STATE ESTIMATION AND PREDICTIVE CONTROL APPLIED TO THE TREATEMENT OF THE HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN NEONATES

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Summary

- **Introduction**
- **Neonate's Bioheat Transfer Model**
- **Actual Temperature Measurements**
- **State Estimation and Predictive Control**
- **Results: Verification and Validation**
- **Conclusions**

Introduction

This work deals with numerical simulations, prediction and stochastic control of state variables. The application of interest is in the treatment of the neonatal hypoxic-ischemic encephalopathy

Causes

- Lack of oxygen | Low blood flow

Treatment

- Cooling of the affected region (temperature reduction ~3ºC)

Cooling Techniques

- Local | Systemic

Phases of the Cooling Treatment

- Fast cooling | Constant cooling | Rewarming

Temperature Measurements

- Forehead | Skin over abdomen | Rectum

Olympic Cool-Cap System(https://natus.com)

Kool-Kit Neonate (https://www.gentherm.com)

Introduction

Motivation:

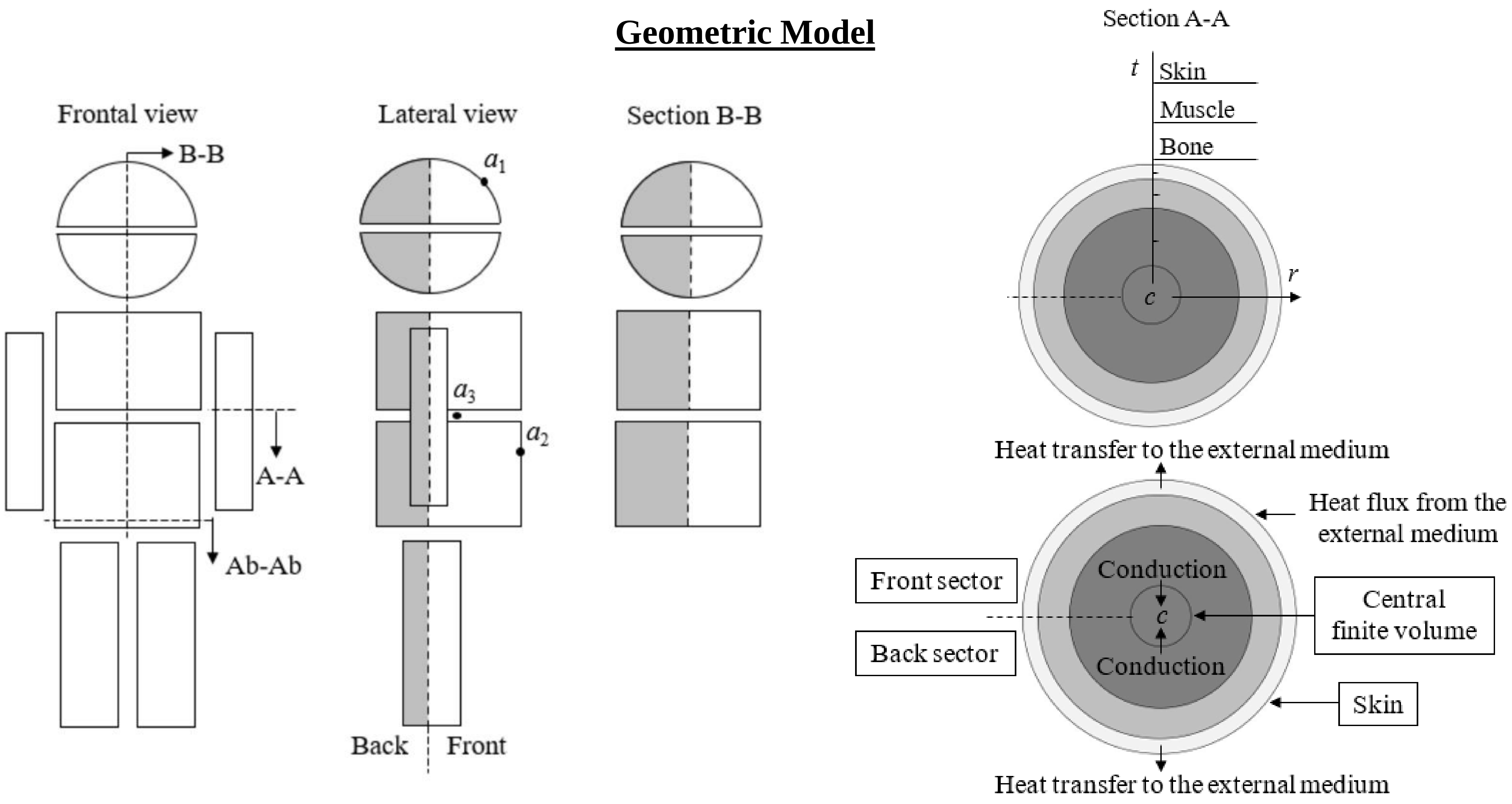
- Non-intrusive temperature measurements of internal tissues are still not feasible.
- Computational simulations under different types of uncertainties and non-intrusive measurements that intrinsically contain errors can be used together in order to estimate and control state variables of the system under analysis.

Objectives:

- Development of an optimization procedure to build the geometric model by using the actual mass, length and perimeter of the head.
- Application of the SIR to sequentially estimate the internal body temperatures of a newborn and external heat fluxes, by using both simulated and actual temperature measurements.
- Application of the PF-MPC for stochastic control of the internal body temperature by manipulating external heat fluxes imposed as boundary conditions.

Neonate's Bioheat Transfer Model

Geometric Model



Neonate's Bioheat Transfer Model

Mathematical Formulation

t = tissue
s = sector
l = body element.

Pennes' Equation:

$$\underbrace{\rho_{t,s,l} c_{t,s,l} \frac{\partial T_{t,s,l}(r,\tau)}{\partial \tau}}_{\text{Energy Storage}} = \underbrace{\frac{k_{t,s,l}}{r^m} \frac{\partial}{\partial r}\left[r^m \frac{\partial T_{t,s,l}(r,\tau)}{\partial r} \right]}_{\text{Diffusion}} + \underbrace{\rho_b c_b\, \omega_{t,s,l}(T_{t,s,l})\left[T_{a,l} - T_{t,s,l}(r,\tau)\right]}_{\text{Perfusion}} + \underbrace{g_{t,s,l}(T_{t,s,l})}_{\text{Generation}}$$

Lumped model for the central region:

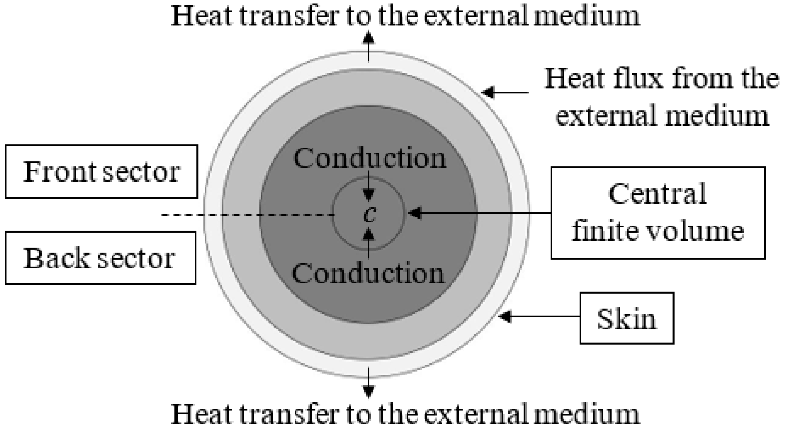
$$\rho_{c,l} c_{c,l} \frac{\partial T_{c,l}(\tau)}{\partial \tau} = \rho_b c_b \omega_{c,l}(T_{c,l})\left[T_{a,l} - T_{c,l}(\tau)\right] + g_{c,l}(T_{c,l}) + \frac{A_{c,l}}{V_{c,l}} \frac{\sum_{s=1}^{2} \phi_s k_{adj,s,l} \frac{\partial T_{adj,s,l}}{\partial r}}{2\pi}$$

Boundary condition:

$$k_{sk,s,l} \frac{\partial T_{sk,s,l}}{\partial r} + h_{s,l} T_{sk,s,l} = h_{s,l} T_{ext,s,l} + q_{ext,s,l}$$

Initial condition:

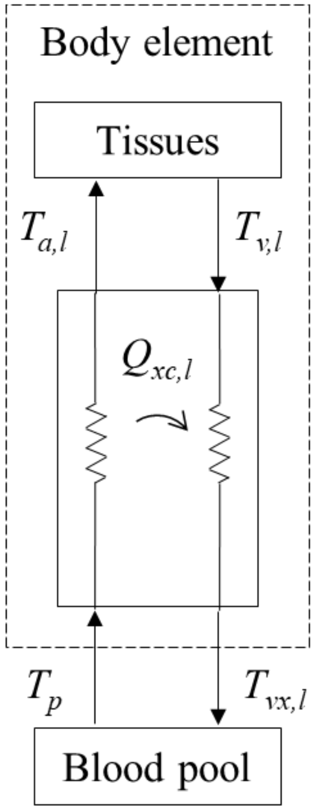
$$T_{t,s,l}(r, \tau = 0) = F_{t,s,l}(r)$$



Neonate's Bioheat Transfer Model

Mathematical Formulation

Blood pool concept



$$Q_{xc,l} = \dot{m}_{b,l} c_b \left[T_p - T_{a,l} \right] = \dot{m}_{b,l} c_b \left[T_{vx,l} - T_{v,l} \right]$$

$$Q_{xc,l} = U_{xc,l} \left[T_{a,l} - T_{v,l} \right]$$

Blood Temperatures

$$T_{v,l} = \frac{\rho_b \sum_{s=1}^{2} \int_{V_{t,s,l}} \omega_{t,s,l} T_{t,s,l} \, dV_{t,s,l}}{\dot{m}_{b,l}}$$

$$T_{a,l} = \frac{\dot{m}_{b,l} c_b T_p + U_{xc,l} T_{v,l}}{\dot{m}_{b,l} c_b + U_{xc,l}}$$

$$T_p = \frac{\sum_{l=1}^{8} \frac{\left(\dot{m}_{b,l}\right)^2 c_b}{\dot{m}_{b,l} c_b + U_l} T_{v,l}}{\sum_{l=1}^{8} \frac{\left(\dot{m}_{b,l}\right)^2 c_b}{\dot{m}_{b,l} c_b + U_{xc,l}}}$$

Fiala, D., Lomas, K.J. and Sthorer, M. (1999), "A computer model of human thermoregulation for a wide range of environmental conditions: the passive system", Journal of Applied Physiology, Vol. 87 No. 5, pp. 1957-1972

Neonate's Bioheat Transfer Model

Mathematical Formulation

Body element	D	L	Tissue	r	k	ρ	c	g^{bas}	ω^{bas}	U
	[mm]			[mm]	[W/mK]	[kg/m^3]	[J/kgK]	[W/m^3]	[s^{-1}]	[W/K]
head	102	-	brain	47	0.5	1000	3805	6454.4	0.017	0
			bone	49	0.8	1030	1796	0	0	
			skin	51	0.3	1000	3631	445.5	0.008	
thorax	92	90	lung	27	0.4	700	3719	858.5	0.39	0
			bone	32	0.8	1030	1796	0	0	
			muscle	44	0.5	1000	3645	363.6	0.001	
			skin	46	0.3	1000	3631	445.5	0.008	
abdomen	92	90	viscera	27	0.5	1005	3697	4038.5	0.004	0
			bone	32	0.8	1030	1796	0	0	
			muscle	44	0.5	1000	3645	363.6	0.001	
			skin	46	0.3	1000	3631	445.5	0.008	
arm	38	160	bone	4	0.8	1030	1796	0	0	1.652
			muscle	17	0.5	1000	3645	363.6	0.001	
			skin	19	0.3	1000	3631	445.5	0.008	
leg	48	180	bone	5	0.8	1030	1796	0	0	2.76
			muscle	22	0.5	1000	3645	363.6	0.001	
			skin	24	0.3	1000	3631	445.5	0.008	

Łaszczyk, J. E., Nowak, A. J. "Computational Modeling of Neonate's Brain Cooling", *International Journal of Numerical Methods for Heat and Fluid Flow*, v. 26, n. 2, pp. 1-23, 2016.

Neonate's Bioheat Transfer Model

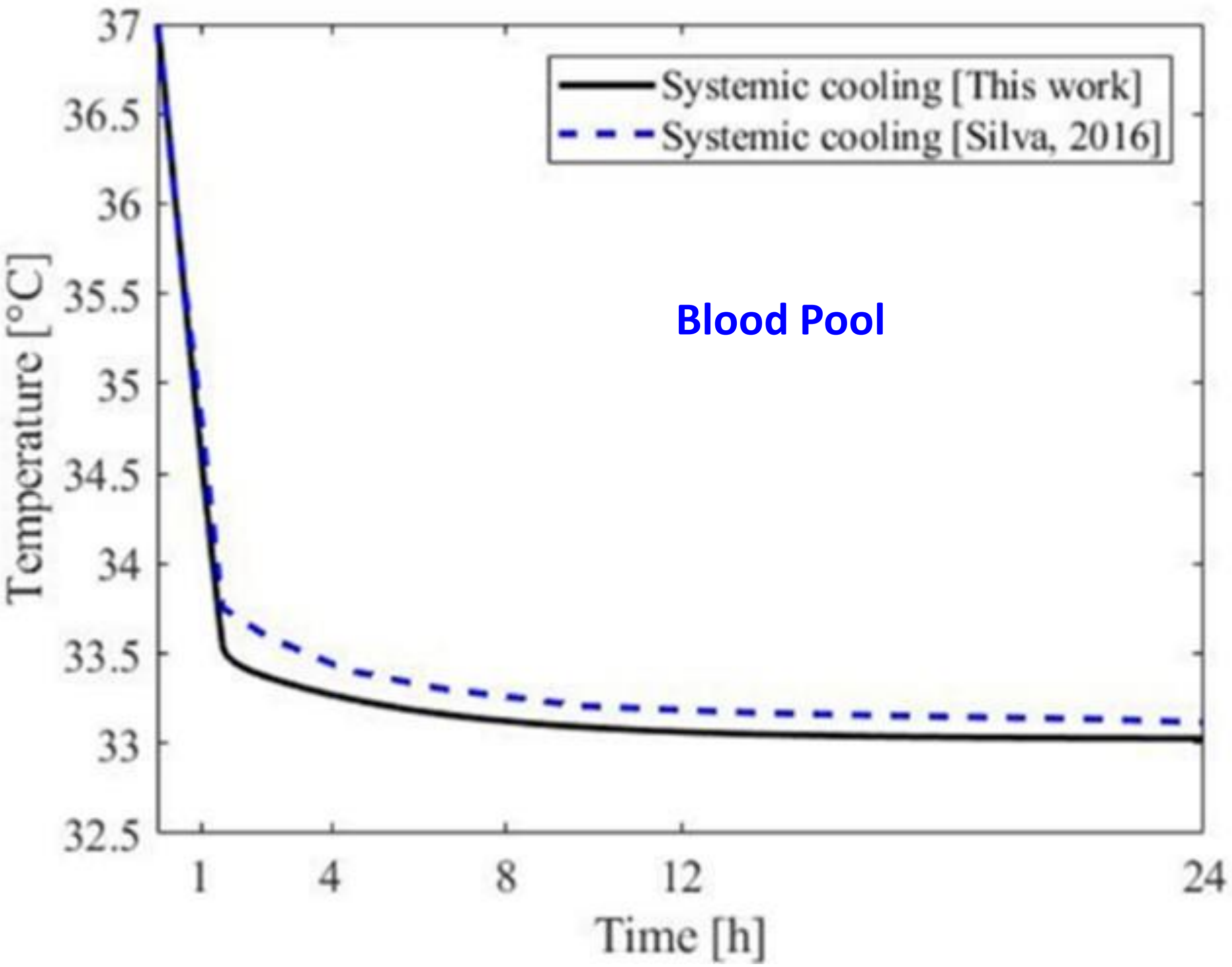
Code Verification

Metabolic heat generation

$$g_{t,s,l} = g_{t,s,l}^{bas}\, Q_{10}^{\frac{T_{t,s,l}-T_0}{10}}$$

Blood perfusion

$$\omega_{t,s,l} = \omega_{t,s,l}^{bas}\, Q_{10}^{\frac{T_{t,s,l}-T_0}{10}}$$

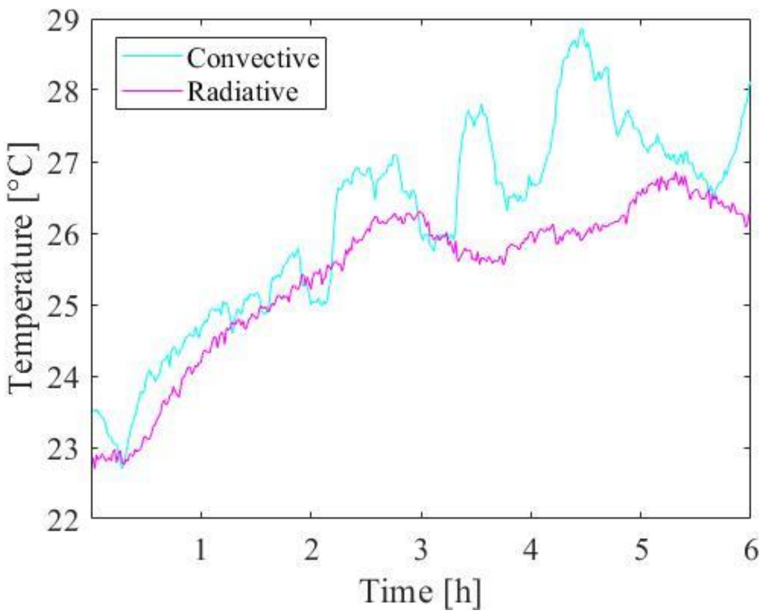


Silva, A.B.C.G., Wrobel, L.C. and Ribeiro, F.L.B. (2018), "A thermoregulation model for whole body cooling hypothermia", Journal of Thermal Biology, Vol. 78, pp. 122-130.

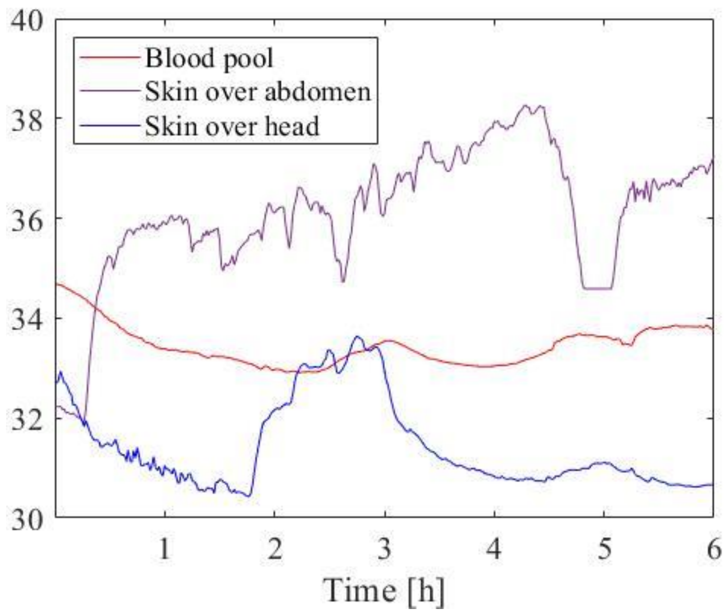
Actual Measurements During the Local Treatment

University Clinical Hospital of Opole, Poland

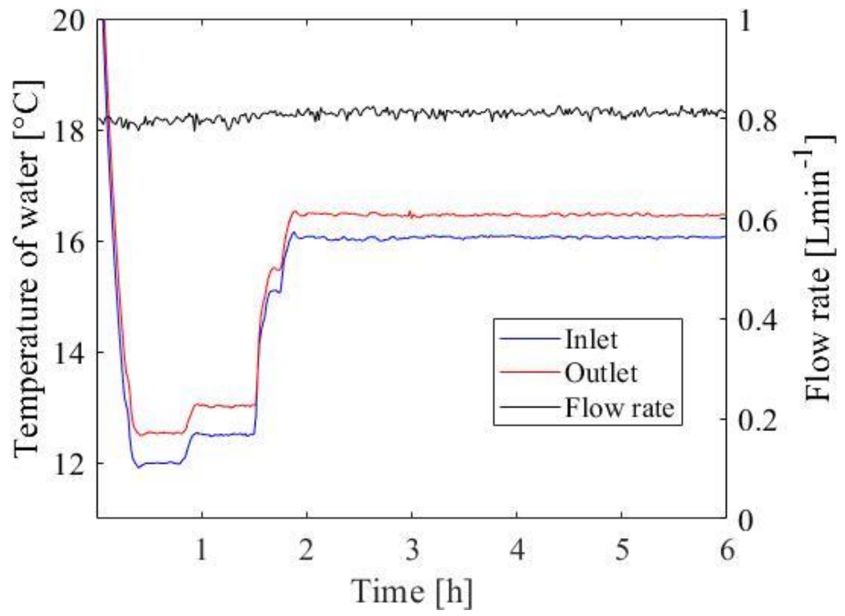
Surrounding temperatures



Body temperatures



Water temperatures and flow rate



Tumidajski, J., Wagstyl, D., Bandola, M. Bojdol, M., Ostrowski, Z., Rojczyk, M., Walas, W. "Non-Invasive Thermal Measurements During Newborn's Therapeutic Hypothermia and Processing of Their Results", In: 9th European Thermal Sciences Conference, Jun 10 – 13, Bled, Slovenia, 2024

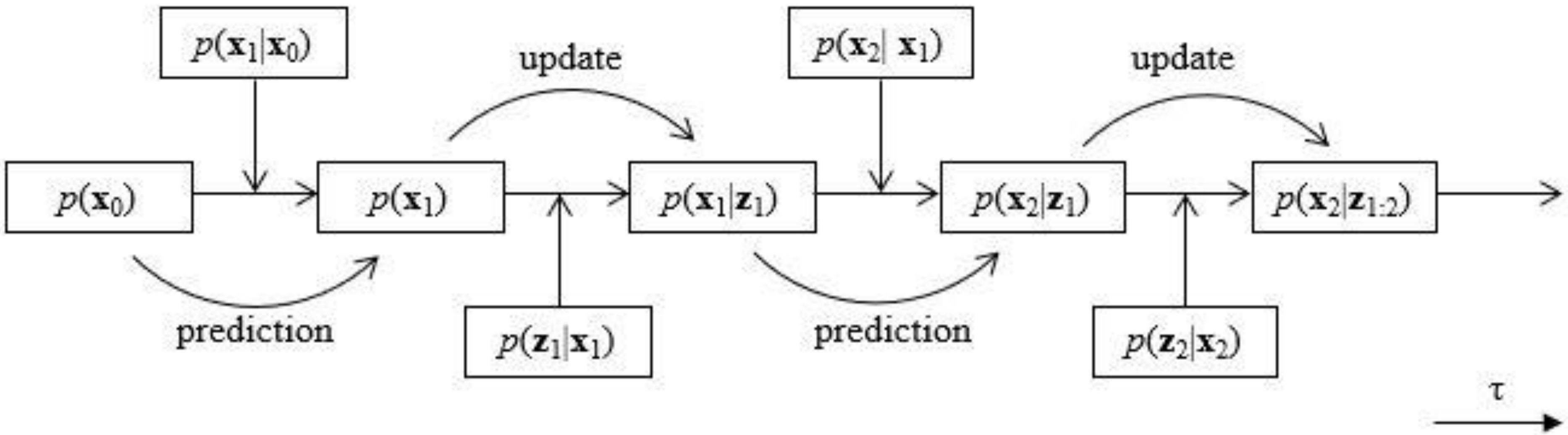
State Estimation Problem

Evolution model: $\mathbf{x}_k = \mathbf{f}_k\left(\mathbf{x}_{k-1}, \mathbf{u}_{k-1}, \mathbf{v}_{k-1}\right)$

Observation model: $\mathbf{z}_k = \mathbf{h}_k\left(\mathbf{x}_k, \mathbf{n}_k\right)$

$\mathbf{x}_k$ = state vector
$\mathbf{u}_k$ = control input vector
$\mathbf{z}_k$ = prediction of the measurements
$\mathbf{v}_k$ = noises of the evolution model
$\mathbf{n}_k$ = noises of the observation model
$\mathbf{f}_k$ = nonlinear function
$\mathbf{h}_k$ = nonlinear function

Prediction and Update Steps:

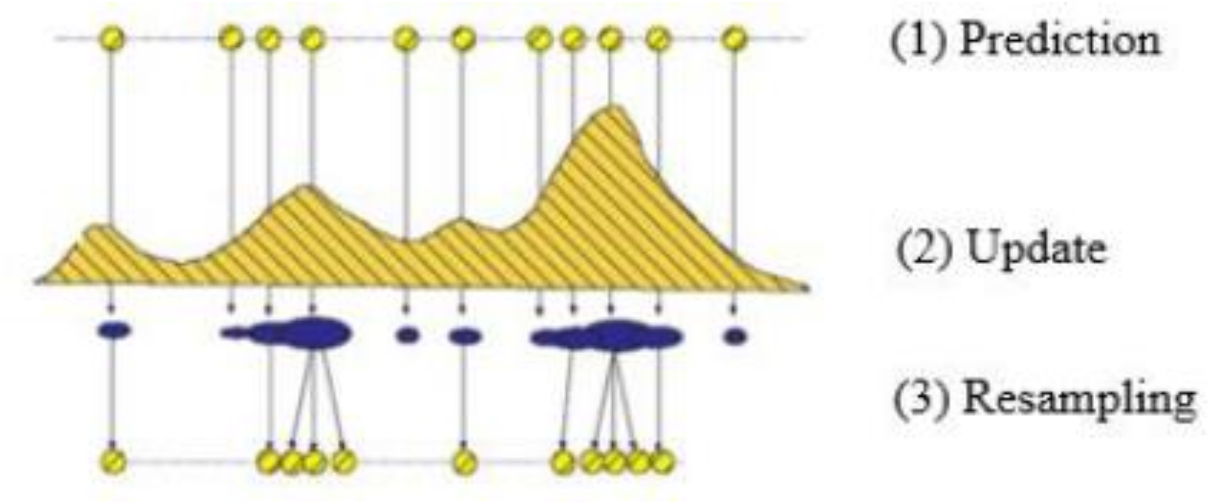


Bayesian Framework: $p_{posterior}\left(\mathbf{x}_k\right) = p\left(\mathbf{x}_k \mid \mathbf{z}_k\right) \propto p\left(\mathbf{x}_k\right) p\left(\mathbf{z}_k \mid \mathbf{x}_k\right)$

State Estimation Problem

Particle Filter - SIR

Represent the posterior probability density function by a set of random samples with associated weights and obtain the estimates based on these samples and weights.



