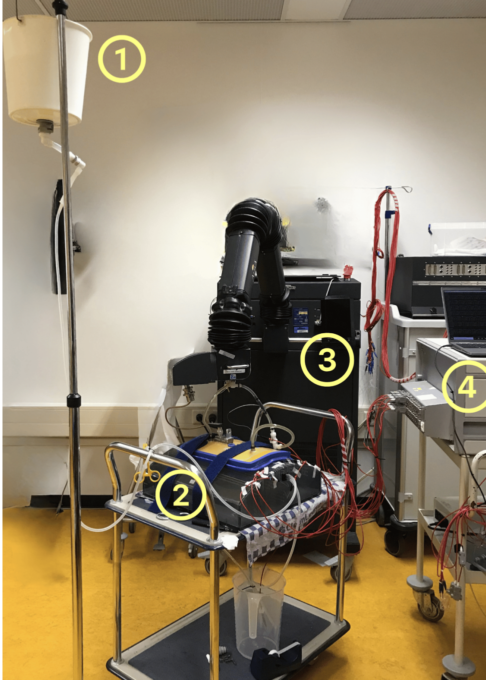
Overcoming MATLAB.

Experiments at AMC [8]

4 Adaptive Estimation for Hyperthermia

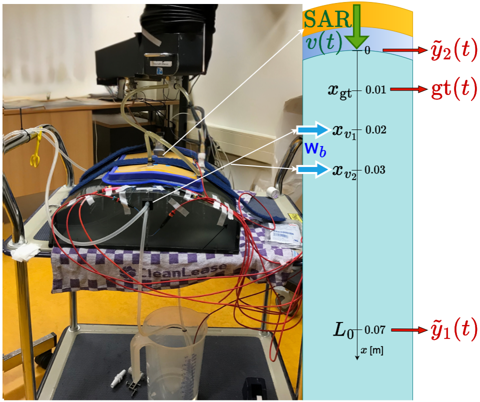
Experimental setup:

1. Bucket with adjustable height;
2. Curved muscle-equivalent phantom;
3. ALBA on4000D and 3H applicator;
4. Hyp3 in-house build thermometry system.



[8] **Cappellini** et al., submitted to IEEE TCST.

Working conditions

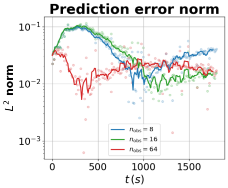


After heating, applicator and water bolus are removed. Cooling is measured for 30 [min]. gt is placed where the tumor to be treated is generally located.
The effect of perfusion w_b is controlled by:

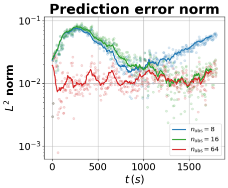
- number of catheters for water n_{cat};
- height of the bucket $\mathbf{H}$.

Set	$\mathbf{H}$ [m]	n_{cat}	v_{cat} [m s^{-1}]
Cooling 1	0.235	1	5.0e−1
Cooling 2	1.085	2	1.2

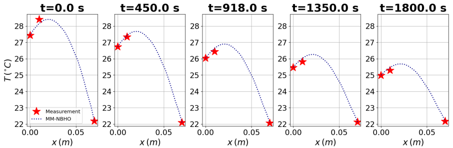
As the number of observers n_{obs} increases, observation error decreases.



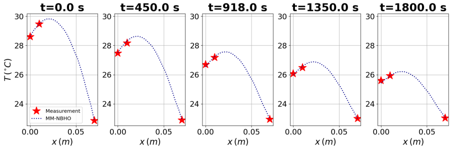
(a) Cooling 1.



(b) Cooling 2.



(a) Cooling 1, n_{obs}=64.



(b) Cooling 2, n_{obs}=64.

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5 Current Work

Extension of the model comprehends:

- Multilayer composition and 2-D case;
- Introduction of heat source: experimental characterization and measurements.

It can be achieved combining more complex NN architectures:

Graph Convolutional Networks (GCNs)

for irregular domains;

Gate Recurrent Unit (GRU)

to capture temporal dependence.

Real-time simulation of deformable tissues using PINNs [9]

Case Study: Wave Equation Applications

Context: Interactive virtual reality models for medical training simulations that require real-time tissue deformation.

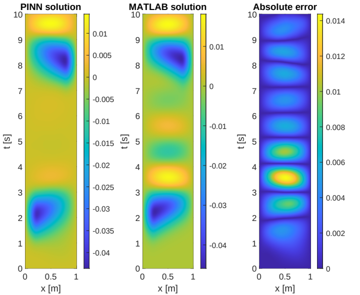
Random Fourier Features encoding enables PINNs to capture high-frequency solutions.

Validation of PINNs: String and membrane deformation

✓ Comparable accuracy to traditional PDE solvers

△ Scale better with increasing problem dimensionality

Mesh-free approach let PINNs avoid limitations encountered in MATLAB, which relies on discretization and suffers from mesh-size constraints



[9] De Santis, **Cappellini**, and Vendittelli, submitted to RO-MAN25.

Contributions

The work conducted throughout this thesis led to the following publications:

- Cristofaro, **Cappellini**, Staffetti, Trappolini, Vendittelli. *"Adaptive Estimation of the Pennes' Bio-Heat Equation - I: Observer Design."* In: 2023 62nd IEEE Conference on Decision and Control (CDC), Singapore, 2023.
- **Cappellini**, Trappolini, Staffetti, Cristofaro, Vendittelli. *"Adaptive Estimation of the Pennes' Bio-Heat Equation - II: A NN-Based Implementation for Real-Time Applications."* In: 2023 62nd IEEE Conference on Decision and Control (CDC), Singapore, 2023.

The following works have been submitted and are currently under review:

- De Santis, **Cappellini**, Vendittelli. *"Real-time Simulation of Deformable Tissues Using PINNs."* Submitted to RO-MAN 2025.
- **Cappellini**, Cristofaro, De Santis, Staffetti, Trappolini, Vendittelli. *"Adaptive Estimation of the Pennes' Bio-Heat Equation: Observer Design and PINNs Implementation."* Submitted to IEEE Transactions on Control Systems Technology (TCST).

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