(1) Particles have uniform weights;
(2) Particles have updated weights after observations by using the likelihood function;
(3) Particles with smaller weights are discarded and new particles are generated from the particles closer to regions of large probability.

State Estimation

Step 1 - Generate new particles and compute weights

for $i = 1, \ldots, N_i$

Sample $\mathbf{x}_k^i \sim p\left(\mathbf{x}_k \mid \mathbf{x}_{k-1}^i, \mathbf{u}_{k-1}\right)$

Compute weights as $w_k^i = p\left(\mathbf{z}_k \mid \mathbf{x}_k^i\right)$

Normalize the weights as $w_k^i = w_k^i \left(w_{tot}\right)^{-1}$

Step 2 - Resample

for $i = 1, \ldots, N_i$

Construct the cumulative sum of weights

Let $i = 1$ and draw u_1 from the uniform distribution $\mathcal{U}\left(0, N^{-1}\right)$

for $i = 1, \ldots, N_i$

Compute $u_j = u_1 + N_i^{-1}\left[j-1\right]$

while $u_j > c_i$

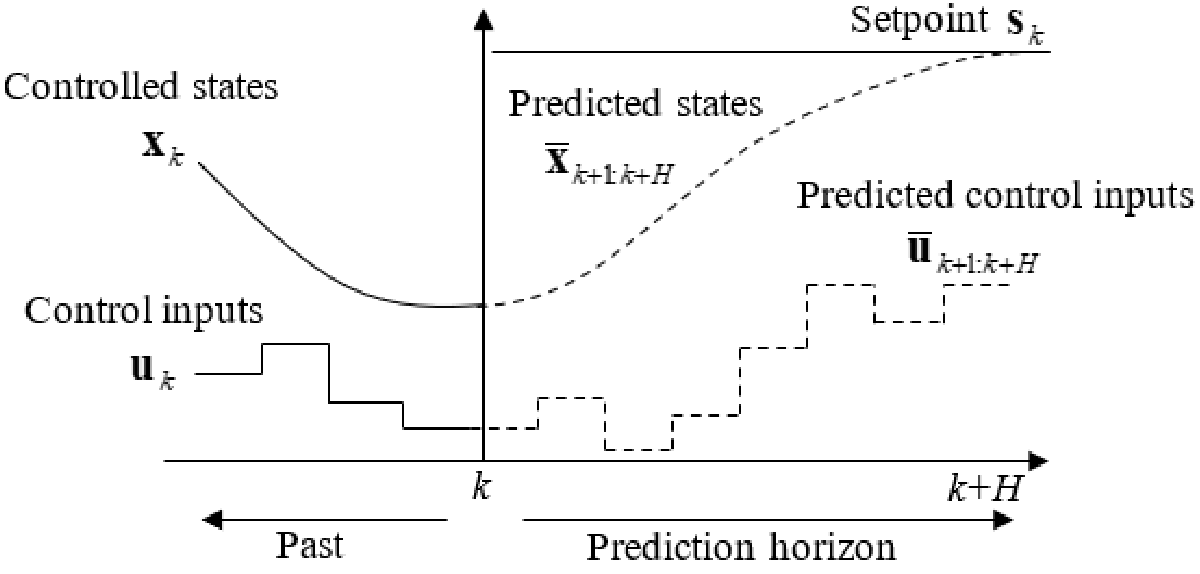
$i = i + 1$

Assign sample $\mathbf{x}_k^j = \mathbf{x}_k^i$

Assign sample weight $w_k^j = N_i^{-1}$

Ristic, B., Arulampalam, S., Gordon, N., *Beyond the Kalman Filter*, Boston: Artech House, (2004).

State Estimation Problem and Model Predictive Control



Stahl, D., Hauth, J., "PF-MPC: Particle filter-model predictive control", *Systems & Control Letters*, 60, pp. 632-643, (2011).

Stochastic Control

Step 3 - Initialize states and control inputs

for $i = 1, \ldots, N_i$

Set $\bar{\mathbf{x}}_k^i = \mathbf{x}_k^i$

Sample $\bar{\mathbf{u}}_k^i \sim p\left(\bar{\mathbf{u}}_k \mid \mathbf{u}_{k-1}\right)$

Step 4 - Prediction horizon loop

for $h = k+1, \ldots, k+H$

Step 5 - Generate new particles and compute weights

for $i = 1, \ldots, N_i$

Sample $\bar{\mathbf{x}}_h^i \sim p\left(\bar{\mathbf{x}}_h \mid \bar{\mathbf{x}}_{h-1}^i, \bar{\mathbf{u}}_{h-1}^i\right)$

Sample $\bar{\mathbf{u}}_h^i \sim p\left(\bar{\mathbf{u}}_h \mid \bar{\mathbf{u}}_{h-1}\right)$

Compute weights $w_h^i = p\left(\mathbf{s}_k \mid \bar{\mathbf{x}}_h^i\right)$

Normalize the particle weights

Step 6 - Resample

Resample as Step 2 for the respective state variables

Assign sample $\bar{\mathbf{x}}_h^j = \bar{\mathbf{x}}_h^i$ and $\bar{\mathbf{u}}_h^j = \bar{\mathbf{u}}_h^i$

Step 7 - Compute statistical point estimates

Mean states

$$\mathbf{x}_k = \sum_{i=1}^{N_i} \mathbf{x}_k^i w_k^i$$

Standard deviation

$$\boldsymbol{\sigma}_k = \sqrt{\frac{1}{N_i} \sum_{i=1}^{N_i} \left(\mathbf{x}_k^i - \mathbf{x}_k\right)^2}$$

Mean control inputs

$$\mathbf{u}_k = \sum_{i=1}^{N_i} \bar{\mathbf{u}}_{k+H} \bar{w}_{k+H}$$

Results and Discussions: VERIFICATION

State Estimation Using Simulated Temperature Measurements

Evolution model: $\mathbf{x}_k = [\mathbf{T}_k] = \mathbf{f}_k(\mathbf{x}_{k-1}, \mathbf{u}_{k-1}) + \mathbf{v}_k$

Observation model: $\mathbf{z}_k = \mathbf{h}_k(\mathbf{x}_k) + \mathbf{n}_k$

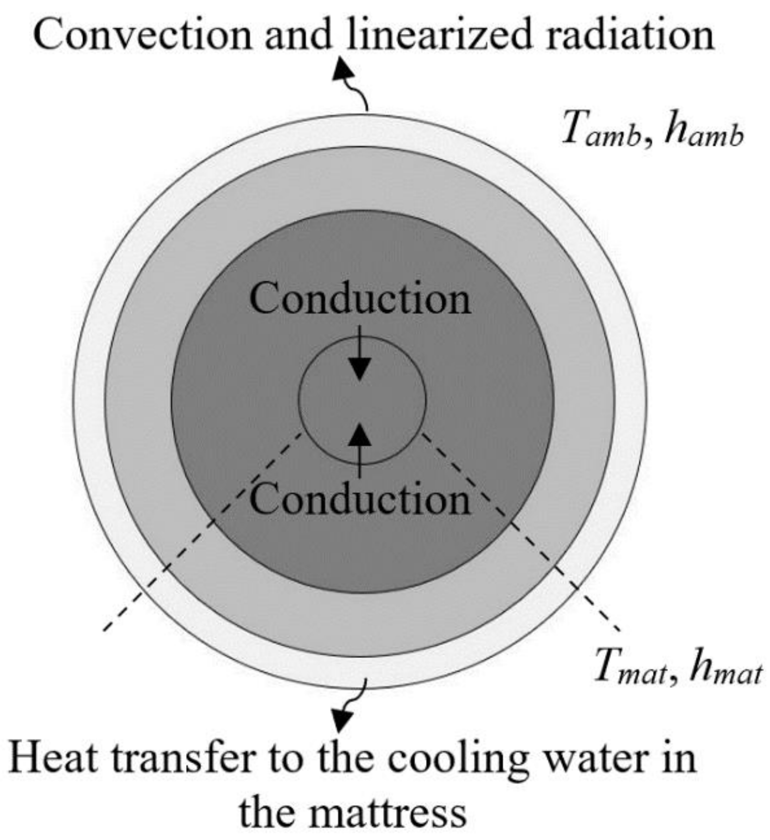
Likelihood: $w_k \propto p(\mathbf{z}_k \mid \mathbf{x}_k) = \exp\left\{ -\frac{1}{2} \frac{\left[\mathbf{z}_k^{meas} - \mathbf{h}(\mathbf{x}_k)\right]^{\mathrm{T}} \left[\mathbf{z}_k^{meas} - \mathbf{h}(\mathbf{x}_k)\right]}{\sigma_{meas}^2} \right\}$

Noise: $\mathbf{n}_k = N(0, \sigma_{meas})$, $\mathbf{v}_k = N(0, \sigma_{mod})$

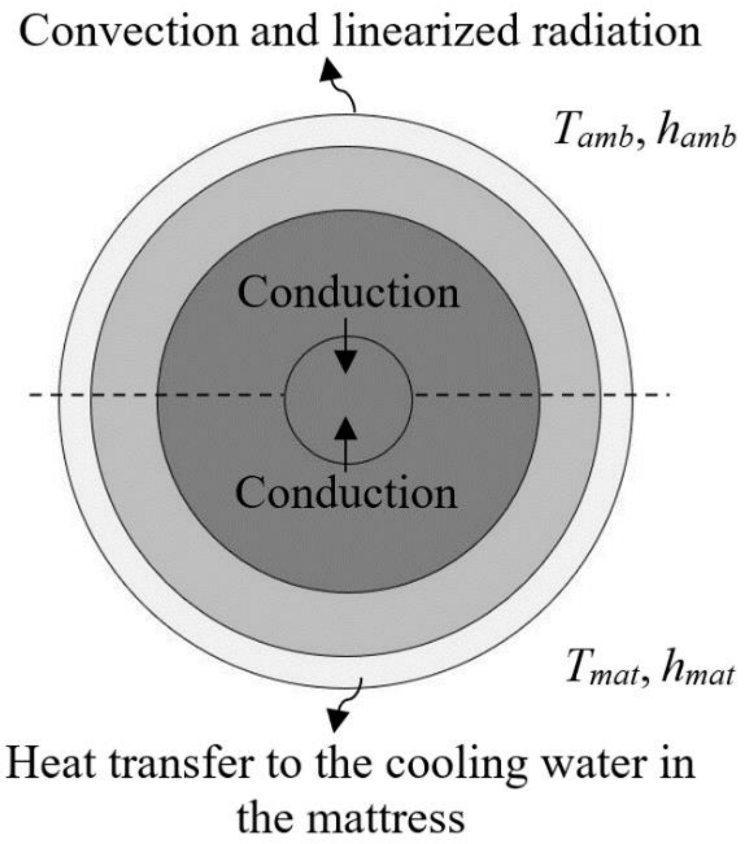
Results and Discussions: VERIFICATION

State Estimation Using Simulated Temperature Measurements

Systemic Cooling: Heat transfer processes



Upper Hemisphere of the Head



Other Body Elements

T_0 = 37°C
T_{amb} = 25°C
h_{amb} = 5 W/m^{2}K

Fast cooling
T_{mat} = 20°C
h_{mat} = 5 W/m^{2}K

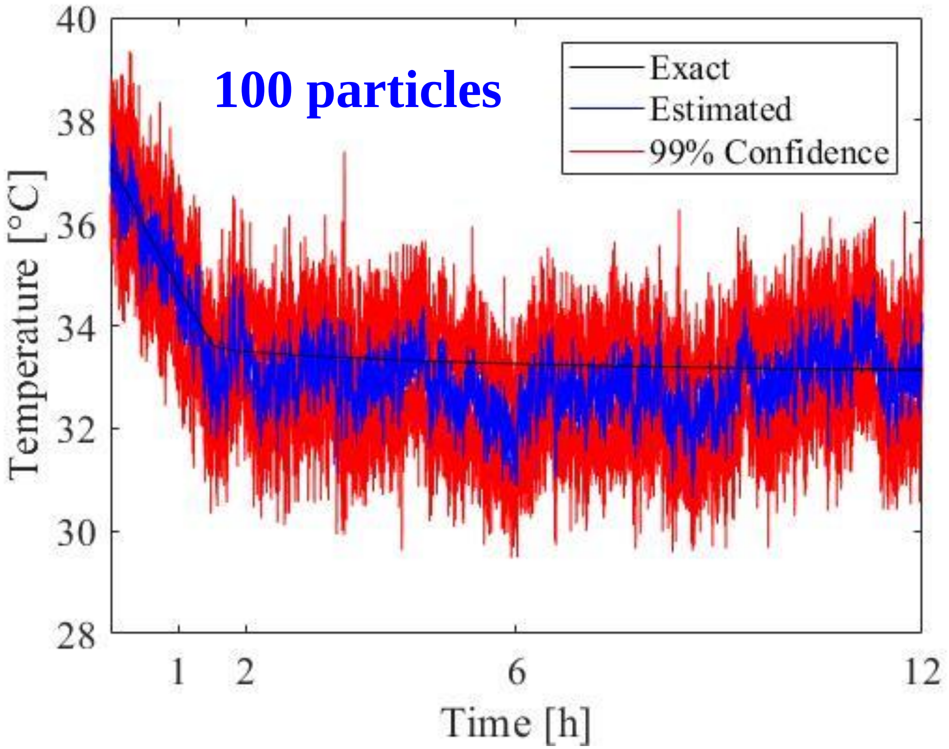
Constant cooling
T_{mat} = 34°C
h_{mat} = 5 W/m^{2}K

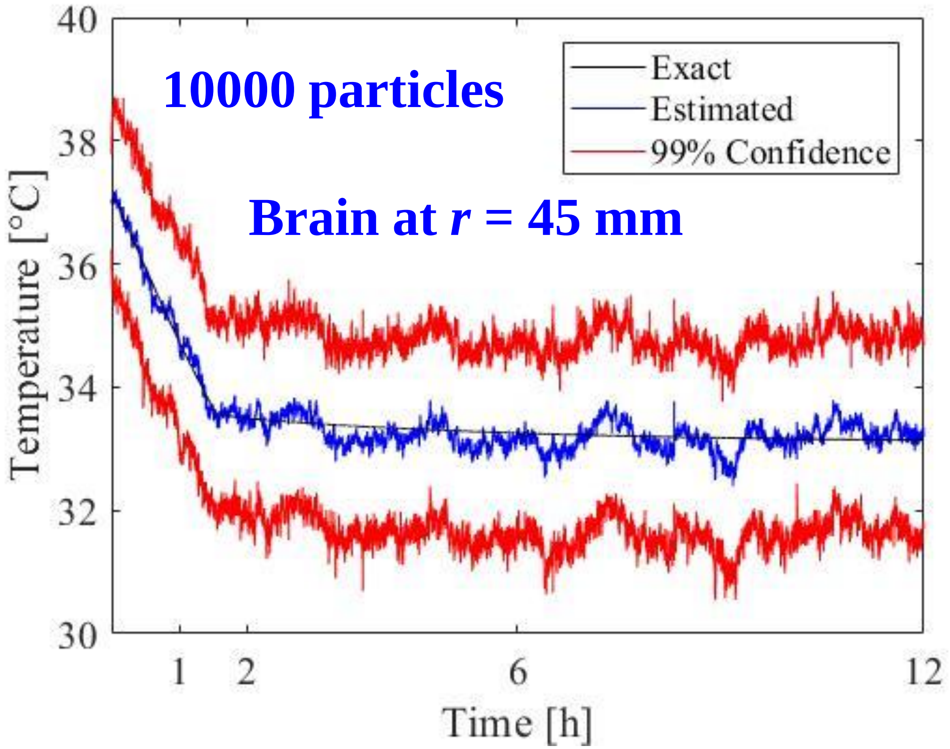
Results and Discussions: VERIFICATION

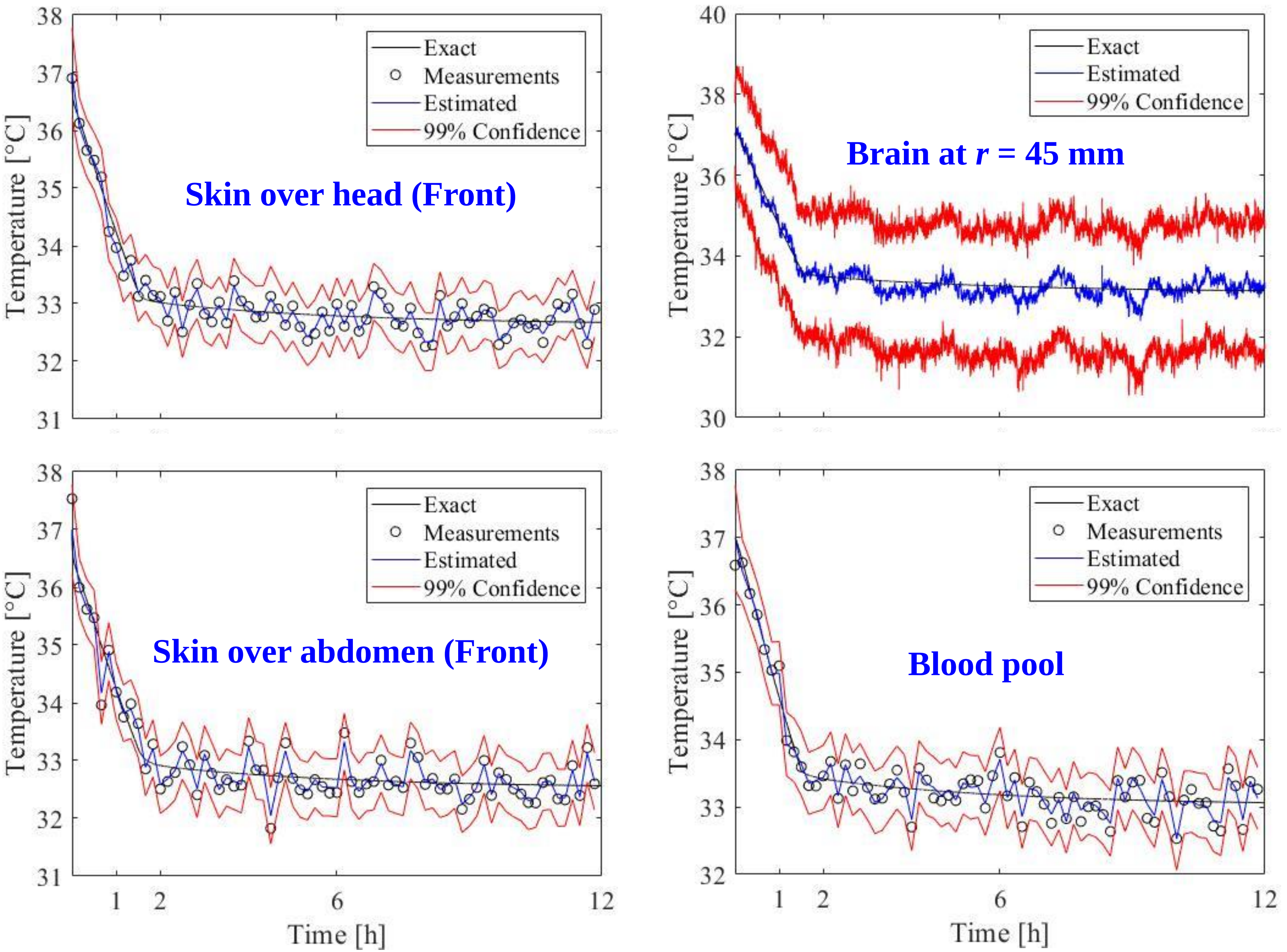
State Estimation Using Simulated Temperature Measurements

Systemic Cooling: The influence of the number of particles

	Number of particles			
	100	1000	10000	15000
RMSE [°C]	0.97	0.74	0.46	0.40
Computational time	8 min	1h20min	12h30min	24h







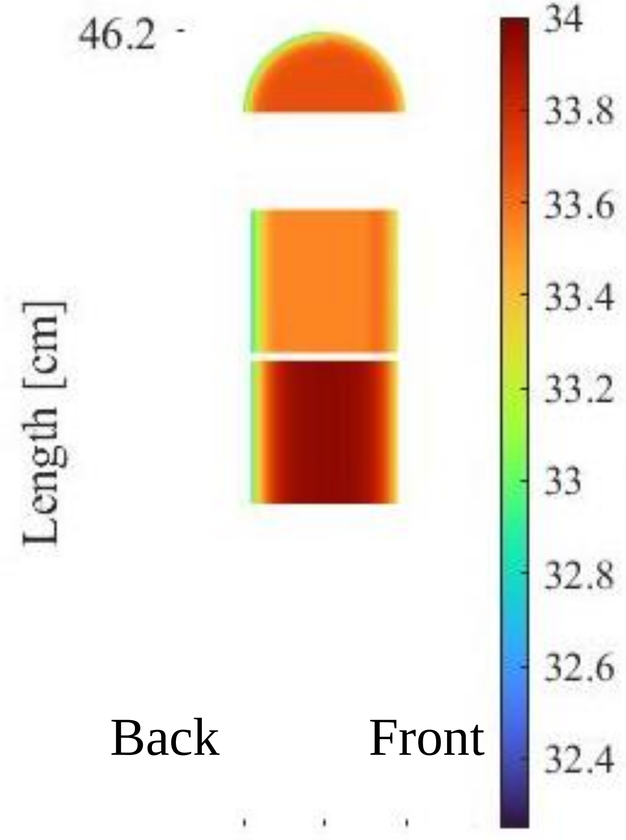
Skin over head (Front)
Brain at r = 45 mm
Skin over abdomen (Front)
Blood pool
Exact
Measurements
Estimated
99% Confidence
Temperature [°C]
Time [h]

Results and Discussions: VERIFICATION

State Estimation Using Simulated Temperature Measurements

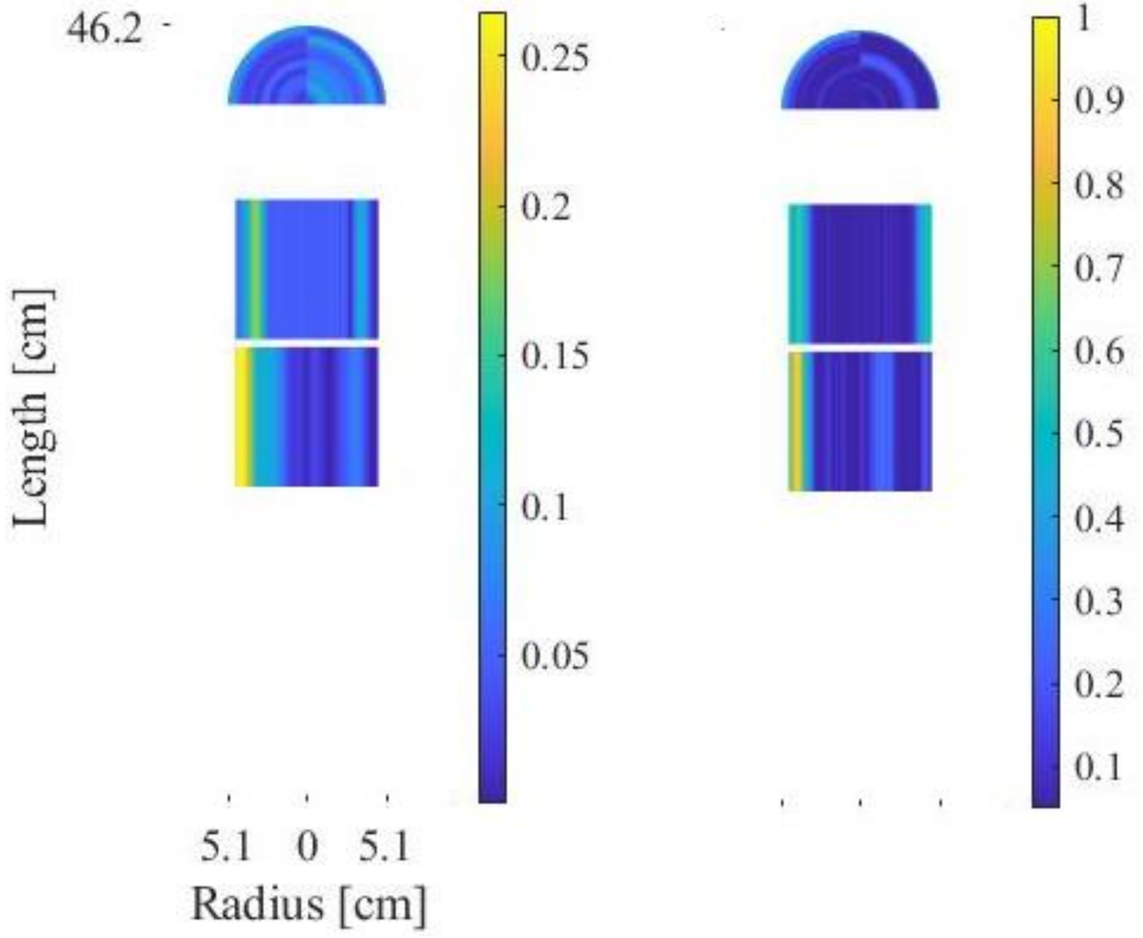
Systemic Cooling: The influence of the uncertainties of the evolution model for the temperatures

Exact



Absolute discrepancies between exact and estimated temperatures

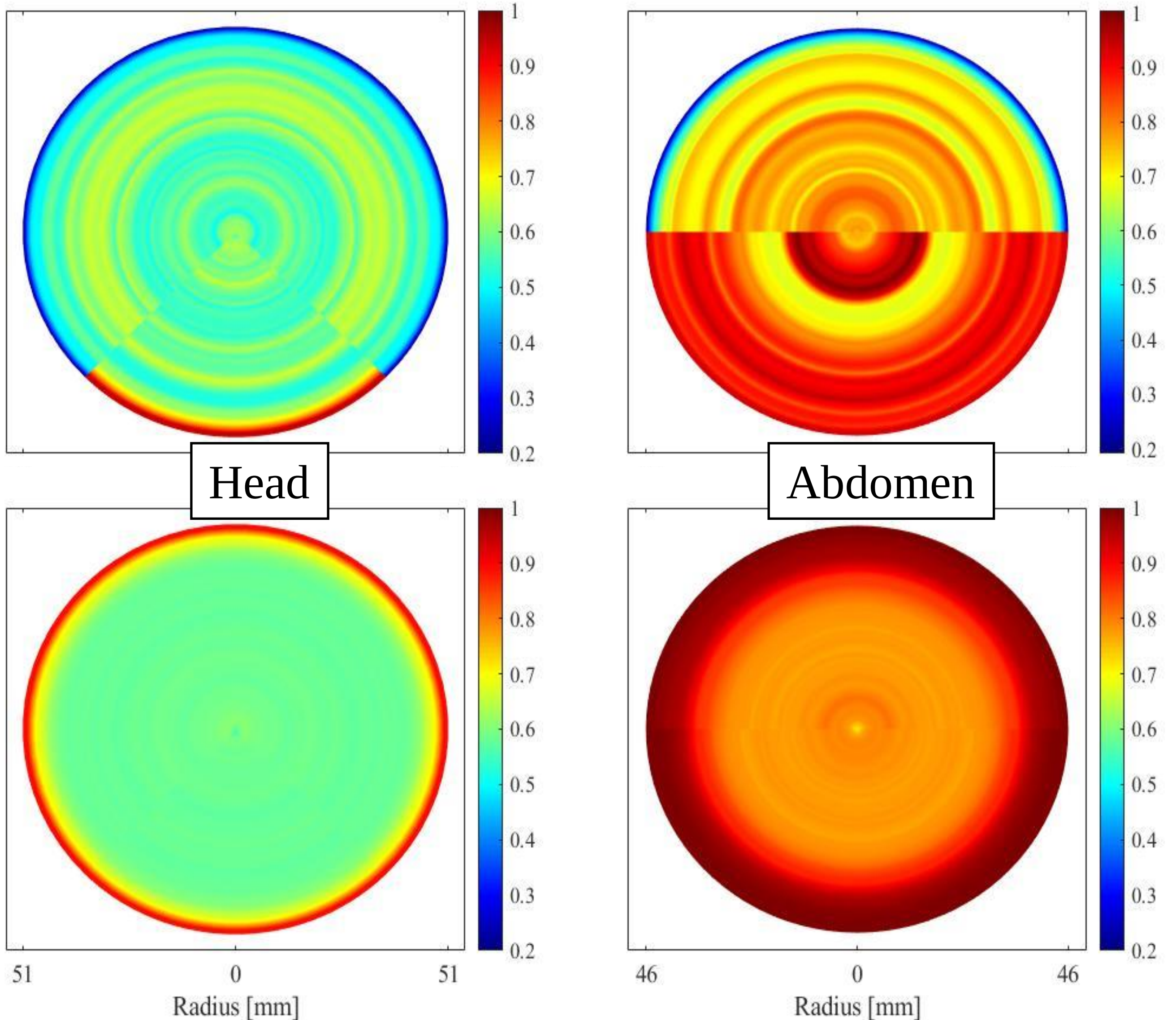
σ_{mod} = 0.1°C σ_{mod} = 0.3°C



Results and Discussions: VERIFICATION

State Estimation Using Simulated Temperature Measurements

Systemic Cooling: The influence of the solution of the estimation problem on the uncertainties



Solution of the State Estimation Problem

10000 Pure Monte Carlo Simulations

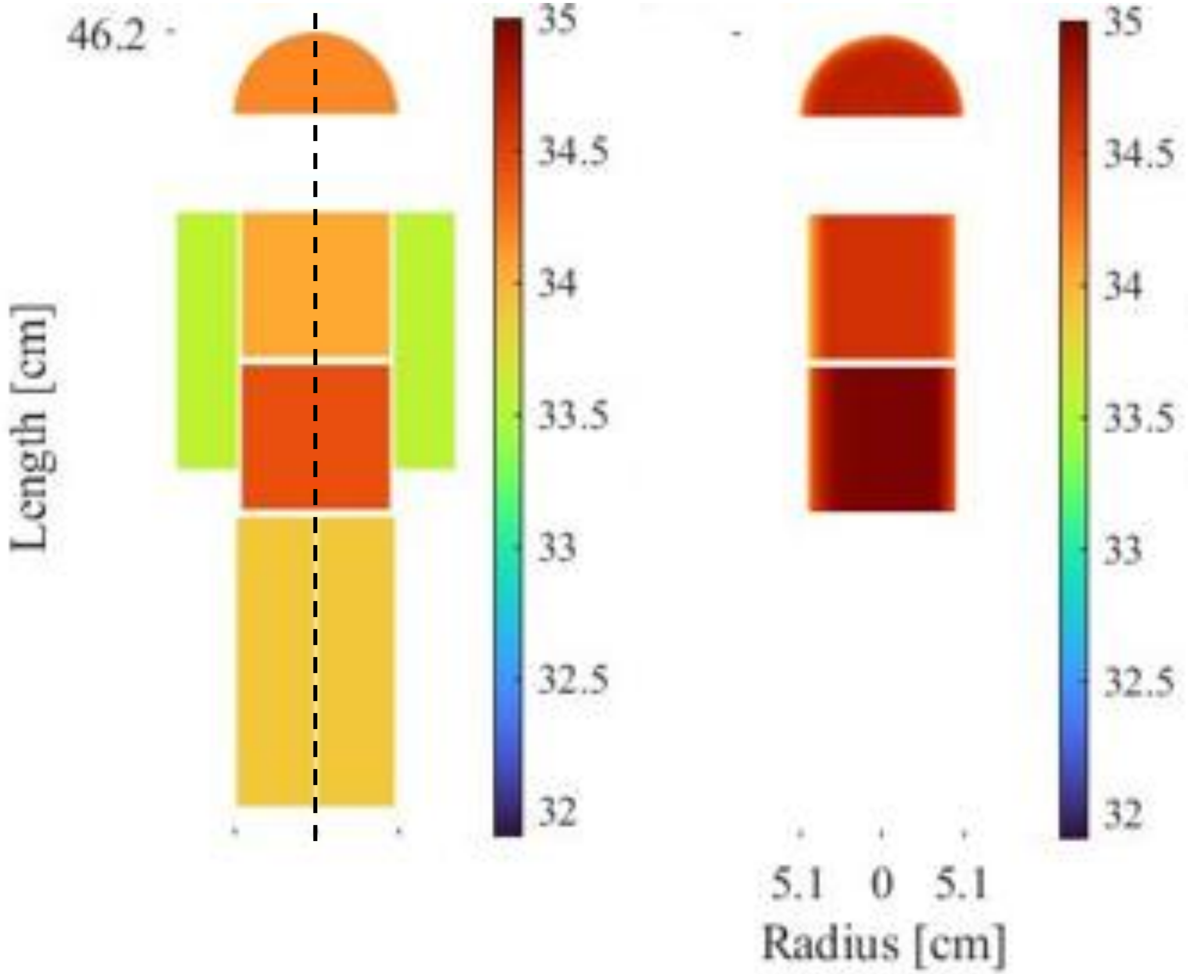
Results and Discussions: VERIFICATION

State Estimation Using Simulated Temperature Measurements

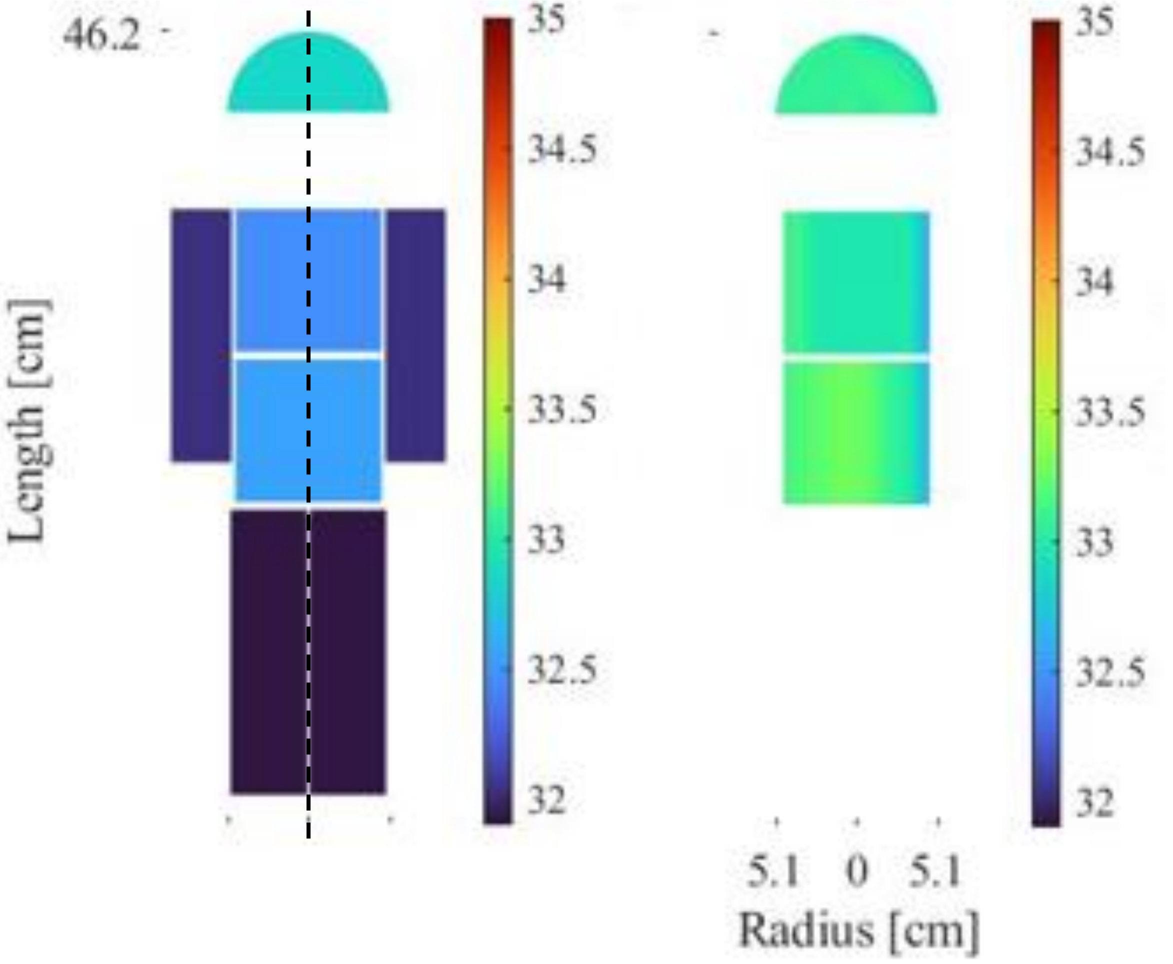
Systemic Cooling: Estimated Temperature Distribution

1 hour of cooling

Frontal view   Section B-B



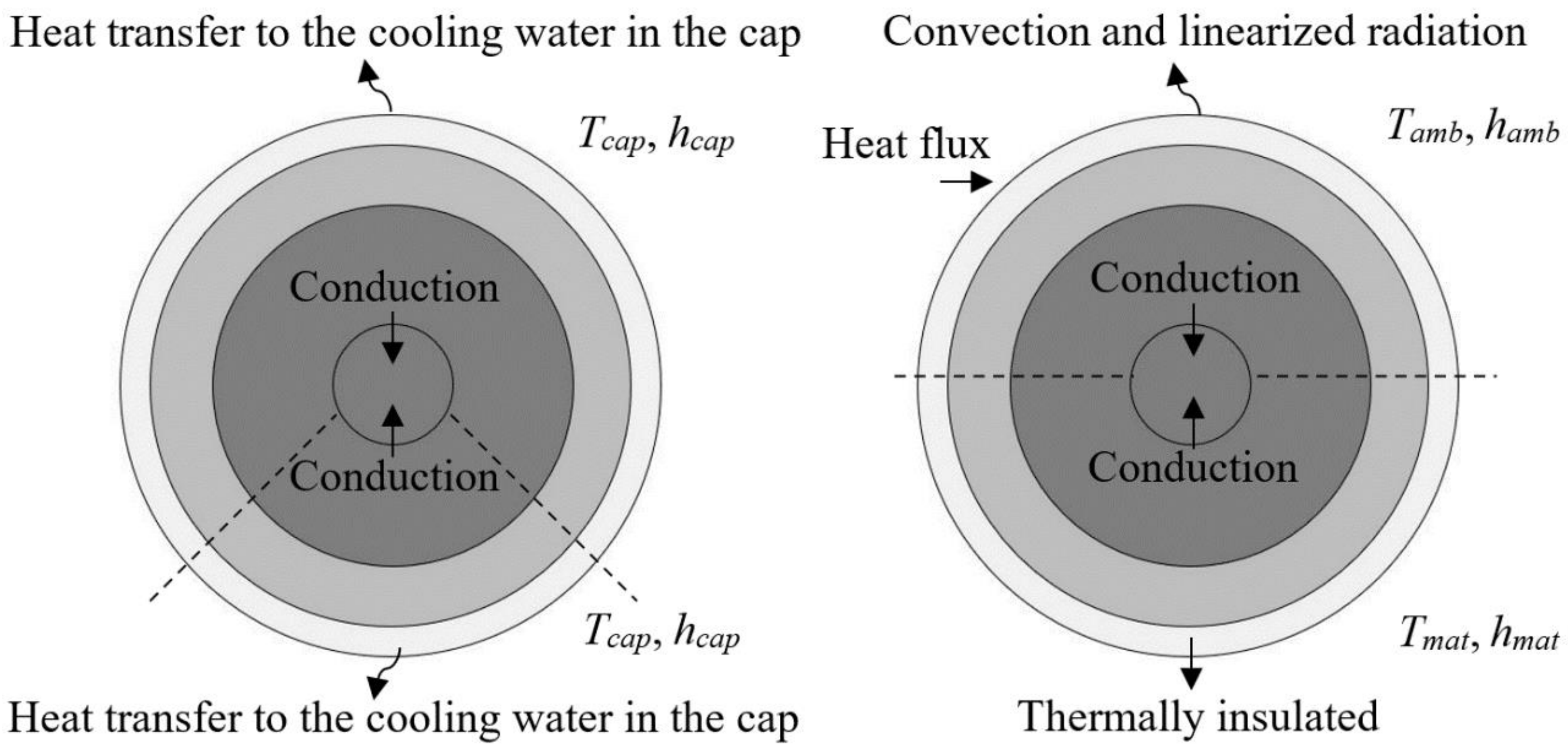
12 hours of cooling



Results and Discussions: VERIFICATION

State Estimation Using Simulated Temperature Measurements

Local Cooling: Heat transfer processes



Upper Hemisphere of the Head

Other Body Elements

$T_0 = 37°C$
$T_{amb} = 25°C$
$h_{amb} = 5\ W/m^2K$

Fast cooling

$T_{cap} = 10.8°C$
$h_{cap} = 19.5\ W/m^2K$
$q_{war} = 0\ W/m^2$

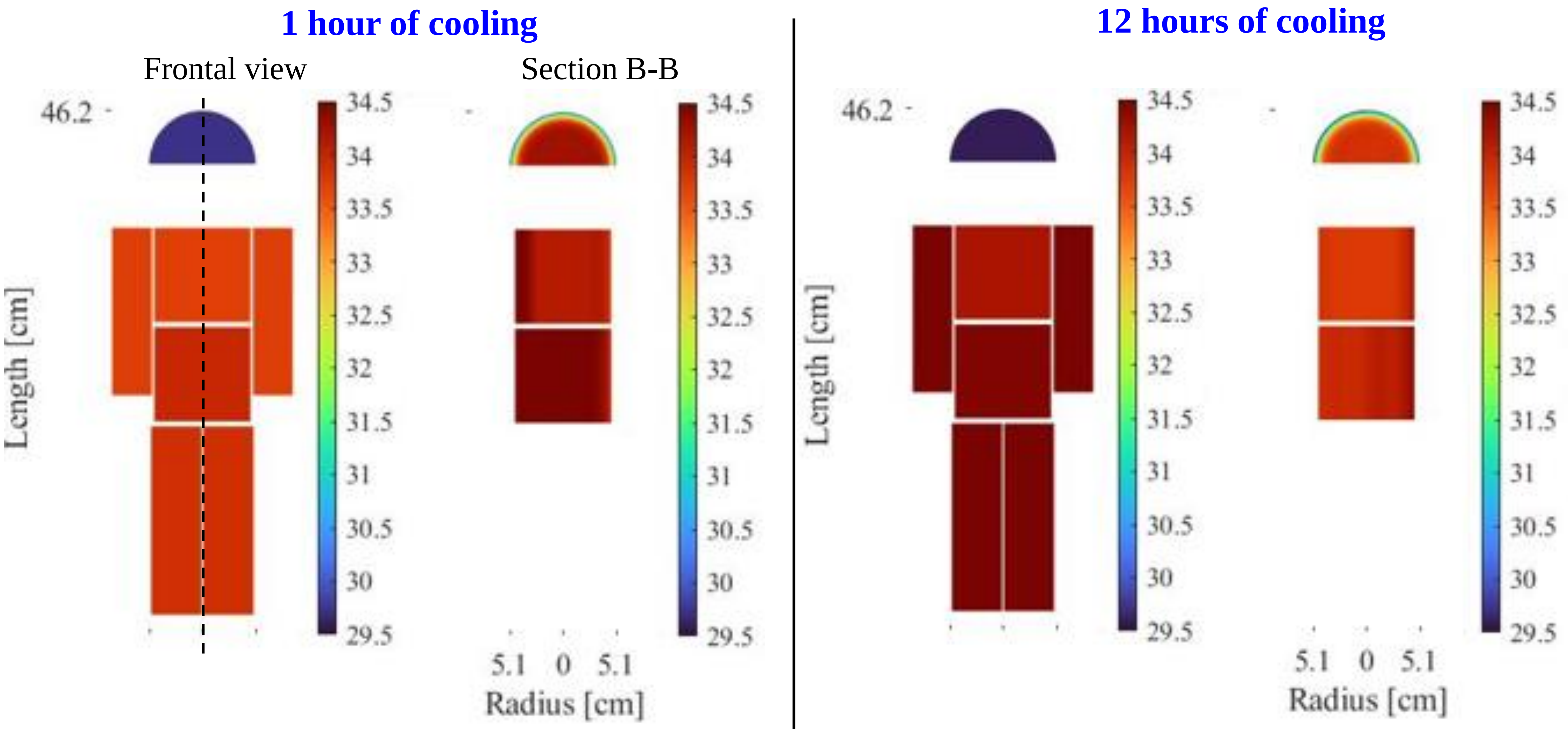
Constant cooling

$q_{war} = 90\ W/m^2$

Results and Discussions: VERIFICATION

State Estimation Using Simulated Temperature Measurements

Local Cooling: Estimated Temperature Distribution



Results and Discussions: VERIFICATION

Stochastic Control of the State Variables with Simulated Measurements

OBSERVER

Evolution model: $\mathbf{x}_k = [\mathbf{T}_k] = \mathbf{f}_k(\mathbf{x}_{k-1}, \mathbf{u}_{k-1}) + \mathbf{v}_k$

Observation model: $\mathbf{z}_k = \mathbf{h}_k(\mathbf{x}_k) + \mathbf{n}_k$

Likelihood:

$$w_k \propto p(\mathbf{z}_k \mid \mathbf{x}_k) = \exp\left\{-\frac{1}{2}\frac{\left[\mathbf{z}_k^{meas} - \mathbf{h}(\mathbf{x}_k)\right]^{\mathrm{T}}\left[\mathbf{z}_k^{meas} - \mathbf{h}(\mathbf{x}_k)\right]}{\sigma_{meas}^2}\right\}$$

CONTROL

Random walk for the control inputs: $\bar{\mathbf{u}}_h = \bar{\mathbf{u}}_{h-1} + \mathbf{c}_h$

Likelihood:

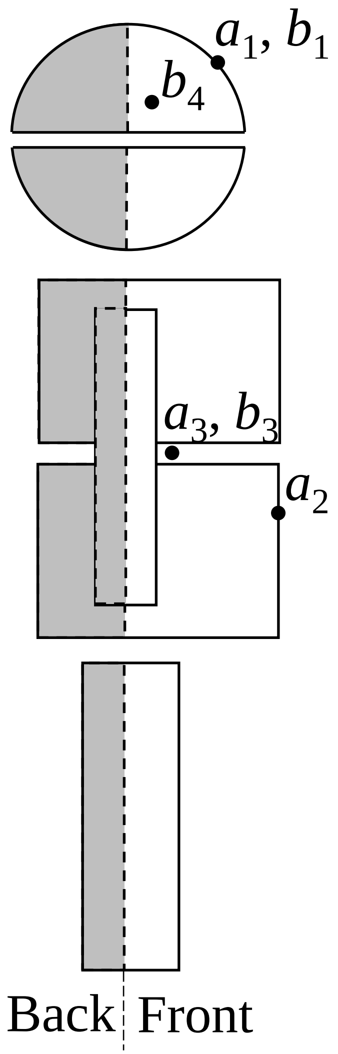
$$p(\mathbf{s}_h \mid \bar{\mathbf{x}}_h) = \exp\left\{-\frac{1}{2}\frac{\left[\mathbf{s}_h - \mathbf{g}(\bar{\mathbf{x}}_h)\right]^{\mathrm{T}}\left[\mathbf{s}_h - \mathbf{g}(\bar{\mathbf{x}}_h)\right]}{\sigma_{set}^2}\right\}$$

Noise: $\mathbf{n}_k = N(0, \sigma_{meas})$, $\mathbf{v}_k = N(0, \sigma_{mod})$, $\mathbf{c}_h = N(0, \sigma_{rw})$

Results and Discussions: VERIFICATION

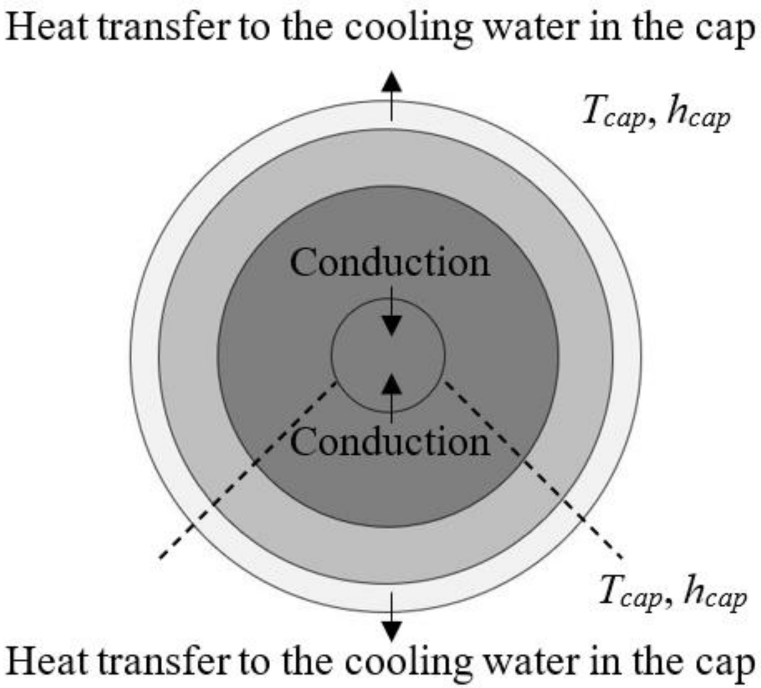
Stochastic Control of the State Variables with Simulated Measurements

Local Treatment: Heat transfer processes for the cooling phase

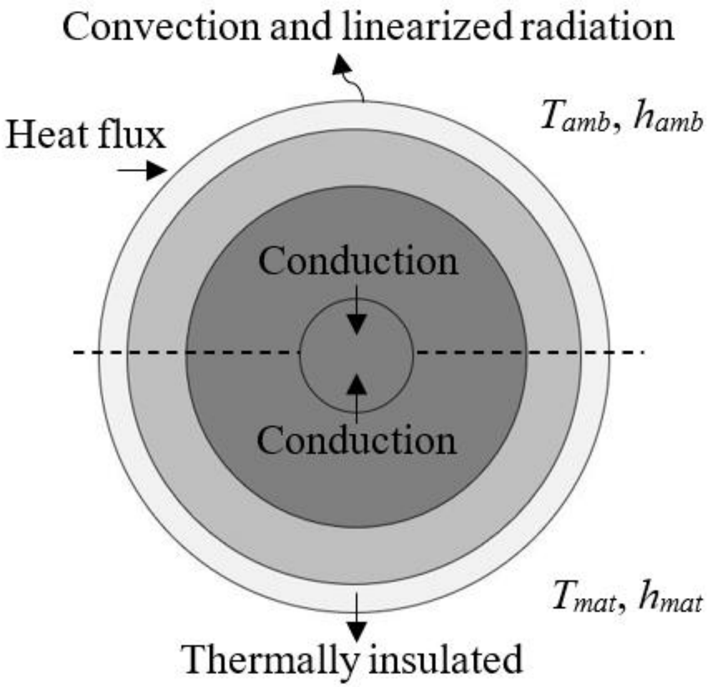


$\mathbf{x}_{ctl} = [b_1; b_3; b_4]$

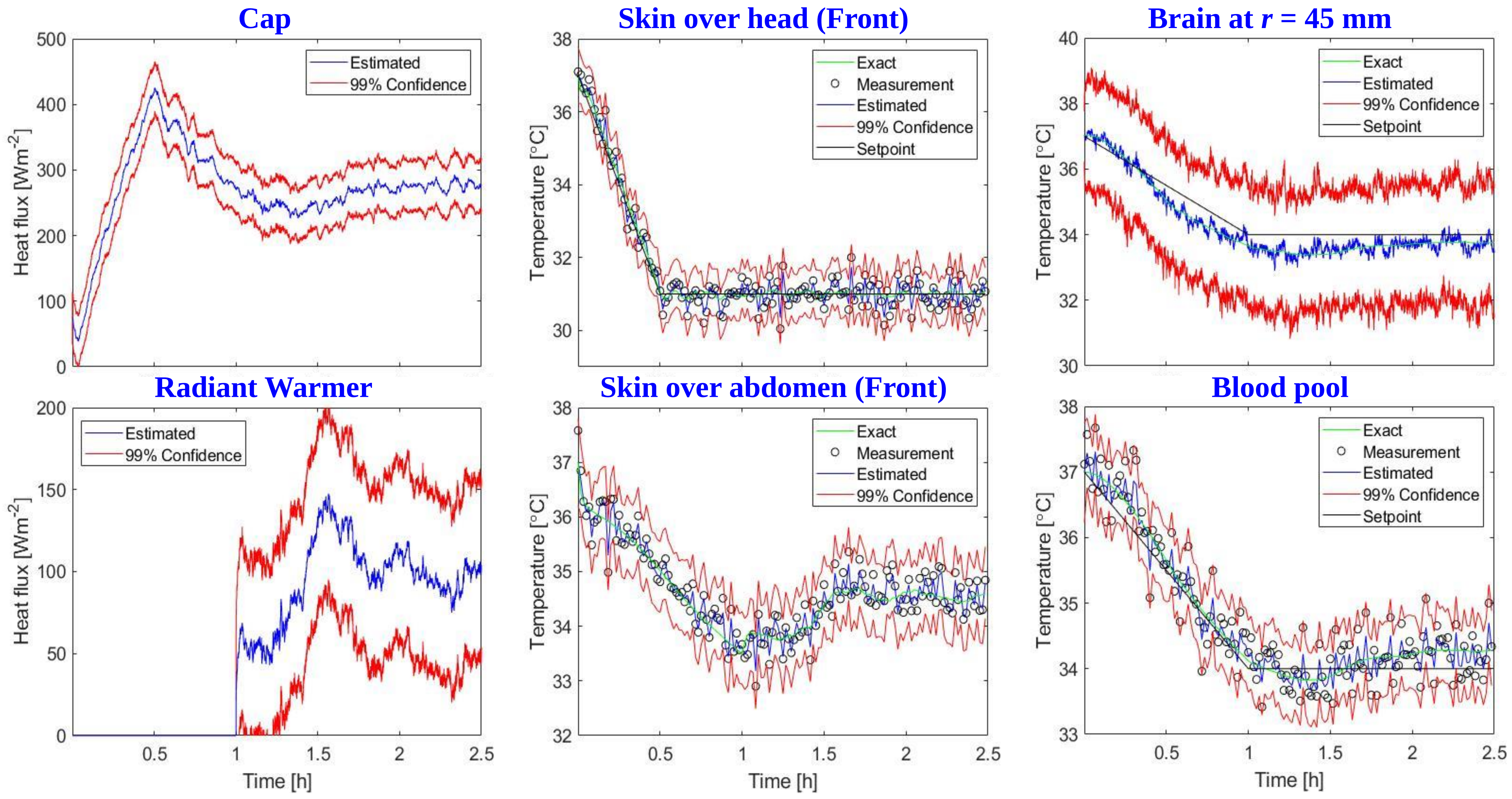
$\mathbf{u} = [q_{cap}; q_{war}]$



Upper Hemisphere of the Head



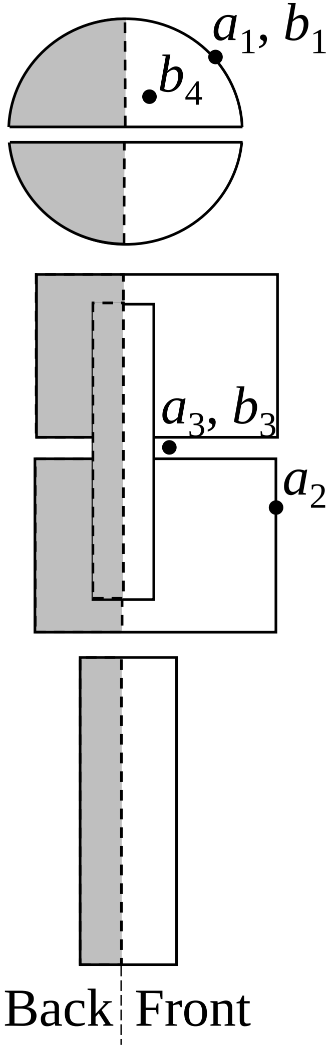
Other Body Elements


Cap
Heat flux [Wm^-2]
Estimated
99% Confidence
Skin over head (Front)
Temperature [°C]
Exact
Measurement
Estimated
99% Confidence
Setpoint
Brain at r = 45 mm
Temperature [°C]
Exact
Estimated
99% Confidence
Setpoint
Radiant Warmer
Heat flux [Wm^-2]
Estimated
99% Confidence
Time [h]
Skin over abdomen (Front)
Temperature [°C]
Exact
Measurement
Estimated
99% Confidence
Time [h]
Blood pool
Temperature [°C]
Exact
Measurement
Estimated
99% Confidence
Setpoint
Time [h]

Results and Discussions: VERIFICATION

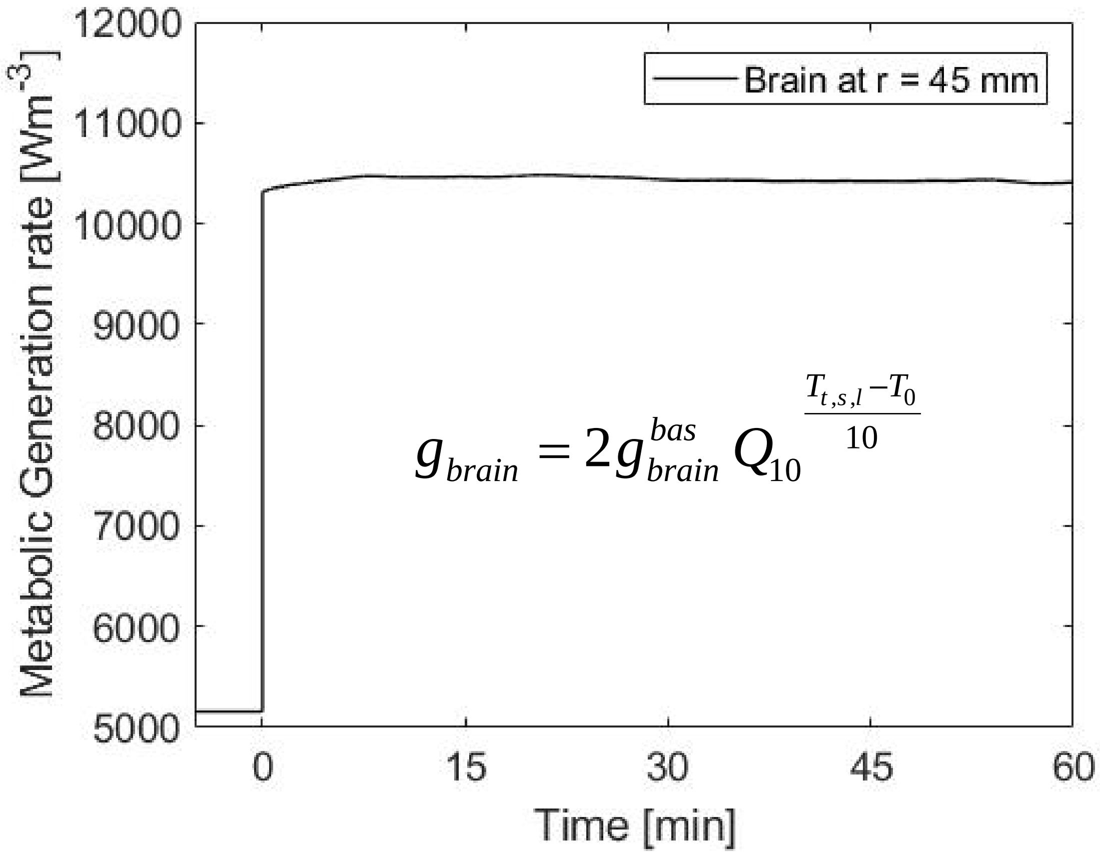
Stochastic Control of the State Variables with Simulated Measurements

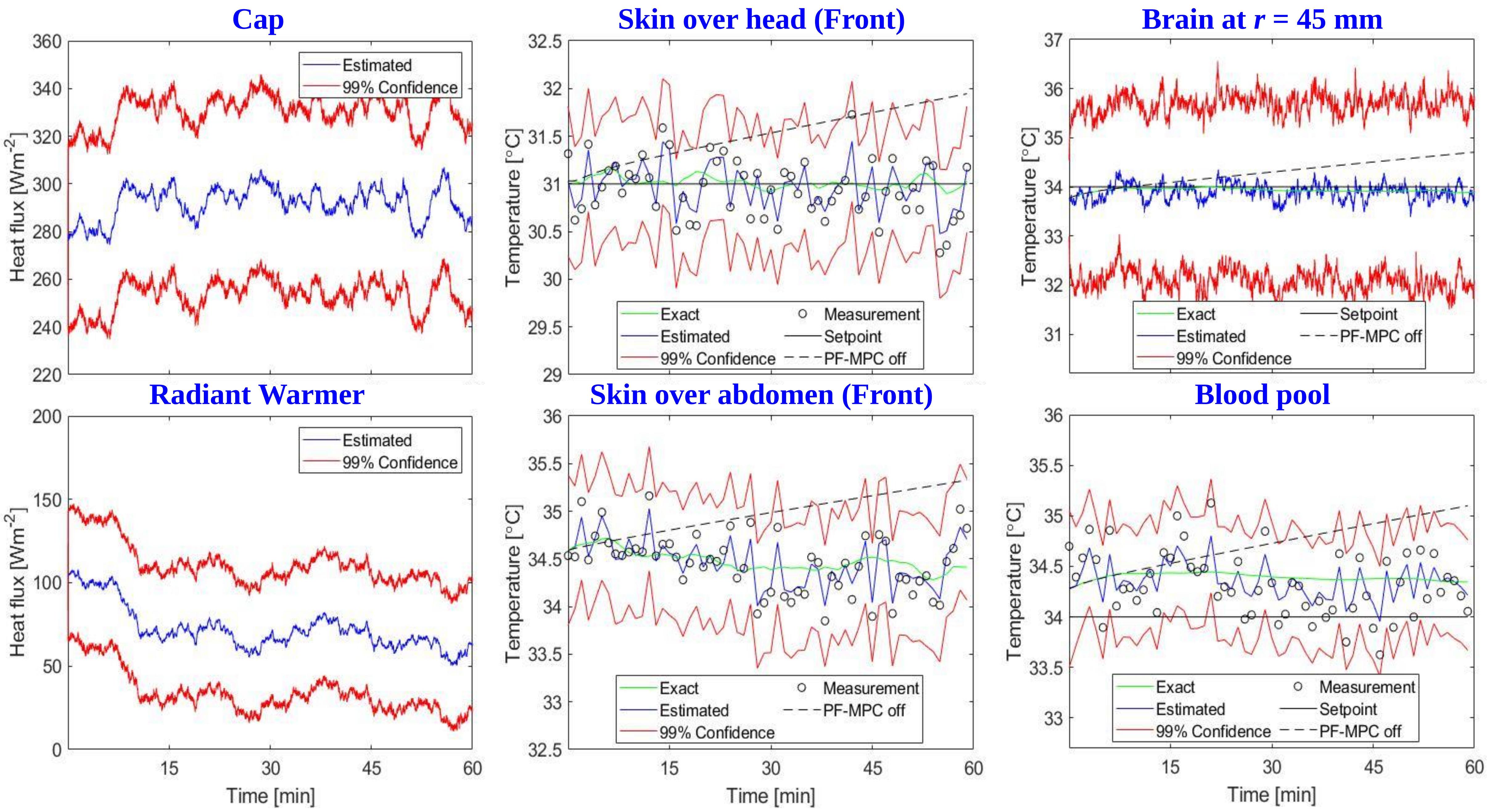
Local Treatment: Undesired metabolic changes



$$\mathbf{x}_{ctl} = [b_1; b_3; b_4]$$

$$\mathbf{u} = [q_{cap}; q_{war}]$$



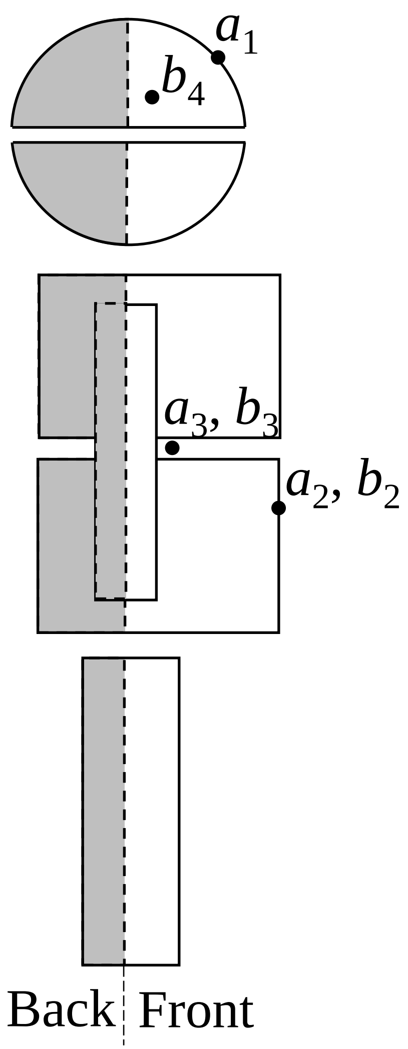


Cap
Heat flux [Wm-2]
Estimated
99% Confidence
Skin over head (Front)
Temperature [°C]
Exact
Estimated
99% Confidence
Measurement
Setpoint
PF-MPC off
Brain at r = 45 mm
Radiant Warmer
Skin over abdomen (Front)
Blood pool
Time [min]

Results and Discussions: VERIFICATION

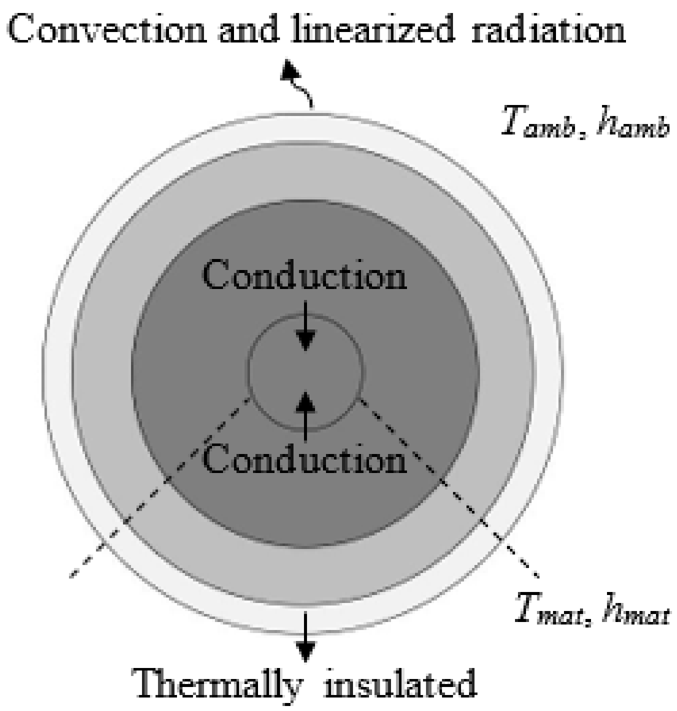
Stochastic Control of the State Variables with Simulated Measurements

Local Treatment: Heat transfer processes for the rewarming phase

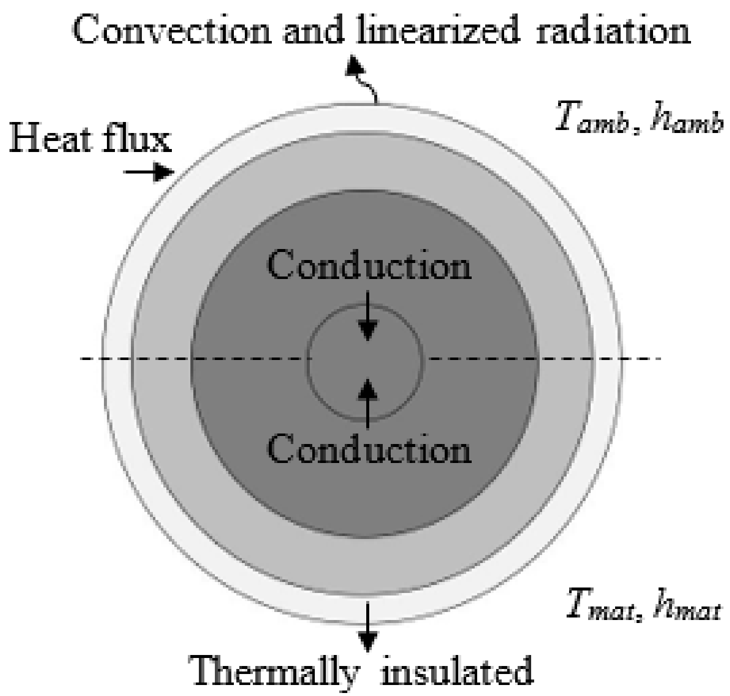


$\mathbf{x}_{ctl} = [b_2; b_3; b_4]$

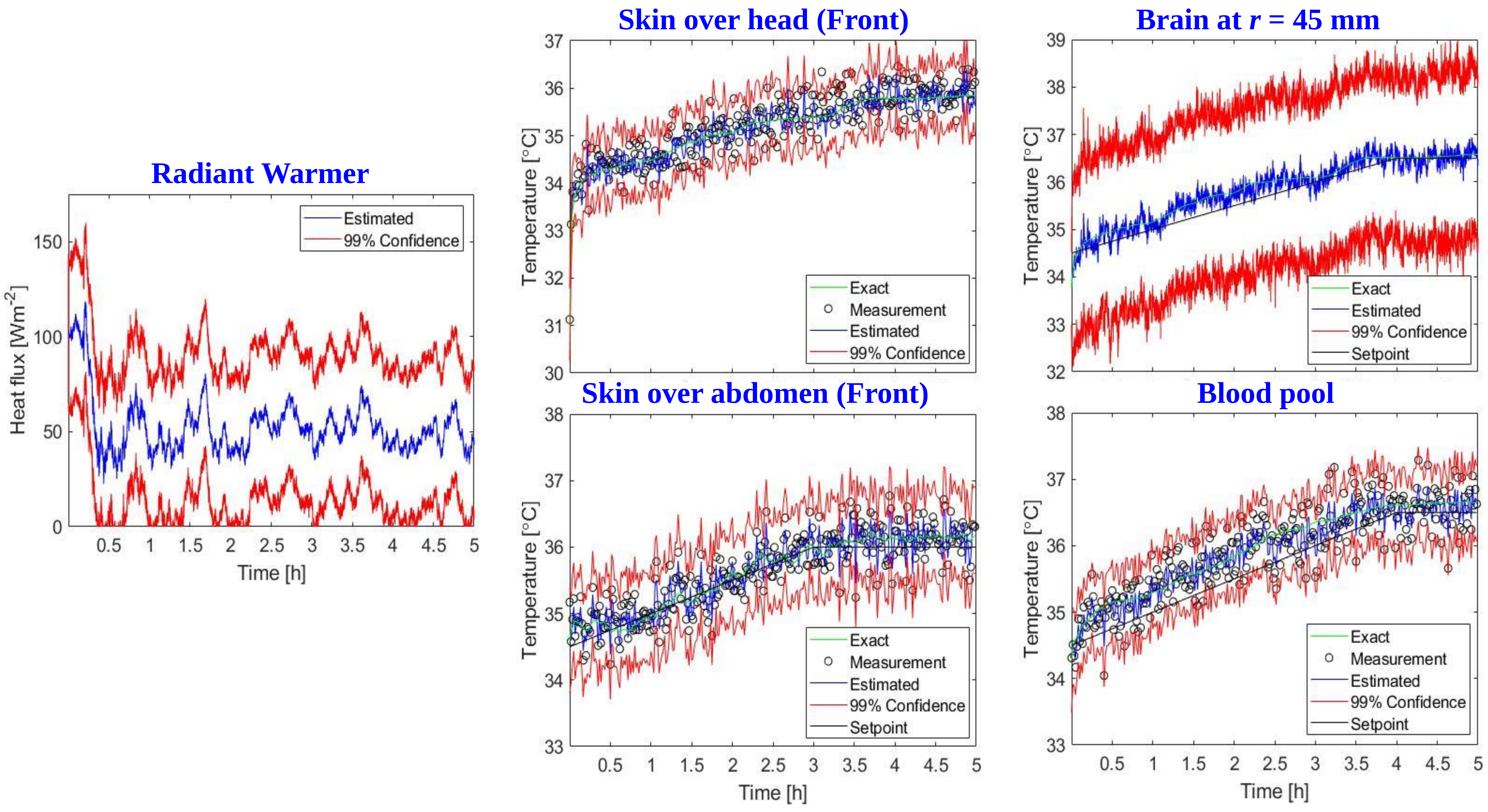
$\mathbf{u} = [q_{war}]$



Upper Hemisphere of the Head



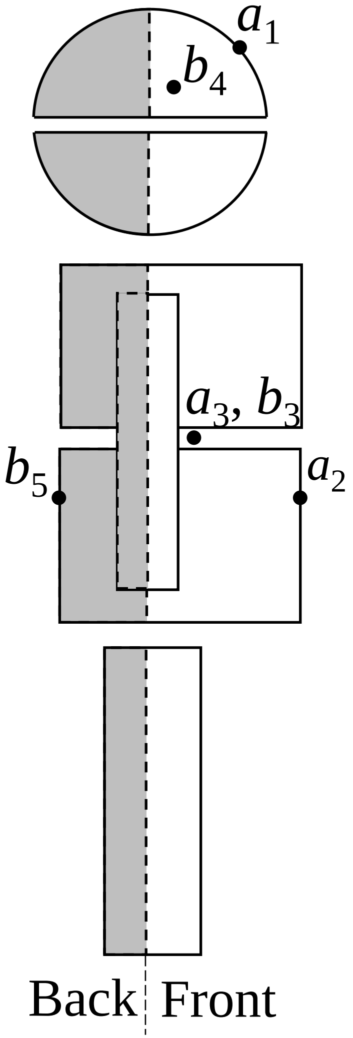
Other Body Elements


Radiant Warmer
Estimated
99% Confidence
Heat flux [Wm^-2]
Time [h]
Skin over head (Front)
Exact
Measurement
Estimated
99% Confidence
Temperature [°C]
Brain at r = 45 mm
Exact
Estimated
99% Confidence
Setpoint
Skin over abdomen (Front)
Exact
Measurement
Estimated
99% Confidence
Setpoint
Blood pool
Exact
Measurement
Estimated
99% Confidence
Setpoint

Results and Discussions: VERIFICATION

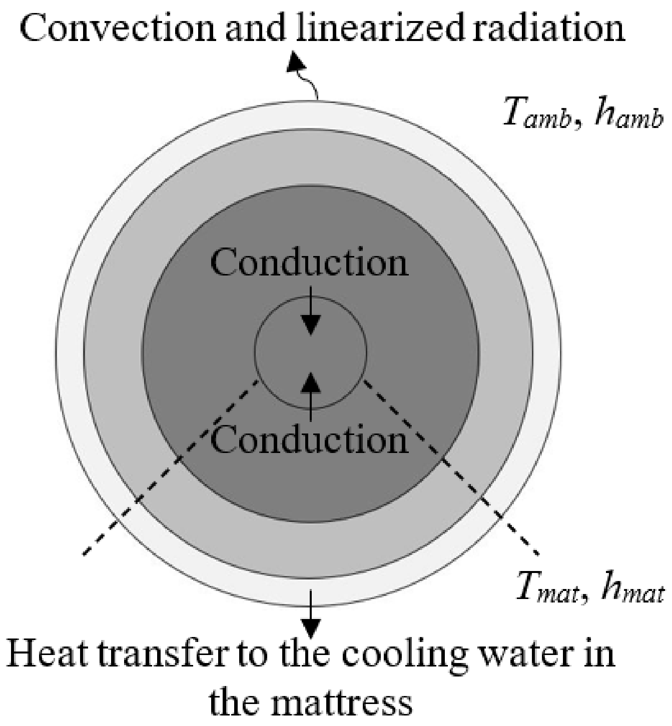
Stochastic Control of the State Variables with Simulated Measurements

Systemic Treatment: Heat transfer processes for the cooling and rewarming phases

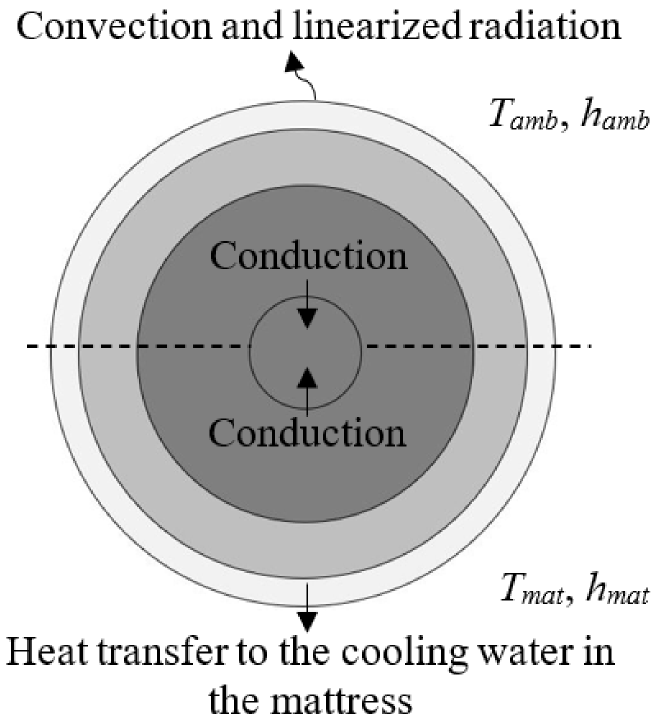


$$\mathbf{x}_{ctl} = [b_3; b_4; b_5]$$

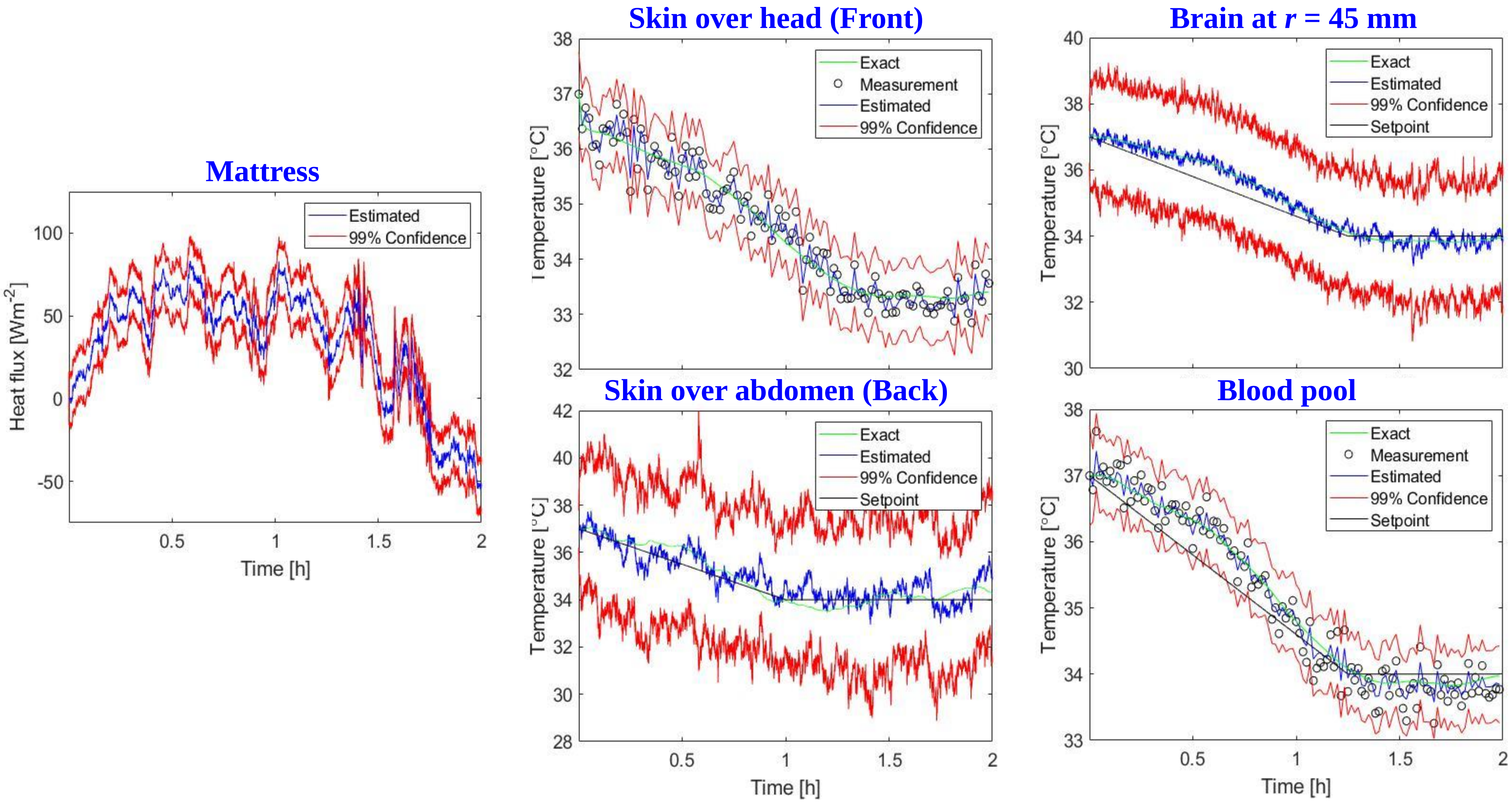
$$\mathbf{u} = [q_{mat}]$$



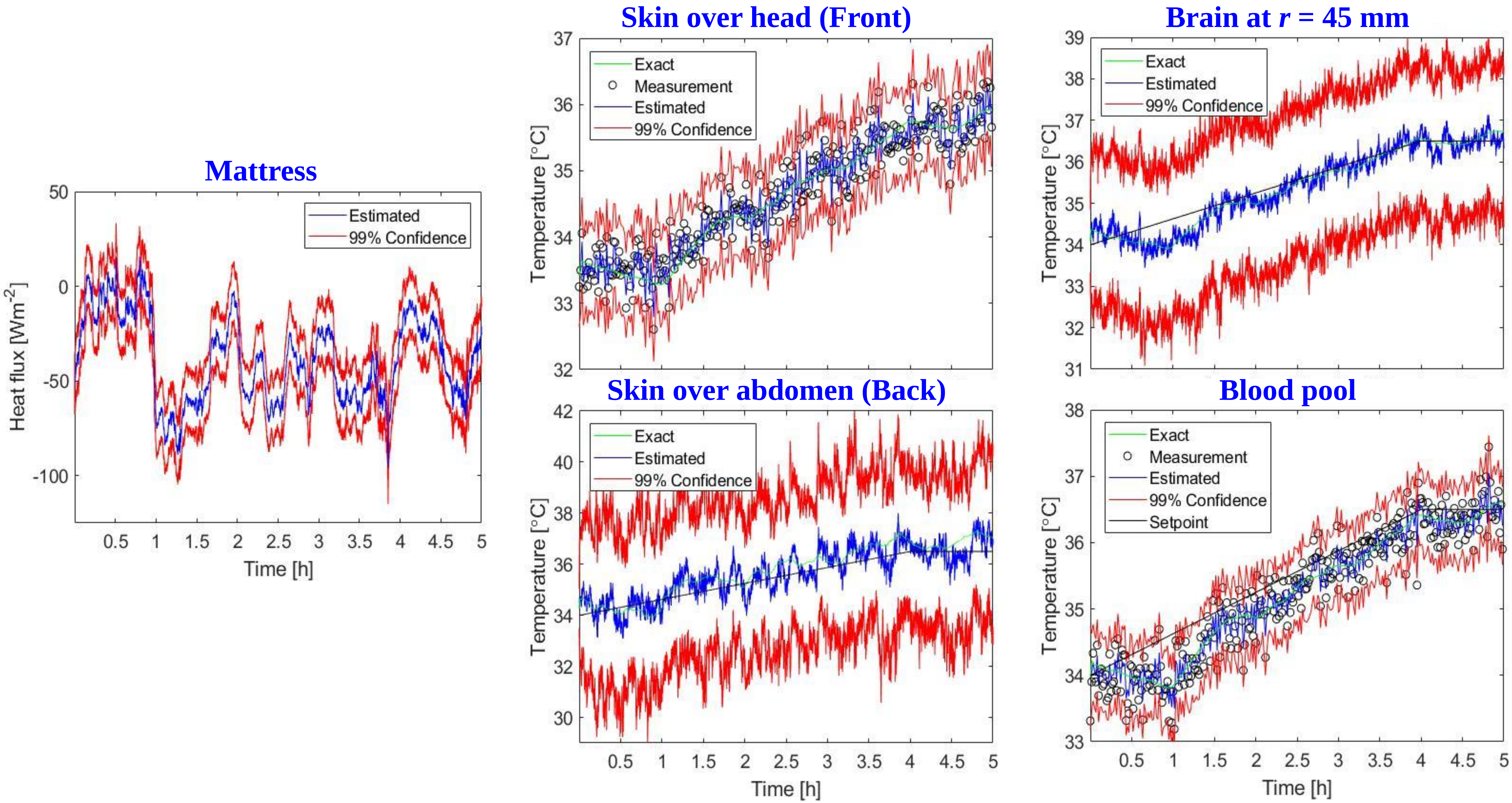
Upper Hemisphere of the Head



Other Body Elements



Mattress
Estimated
99% Confidence
Heat flux [Wm^-2]
Time [h]
Skin over head (Front)
Exact
Measurement
Estimated
99% Confidence
Temperature [°C]
Brain at r = 45 mm
Exact
Estimated
99% Confidence
Setpoint
Temperature [°C]
Skin over abdomen (Back)
Exact
Estimated
99% Confidence
Setpoint
Temperature [°C]
Time [h]
Blood pool
Exact
Measurement
Estimated
99% Confidence
Setpoint
Temperature [°C]
Time [h]



Mattress
Estimated
99% Confidence
Heat flux [Wm^{-2}]
Time [h]
Skin over head (Front)
Exact
Measurement
Estimated
99% Confidence
Temperature [°C]
Brain at r = 45 mm
Exact
Estimated
99% Confidence
Temperature [°C]
Skin over abdomen (Back)
Exact
Estimated
99% Confidence
Temperature [°C]
Time [h]
Blood pool
Exact
Measurement
Estimated
99% Confidence
Setpoint
Temperature [°C]
Time [h]

Results and Discussions: VALIDATION

Construction of the Geometric Model

Input Measurements: Mass, Length, Perimeter of the Head

Parameters: Diameter of the Trunk, Leg and Arm
Percentage of surface area of the Head, Trunk, Leg and Arm

Objective Function:

$$S_{OLS} = \left(BSA_{Model} - BSA_{Meban}\right)^2$$

where:

$$BSA_{Meban} = \left[6.4954\left(10^3 m\right)^{0.562}\left(10^2 L\right)^{0.320}\right]10^{-4}$$

BSA = Body surface area
$fBSA$ = *Fraction* of the body surface area

Results and Discussions: VALIDATION

Construction of the Geometric Model

Restrictions (Medical Data):

$$m_{model} = m_{meas}$$

$$L_{model} = L_{meas}$$

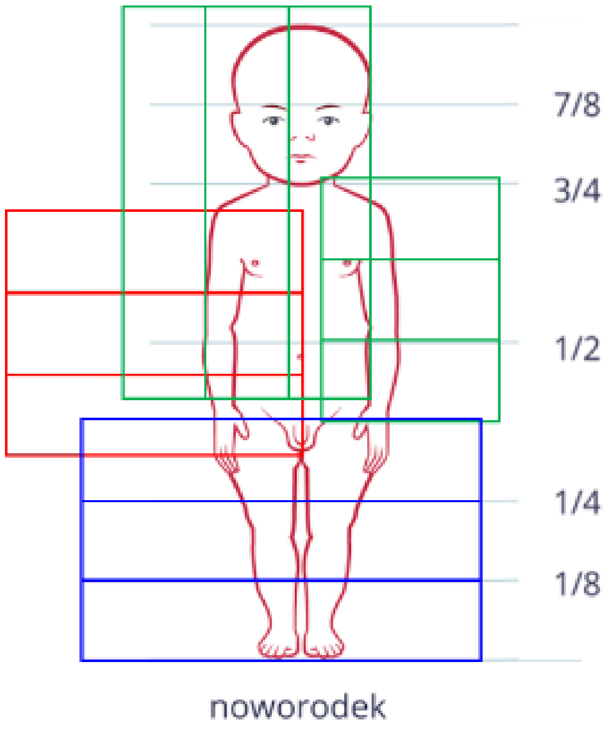
$$2\, d_{leg} \leq d_{trunk}$$

$$d_{arm} \leq d_{leg}$$

$$(P_{head} - 0.02) \leq P_{trunk}$$

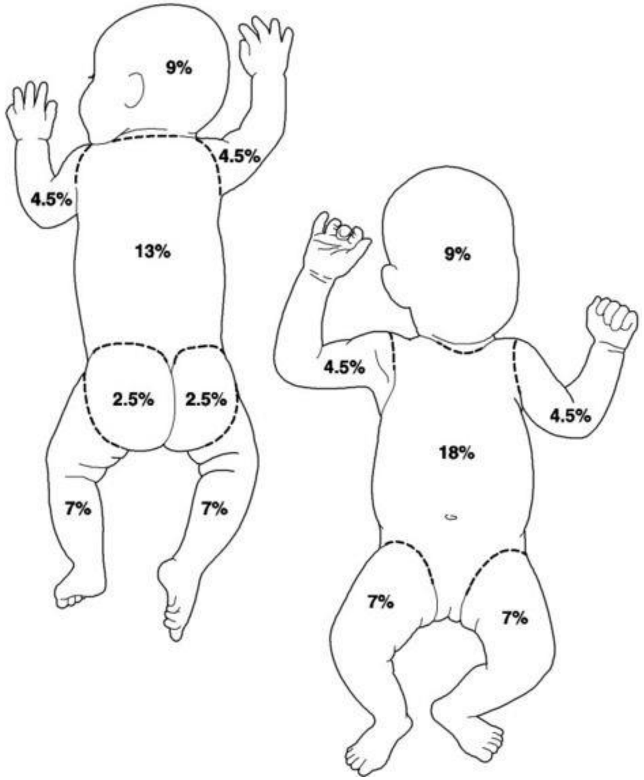
$$0.33 \leq fBSA_{trunk}$$

$$0.13 \leq fBSA_{leg}$$



Length of body elements
(CLEGG and MACKEAN, 1994)

Body measurements
(University Clinical Hospital in Opole)



Rule of Nines
(WALLACE, 1951)

Results and Discussions: VALIDATION

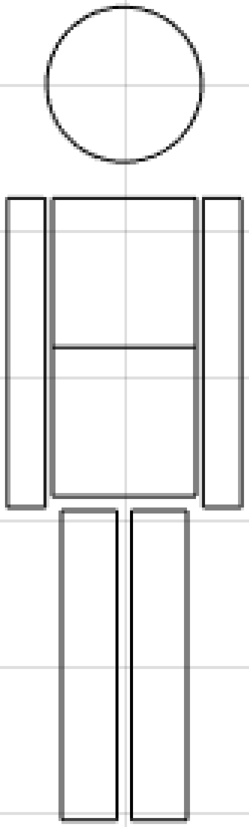
Construction of the Geometric Model

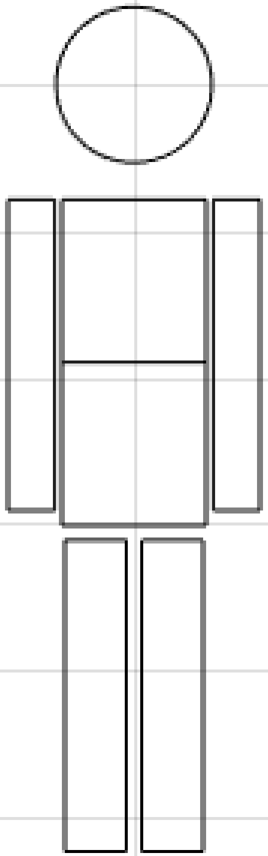
Patient Nº	Model									BSA Discrepancy [%]
	Mass [kg]	Diameter [m]				Length [m]			BSA_{Model} [m^2]	
		Head	Trunk	Leg	Arm	Trunk	Leg	Arm		
1	2.80	0.106	0.098	0.038	0.026	0.202	0.212	0.212	0.183	8.02
2	3.36	0.106	0.098	0.046	0.034	0.230	0.206	0.260	0.210	4.97
3	2.92	0.106	0.098	0.040	0.028	0.208	0.207	0.207	0.188	7.52
4	2.17	0.102	0.096	0.036	0.026	0.188	0.200	0.194	0.166	3.62
5	3.72	0.112	0.106	0.044	0.032	0.228	0.222	0.222	0.221	5.72
6	3.25	0.106	0.098	0.044	0.032	0.226	0.210	0.210	0.205	5.54
7	3.17	0.106	0.098	0.042	0.032	0.222	0.213	0.213	0.203	5.52

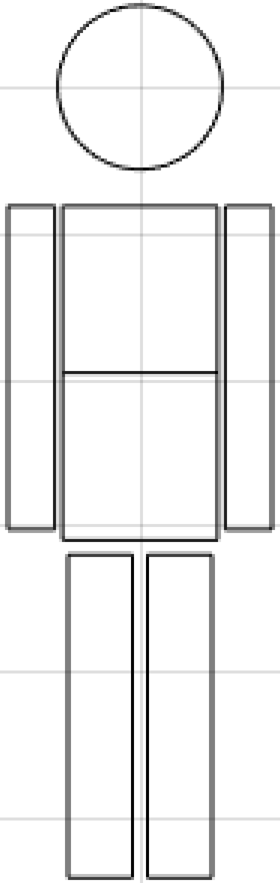
Results and Discussions: VALIDATION

Construction of the Geometric Model

Input	2.79 kg | 52 cm | 33 cm		3.13 kg | 54 cm | 33 cm		3.60 kg | 56 cm | 35 cm	
	Diam. (cm)	Len. (cm)	Diam. (cm)	Len. (cm)	Diam. (cm)	Len. (cm)
Head	10.6		10.6		11.2	
Trunk	9.8	20.2	9.8	22.2	10.6	22.8
Arm	2.6	21.2	3.2	21.3	3.2	22.2
Leg	3.8	21.2	4.2	21.3	4.4	22.2
BSA error	8.0%	Pat. 1	5.5%	Pat. 7	5.7%	Pat. 5







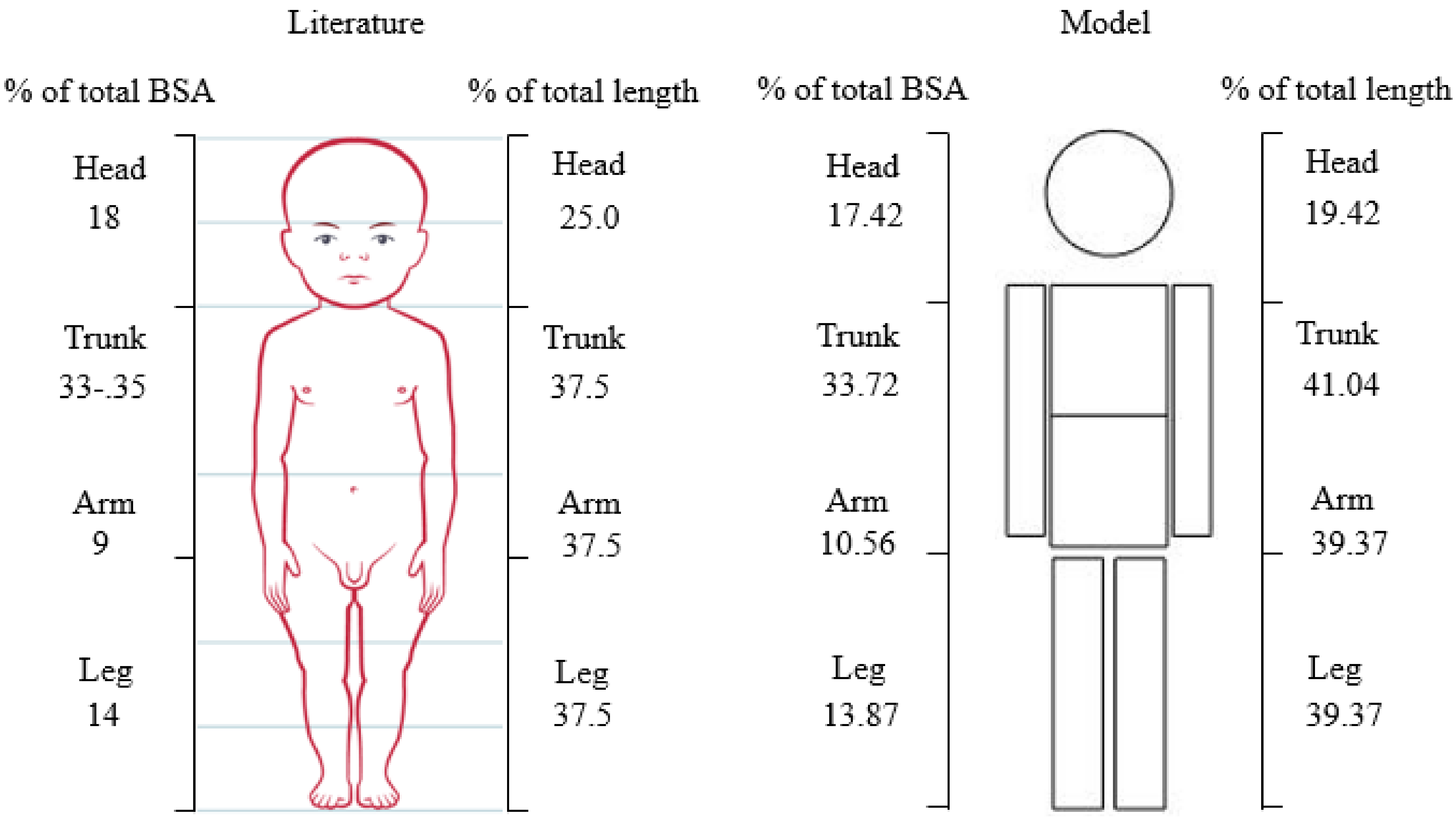
Results and Discussions: VALIDATION

Comparison With Data From Literature

	Surface area (%)				Length (%)			
	Head	Trunk	Leg	Arm	Head	Trunk	Leg	Arm
Literature	18.00	35.00	15.00	9.00	25.00	37.50	37.50	37.50
Patient 1	19.31	34.03	13.85	9.48	20.38	38.85	40.77	40.77
Patient 2	16.84	33.77	14.20	10.50	19.55	42.44	38.00	38.00
Patient 3	18.80	34.10	13.85	9.70	20.34	39.92	39.73	39.73
Patient 4	19.65	34.09	13.60	9.53	20.82	38.37	40.82	37.59
Patient 5	17.80	34.30	13.86	10.08	19.93	40.57	39.50	39.50
Patient 6	17.21	33.91	14.15	10.30	19.55	41.70	38.75	38.75
Patient 7	17.42	33.72	13.87	10.56	19.6	41.03	39.37	39.37

Results and Discussions: VALIDATION

Comparison With Data From Literature



Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

Evolution model:

$$\mathbf{x}_k = \begin{bmatrix} \mathbf{T}_k \\ \dot{Q}_{war,k} \end{bmatrix} = \begin{bmatrix} \mathbf{f}_k(\mathbf{x}_{k-1}, \mathbf{u}_{k-1}) + \mathbf{v}_k \\ -\dot{Q}_{gen,k-1} + \dot{Q}_{conv,k} + \dot{Q}_{rad,k} + \mathbf{v}_{war,k} \end{bmatrix}$$

Observation model:

$$\mathbf{z}_k = \mathbf{h}_k(\mathbf{x}_k) + \mathbf{n}_k$$

Noise:

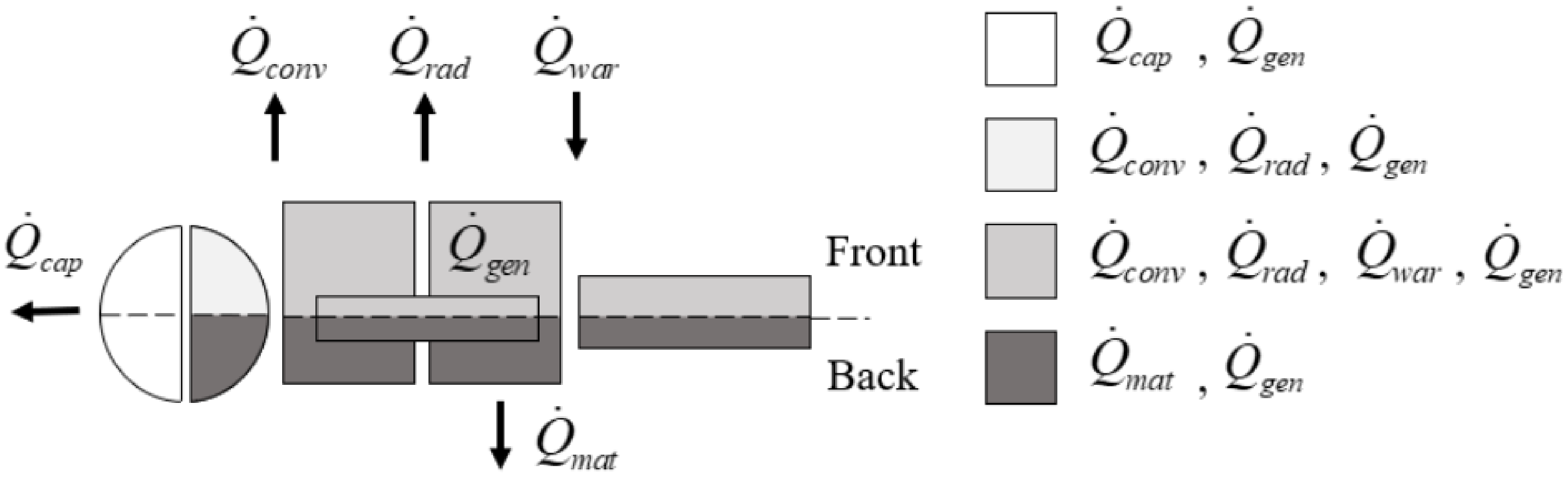
$$\mathbf{v}_k = N(0, \sigma_{mod})$$

$$\mathbf{v}_{war,k} = \dot{Q}_{cap,k} \sim \mathcal{U}\left(\dot{Q}_{cv2,k}, \dot{Q}_{cv1,k}\right)$$

$$\mathbf{n}_k = N(0, \sigma_{meas})$$

Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements



$$\dot{Q}_{mat,k} = 0$$

$$\dot{Q}_{gen,k} = \sum_{l=1}^{8}\sum_{s=1}^{2}\int_{V_{t,s,l}} g_{t,s,l}\, dV_{t,s,l}$$

$$\dot{Q}_{cap,k} \sim \mathcal{U}\left(\dot{Q}_{cv2,k}, \dot{Q}_{cv1,k}\right)$$

$$\dot{Q}_{conv,k} = h_{conv}\left(T_{sk,a_2} - T_{conv}\right)A_{act}$$

$$\dot{Q}_{rad,k} = \varepsilon\beta\left(T_{sk,a_2}^4 - T_{rad}^4\right)A_{act}$$

$$\dot{Q}_{war,k} = -\dot{Q}_{gen,k} + \dot{Q}_{conv,k} + \dot{Q}_{rad,k} + \dot{Q}_{cap,k}$$

Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

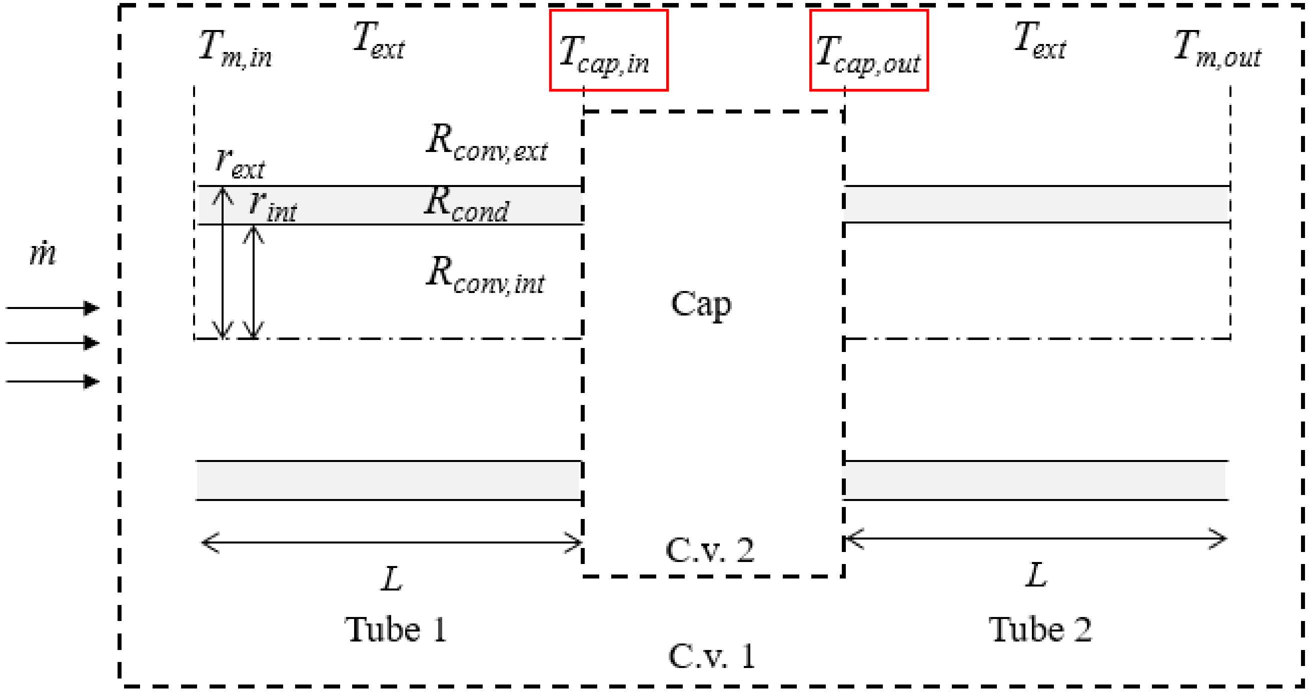
Noise of the random walk function:

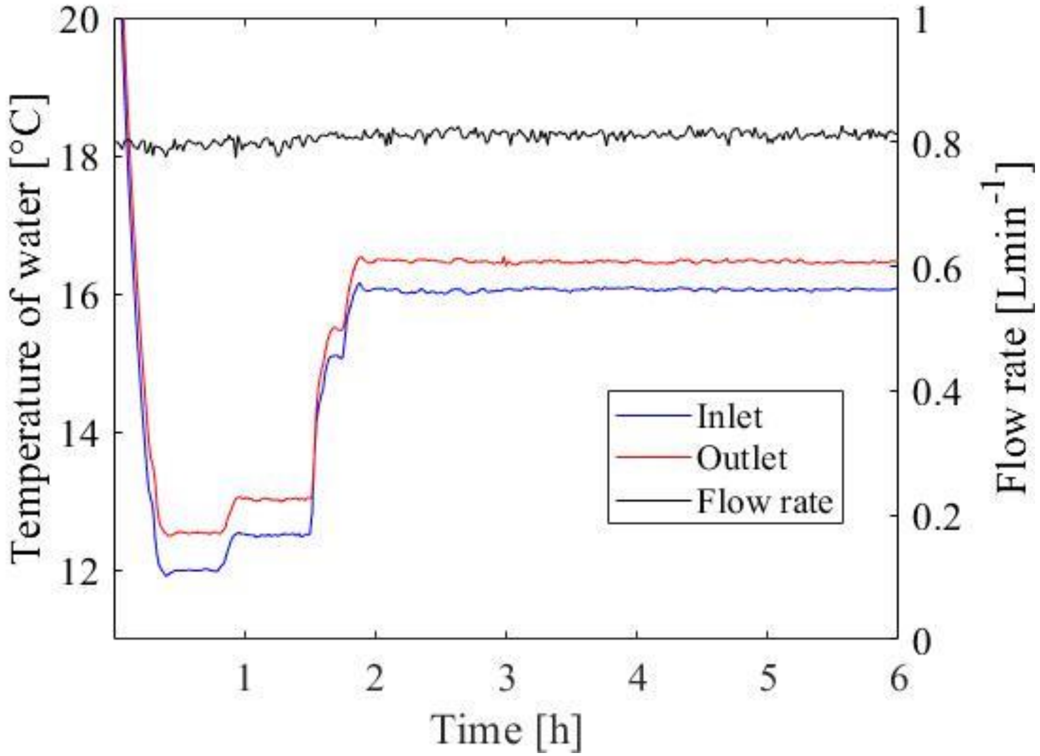
$$\mathbf{v}_{war,k} = \dot{Q}_{cap,k} \sim \mathcal{U}\left(\dot{Q}_{cv2,k}, \dot{Q}_{cv1,k}\right)$$

Heat transfer rate:

$$\dot{Q}_{cv1,k} = \dot{m}c_p\left(T_{m,out} - T_{m,in}\right) = UA_{ext}\left(\Delta T_{\ln 1} + \Delta T_{\ln 2}\right) + \dot{Q}_{cv2,k}$$

$$\dot{Q}_{cv2,k} = \dot{m}c_p\left(T_{cap,out} - T_{cap,in}\right)$$





Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

Noise of the random walk function:

$$\mathbf{v}_{war,k} = \dot{Q}_{cap,k} \sim \mathcal{U}\left(\dot{Q}_{cv2,k}, \dot{Q}_{cv1,k}\right)$$

Heat transfer rates:

$$\dot{Q}_{cv1,k} = \dot{m}c_p\left(T_{m,out} - T_{m,in}\right) = UA_{ext}\left(\Delta T_{\ln 1} + \Delta T_{\ln 2}\right) + \dot{Q}_{cv2,k}$$

$$\dot{Q}_{cv2,k} = \dot{m}c_p\left(T_{cap,out} - T_{cap,in}\right)$$

Expressions to calculate the temperatures of the cooling cap:

$$\left(T_{ext} - T_{cap,in}\right) = \left(T_{ext} - T_{m,in}\right)\exp\left(\frac{-U\pi d_{ext}L}{\dot{m}c_p}\right)$$

$$\left(T_{ext} - T_{m,out}\right) = \left(T_{ext} - T_{cap,out}\right)\exp\left(\frac{-U\pi d_{ext}L}{\dot{m}c_p}\right)$$

Global heat transfer coefficient:

$$U = \frac{1}{(R_{conv,int} + R_{cond} + R_{conv,ext})A_{ext}}$$

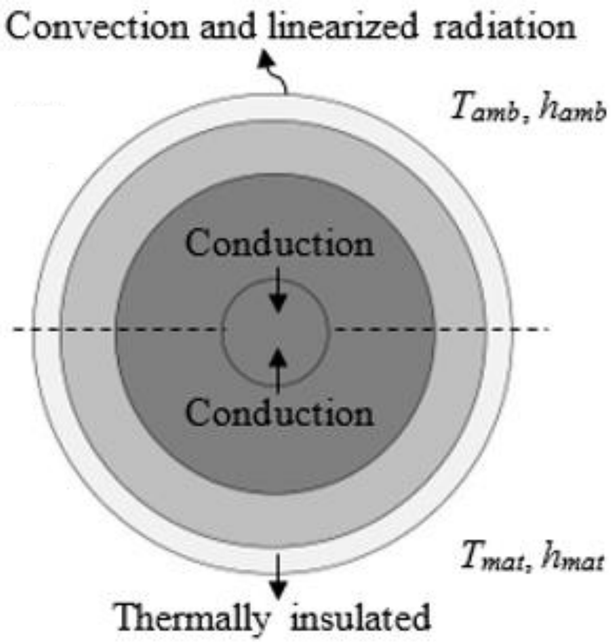
Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

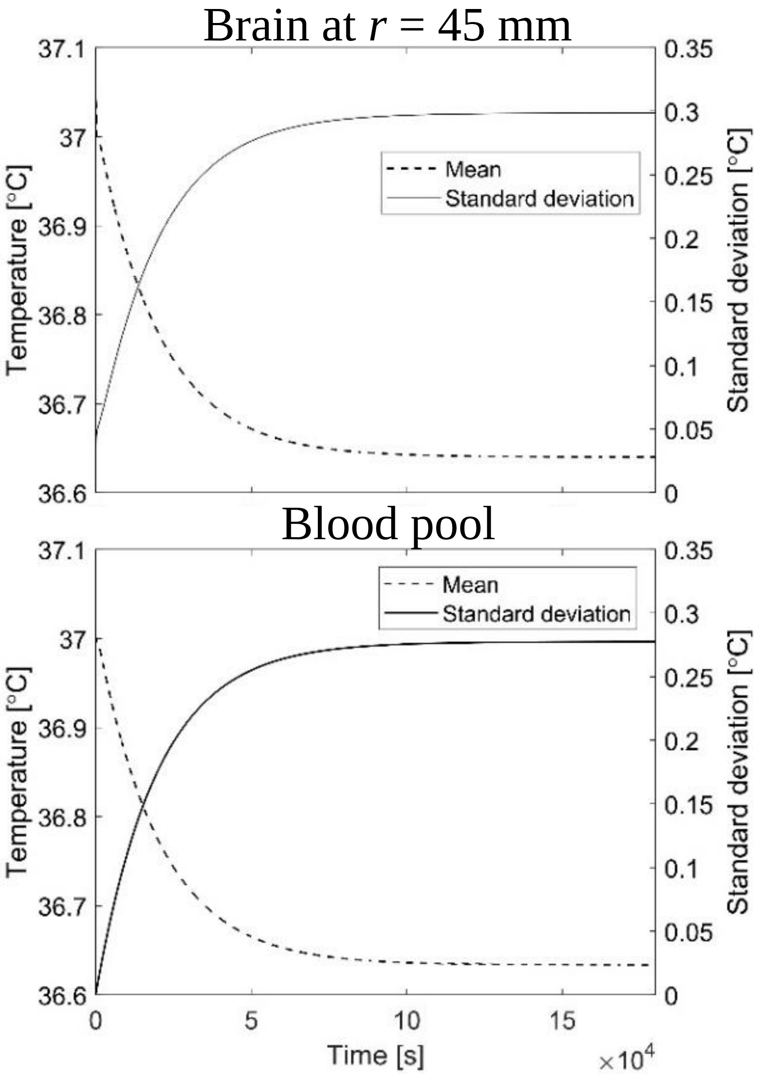
Monte Carlo Simulation for the Uncertainties of the Evolution Model for the Temperatures

- 10000 solutions of the direct problem
- Standard deviation of 1% of the values of the diameters and lengths of each body element

T_0 = 37°C | T_{amb} = 23.5°C | h_{amb} = 8 W/m^{2}K



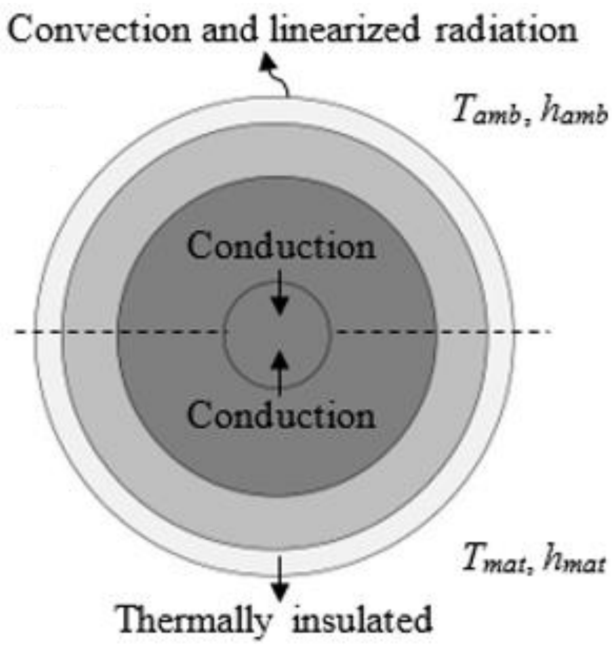
Body Elements



Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

Initial Temperature Distribution: Hypoxic-ischemic condition



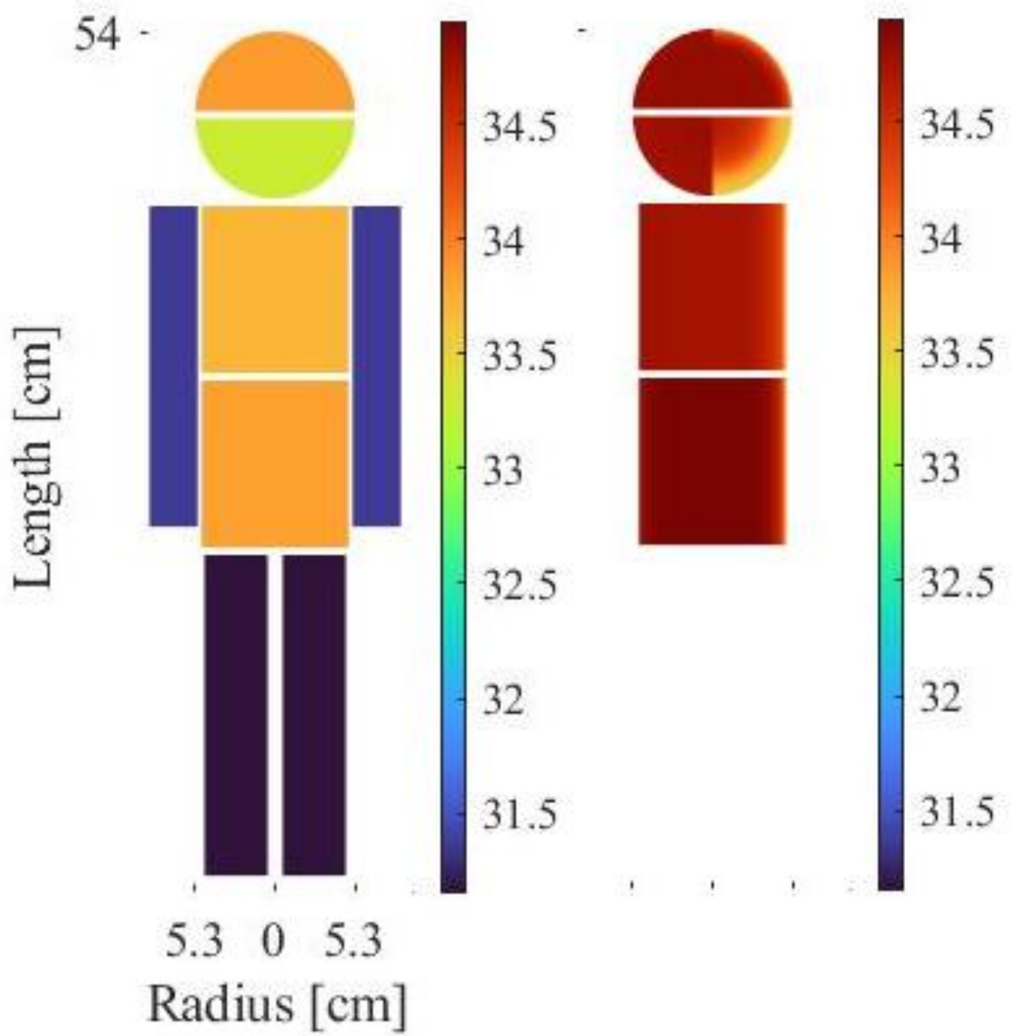
Body Elements

$T_0 = 37°C$

$T_{amb} = 23.5°C$

$h_{amb} = 8\ W/m^2K$

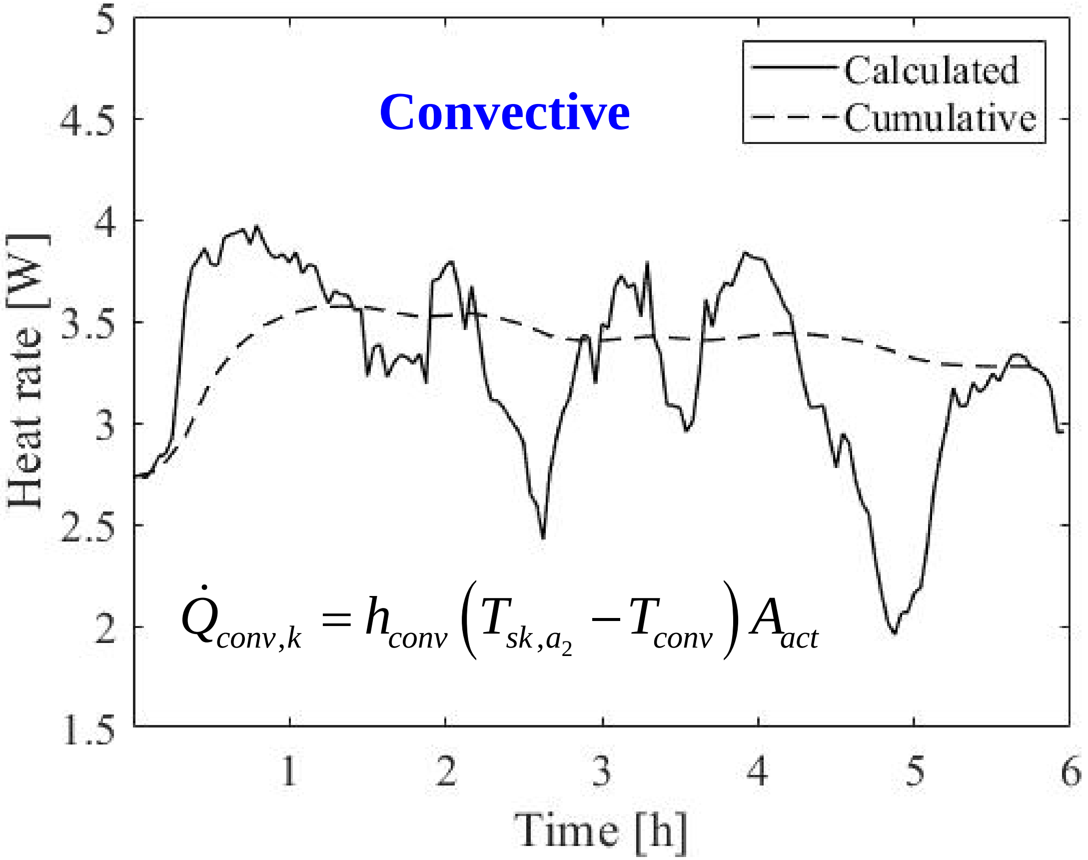
$$g_{brain} = 0.95 g_{brain}^{bas} Q_{10}^{\frac{T_{t,s,l} - T_0}{10}}$$

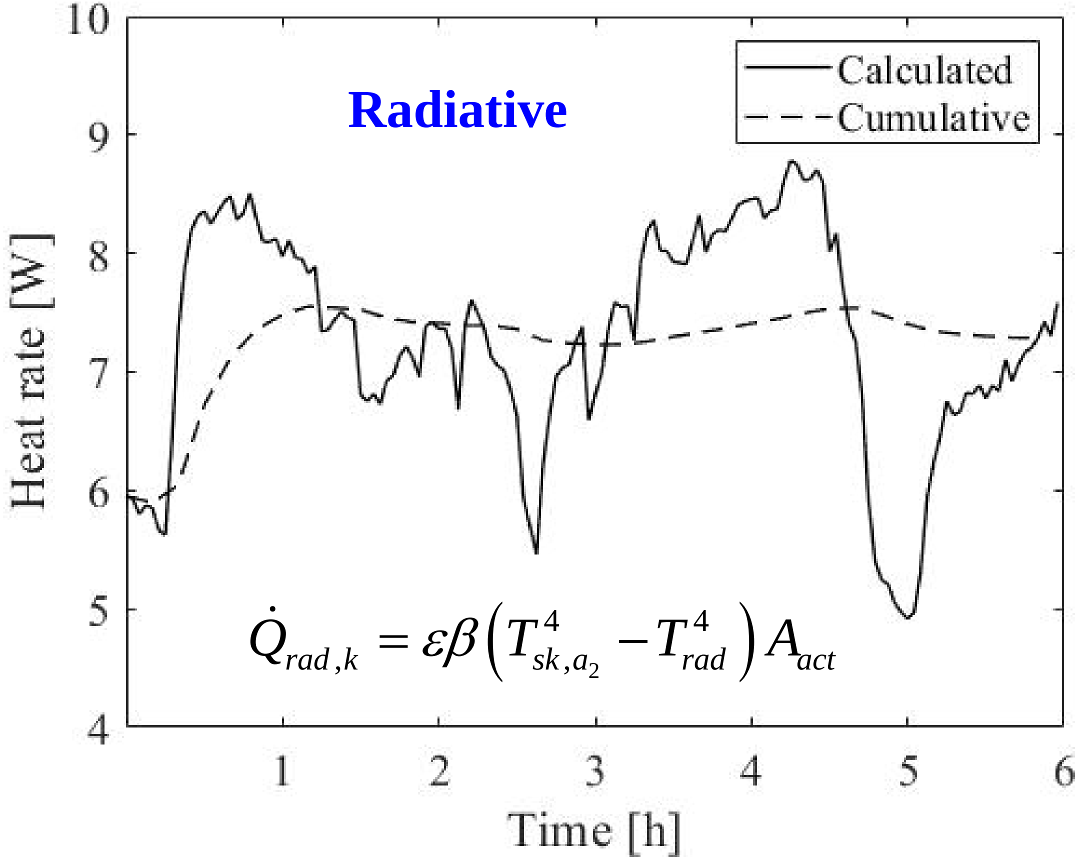


Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

Local Cooling: Estimated heat rates



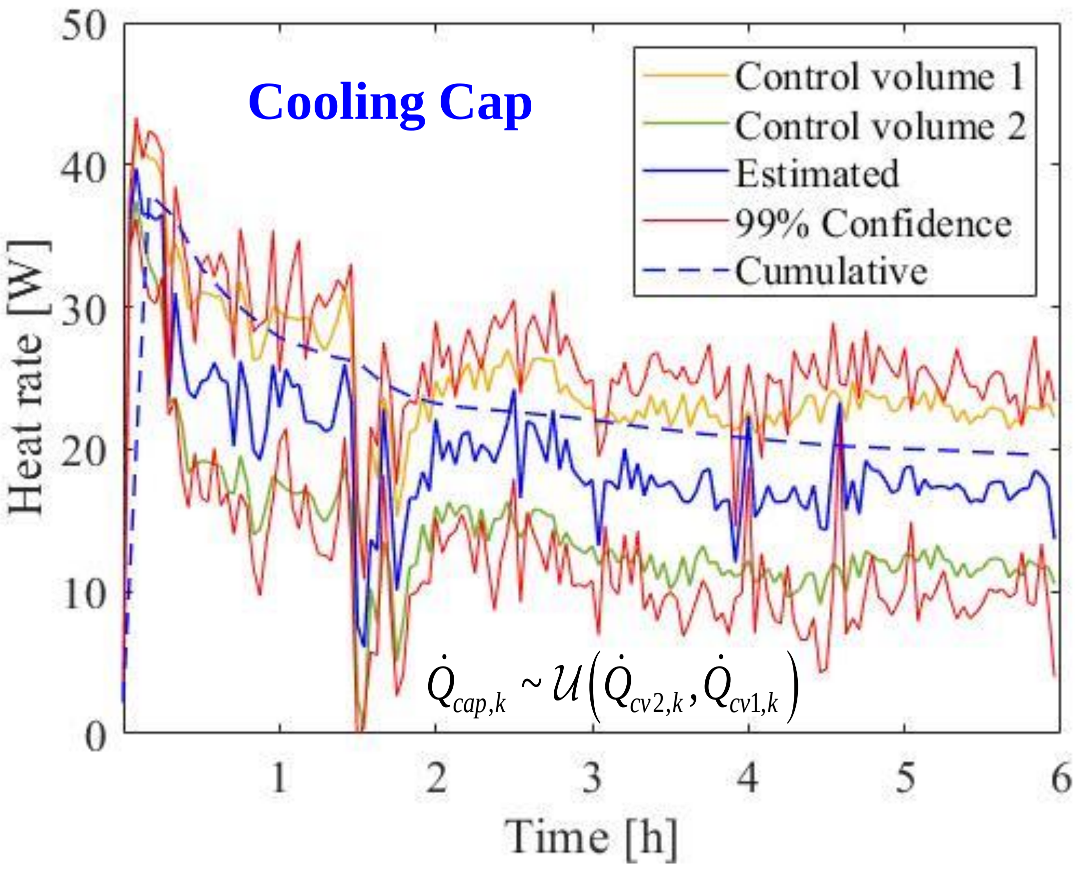


Results and Discussions: VALIDATION

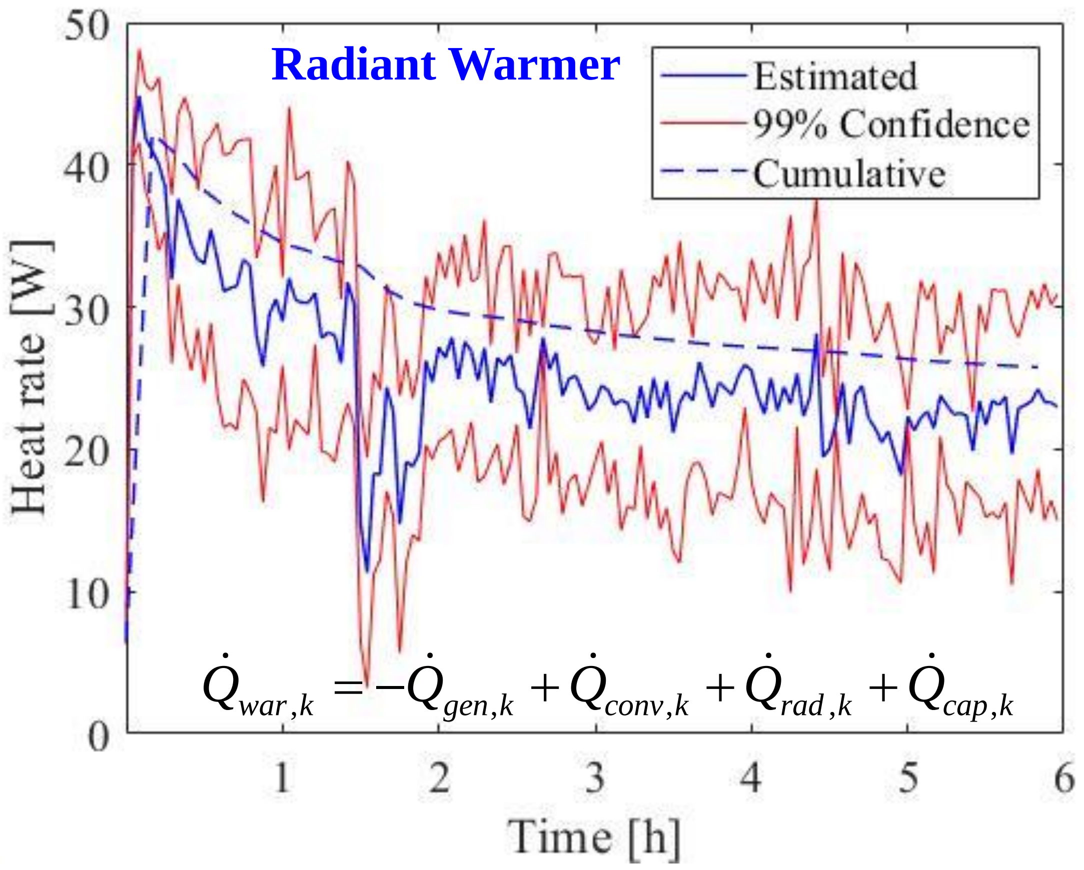
State Estimation Using Actual Temperature Measurements

Local Cooling: Estimated heat rates

Measured temperatures: Blood pool, skins of the head and abdomen.



$$\dot{Q}_{cap,k} \sim \mathcal{U}\left(\dot{Q}_{cv2,k}, \dot{Q}_{cv1,k}\right)$$



$$\dot{Q}_{war,k} = -\dot{Q}_{gen,k} + \dot{Q}_{conv,k} + \dot{Q}_{rad,k} + \dot{Q}_{cap,k}$$

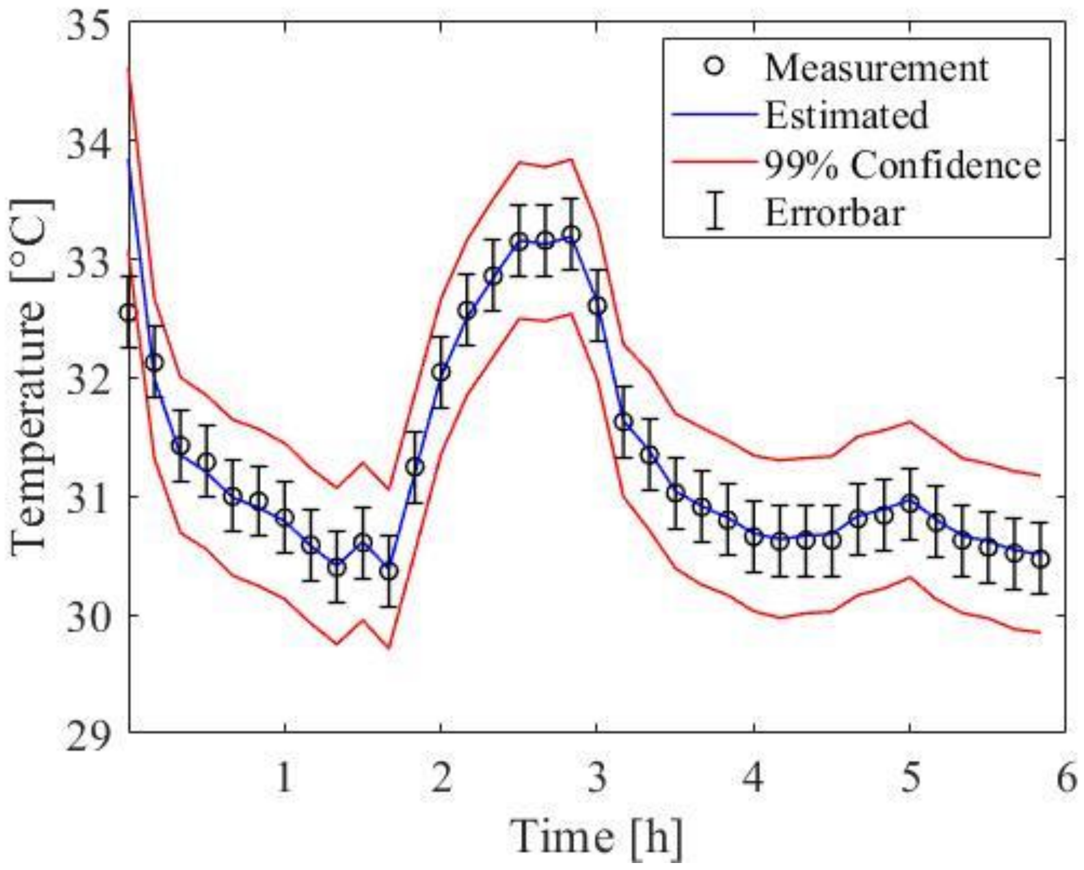
Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

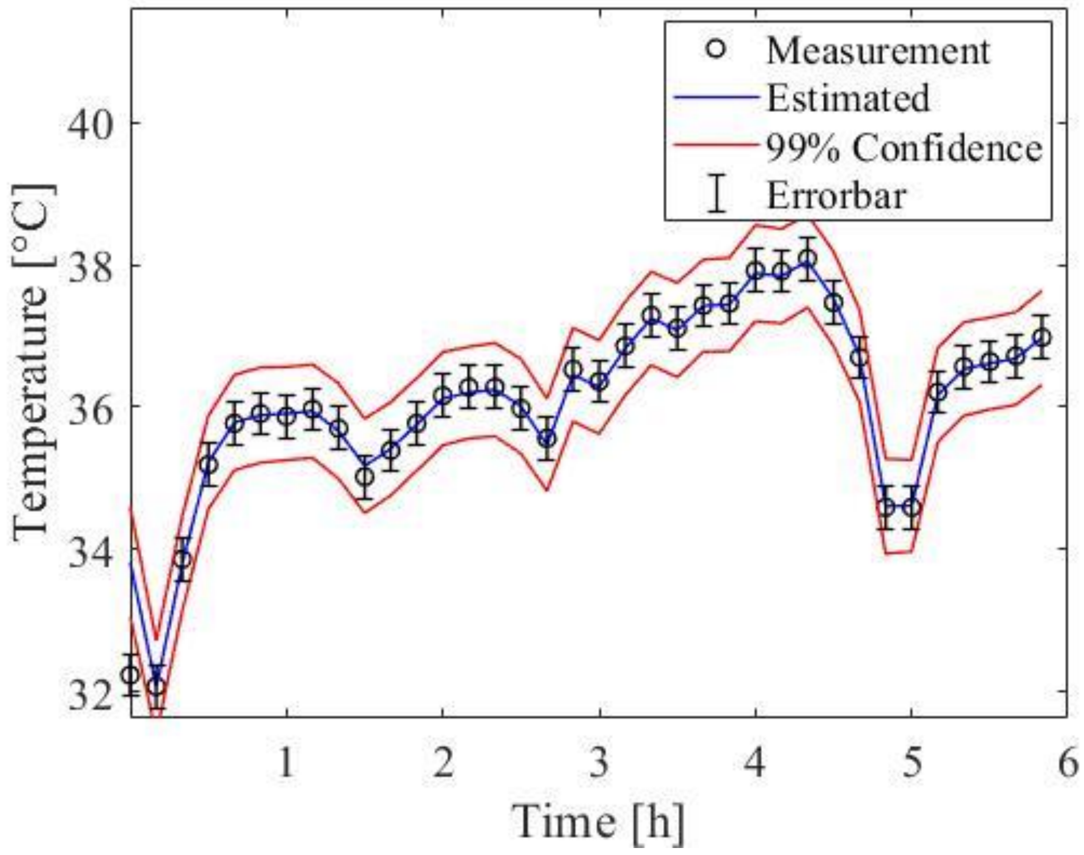
Local Cooling: Estimated temperatures

Measured temperatures: Blood pool, skins of the head and abdomen.

Skin over the head (Front)



Skin over the abdomen (Front)



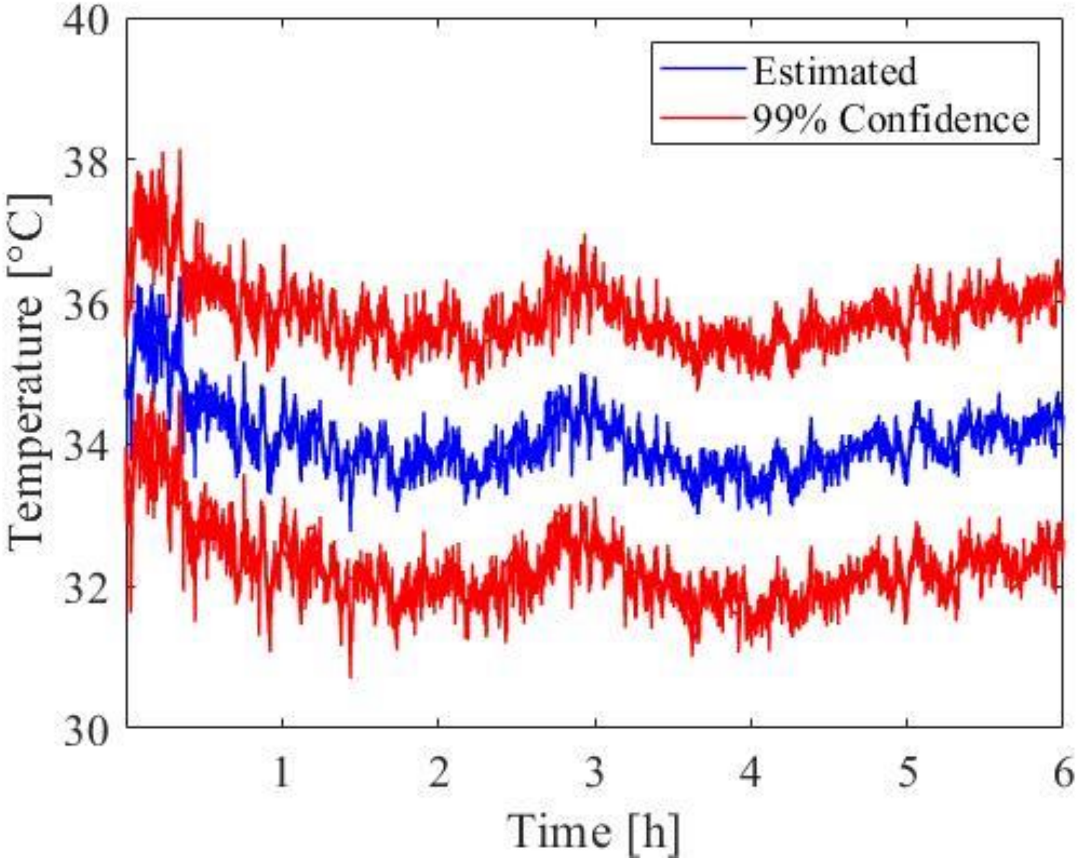
Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

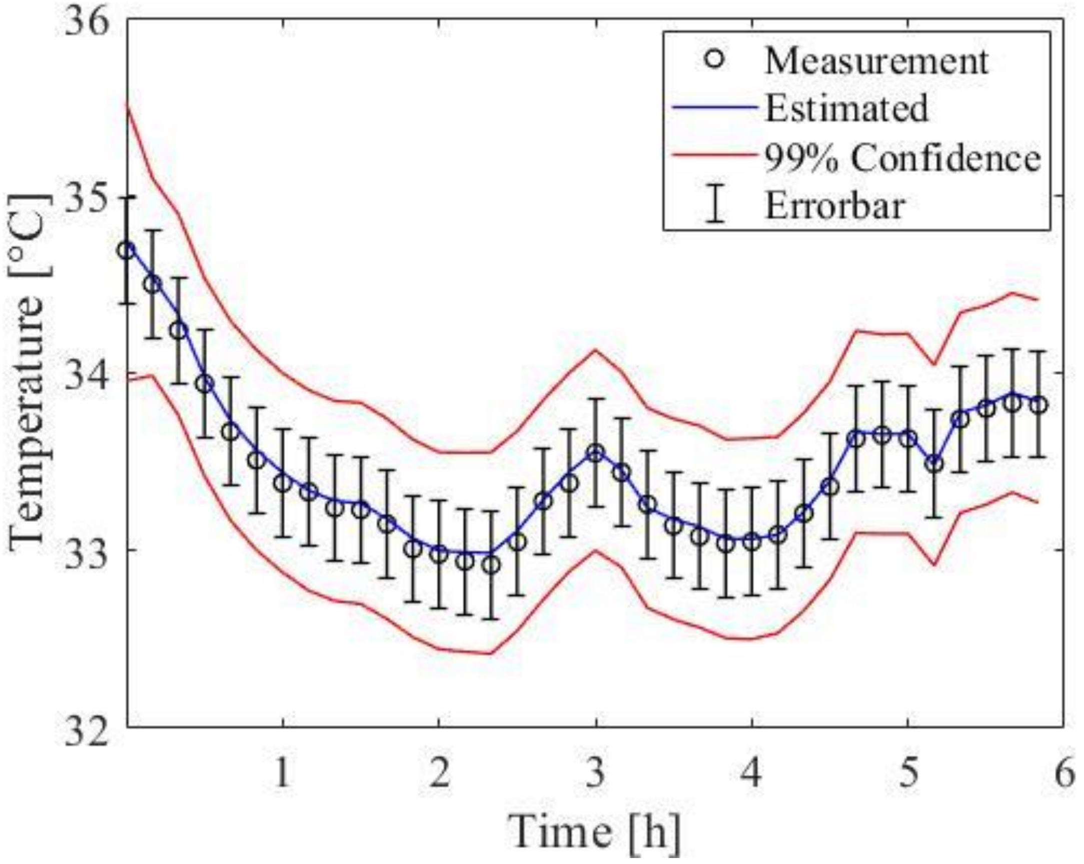
Local Cooling: Estimated temperatures

Measured temperatures: Blood pool, skins of the head and abdomen.

Brain at *r* = 45 mm



Blood pool

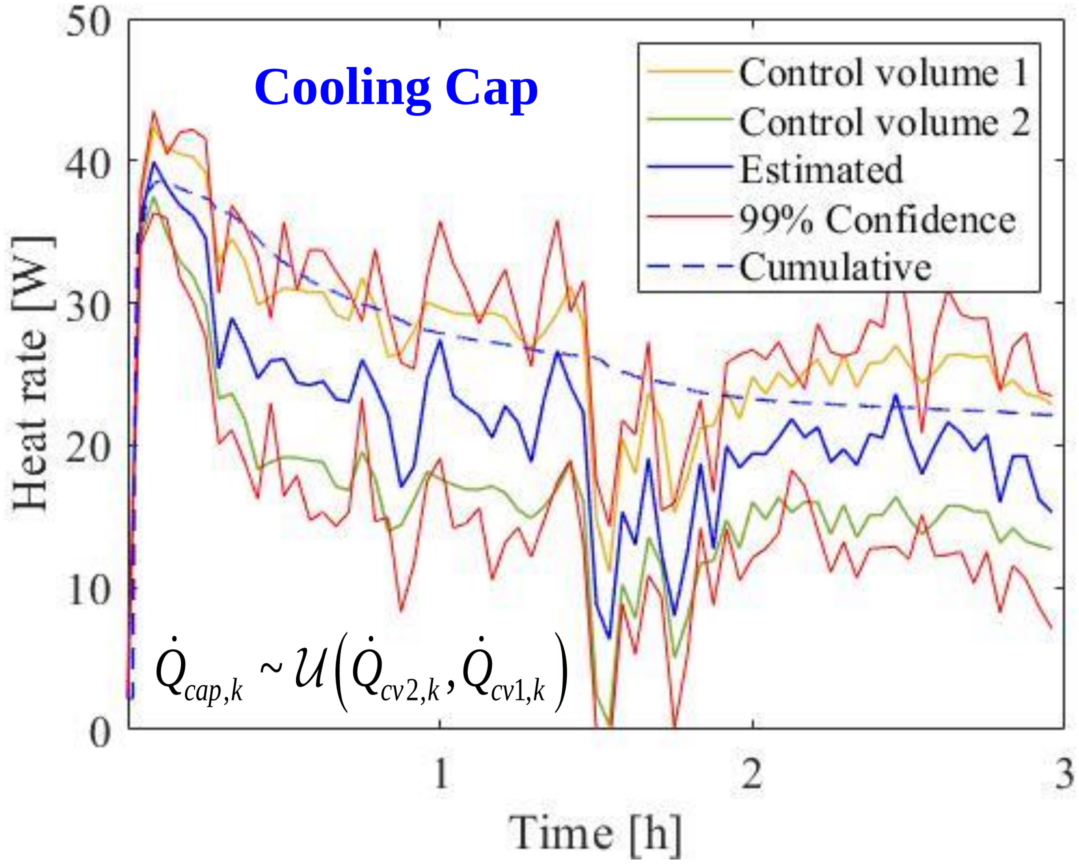


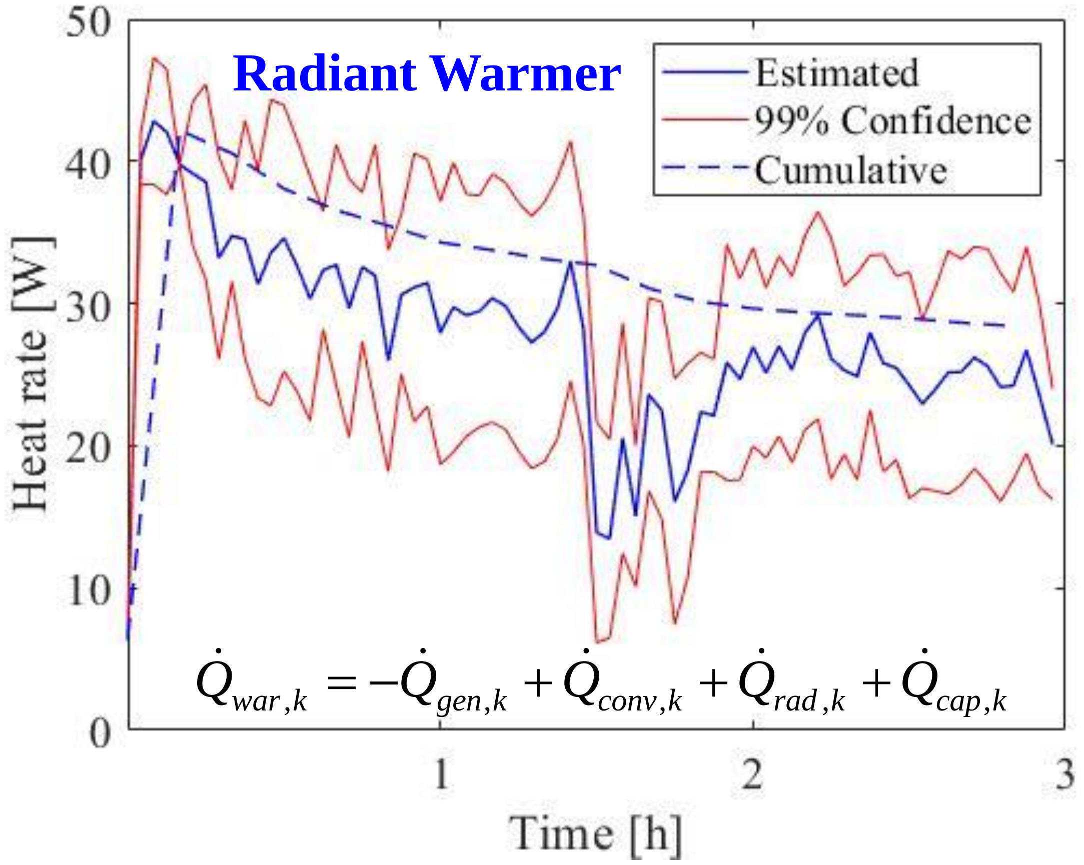
Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

Local Cooling: Estimated heat rates

Measured temperatures: Blood pool and skin of the head ~~and abdomen.~~



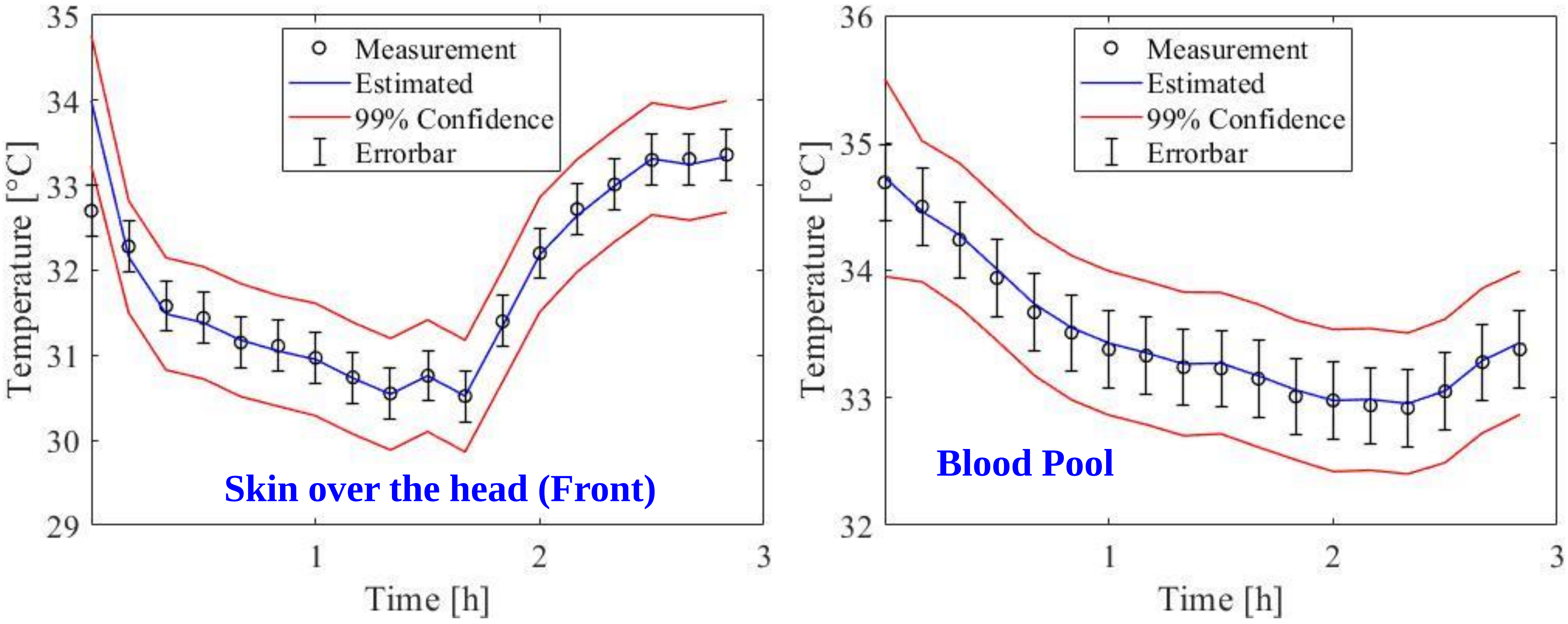


Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

Local Cooling: Estimated temperatures

Measured temperatures: Blood pool and skin of the head ~~and abdomen.~~

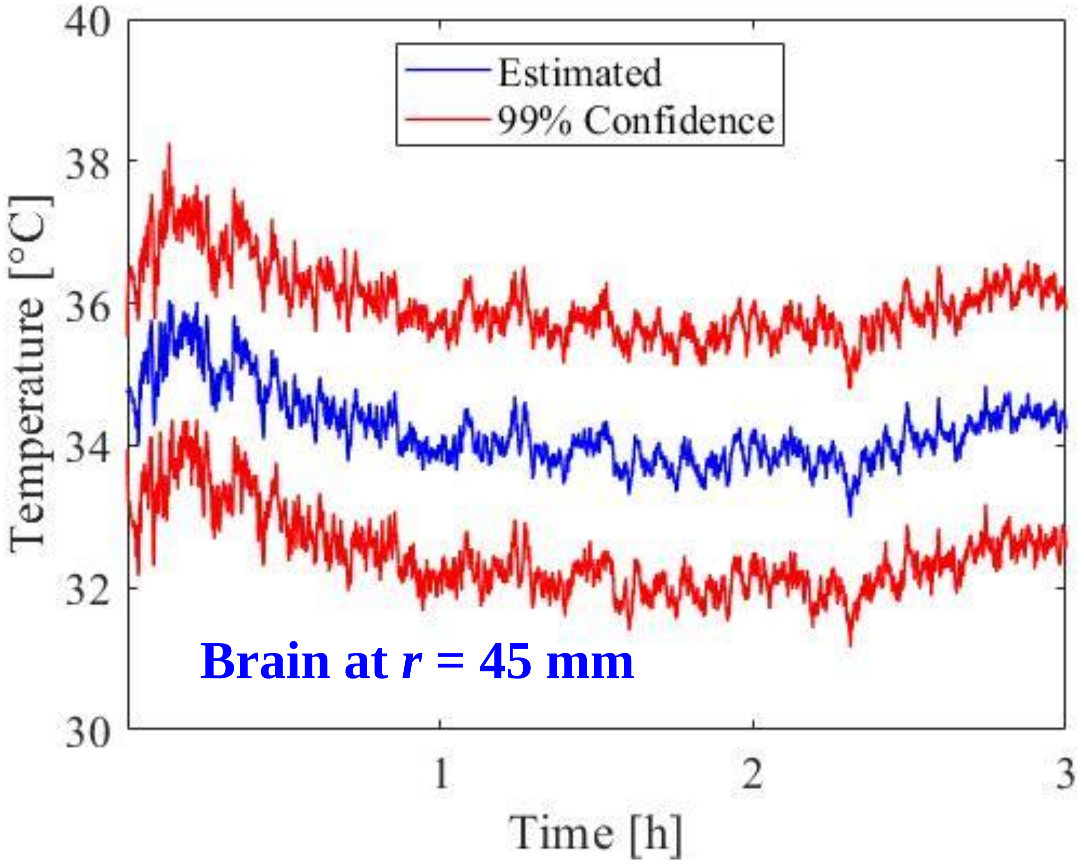


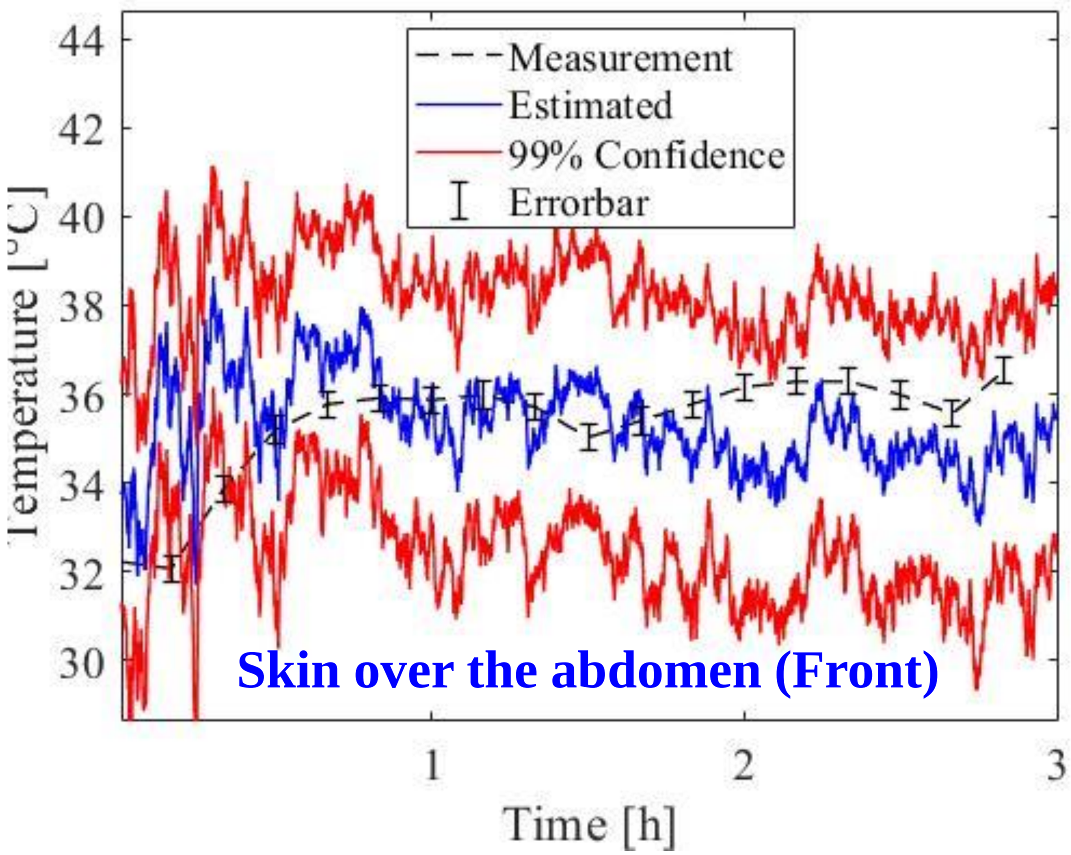
Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

Local Cooling: Estimated temperatures

Measured temperatures: Blood pool and skin of the head ~~and abdomen.~~

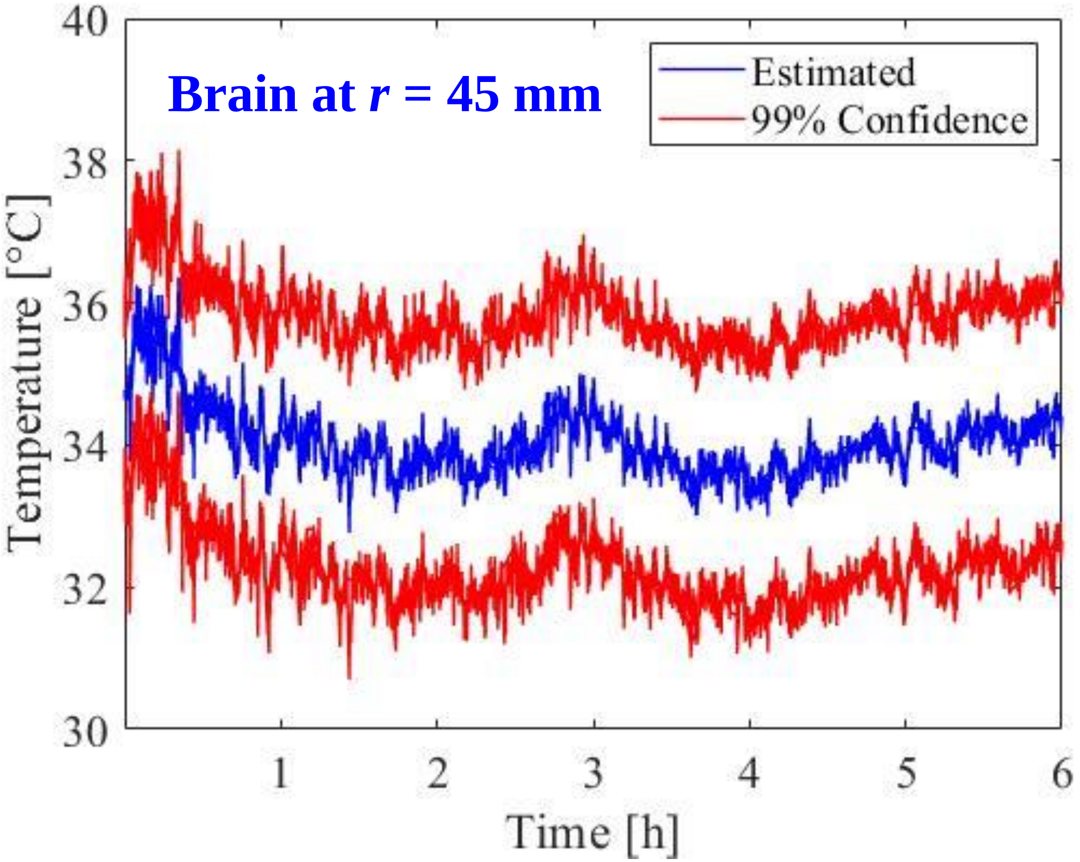




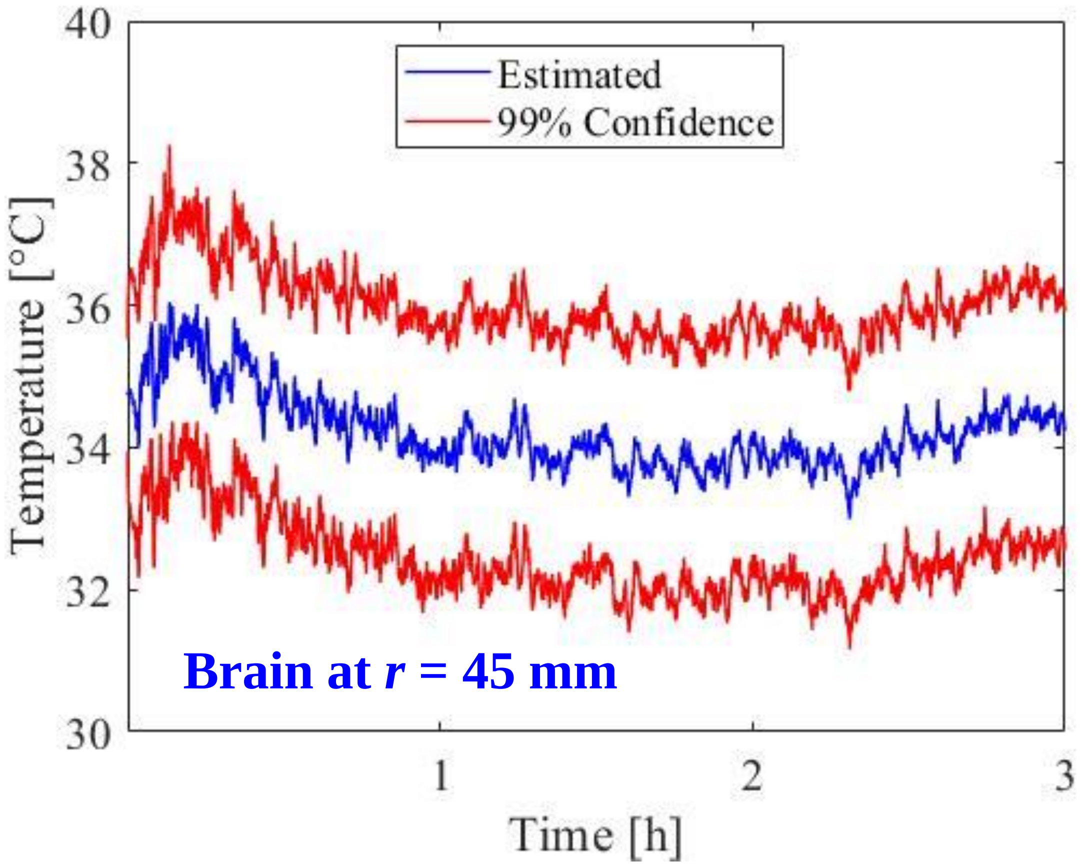
Results and Discussions: VALIDATION

State Estimation Using Actual Temperature Measurements

Measured temperatures: Blood pool, skins of the head and abdomen.



Measured temperatures: Blood pool and skin of the head ~~and abdomen.~~



Conclusions

1. Geometrical Model

- The optimization procedure to build the geometric model was able to produce realistic dimensions for the body elements.
- The mean error between the total surface area calculated with the model and with Meban’s equation was 5.8%.

2. State Estimation Problem Using Simulated Measurements

- The SIR algorithm produced accurate and stable estimated temperatures not only in regions where measurements were available but in the whole body.
- Estimated uncertainties were larger where measurements were not available, since the likelihood function did not contribute significantly.
- The solution was not influenced by the cooling technique.
- Uncertainties from direct Monte Carlo simulations were much larger than those obtained with the particle filter.

Conclusions

3. State Estimation and Model Predictive Control

- The application of two nested particle filters for stochastic control of the body temperatures was able to drive the temperatures of body to the desired setpoints at all phases of the treatment and to avoid undesired temperature variations.
- The combined application of particle filters and stochastic model predictive control, using the SIR algorithm, has great potential to act as an observer and controller of the body temperatures.

4. State Estimation Problem Using Actual Measurements

- Estimated temperatures in excellent agreement with the actual measurements, even during large temperature variations.
- For important internal regions of the body, such as in the brain and in the blood pool, estimated mean temperatures and associated uncertainties were stable (and within the measurement uncertainties, wherever available).
- The application of the SIR algorithm was successfully validated by using temperature measurements of the skin over the abdomen.

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