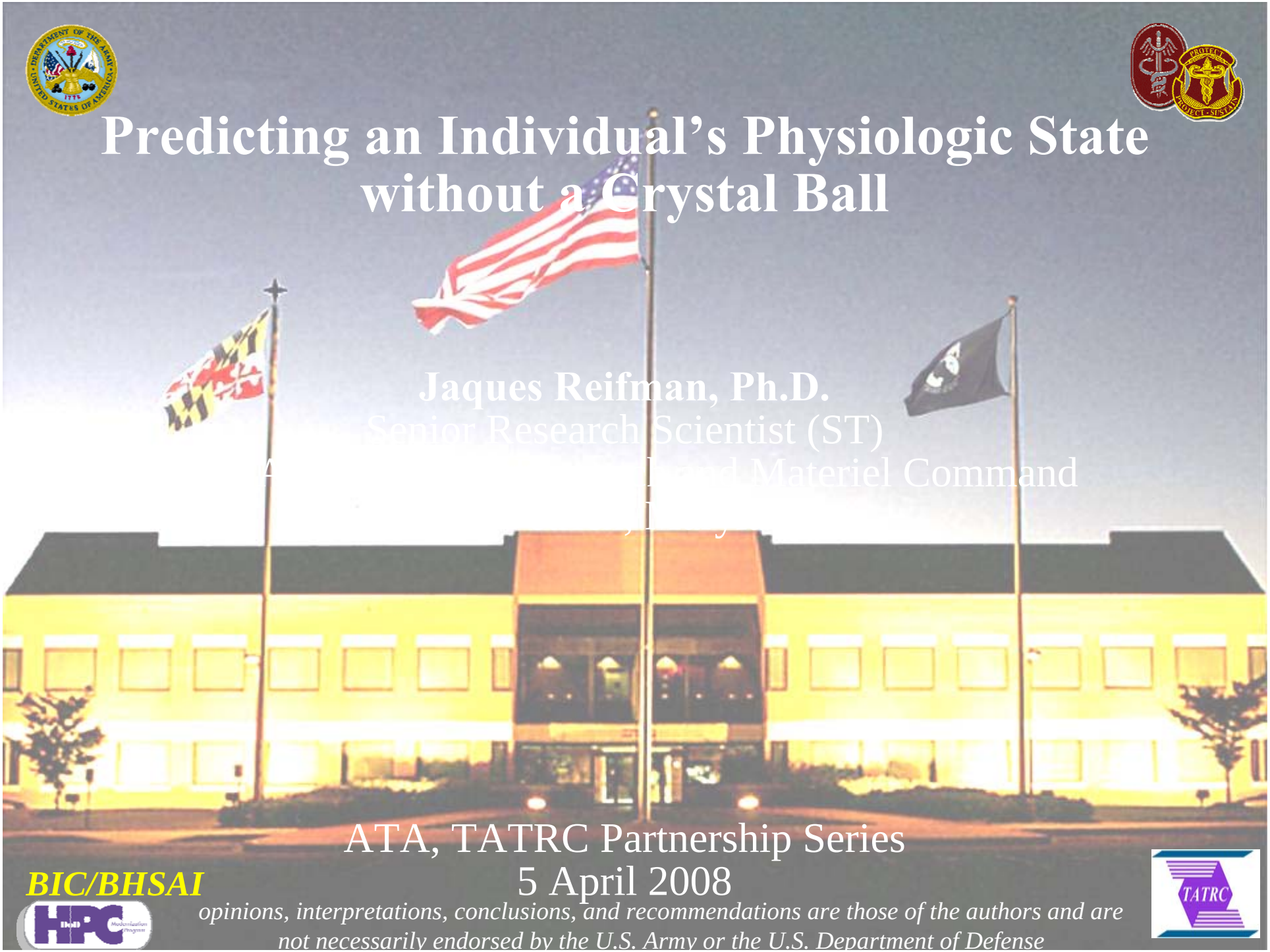

Predicting an Individual's Physiologic State without a Crystal Ball

Jaques Reifman, Ph.D.
Senior Research Scientist (ST)
[illegible] and Materiel Command

ATA, TATRC Partnership Series
5 April 2008

BIC/BHSAI

opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the U.S. Army or the U.S. Department of Defense

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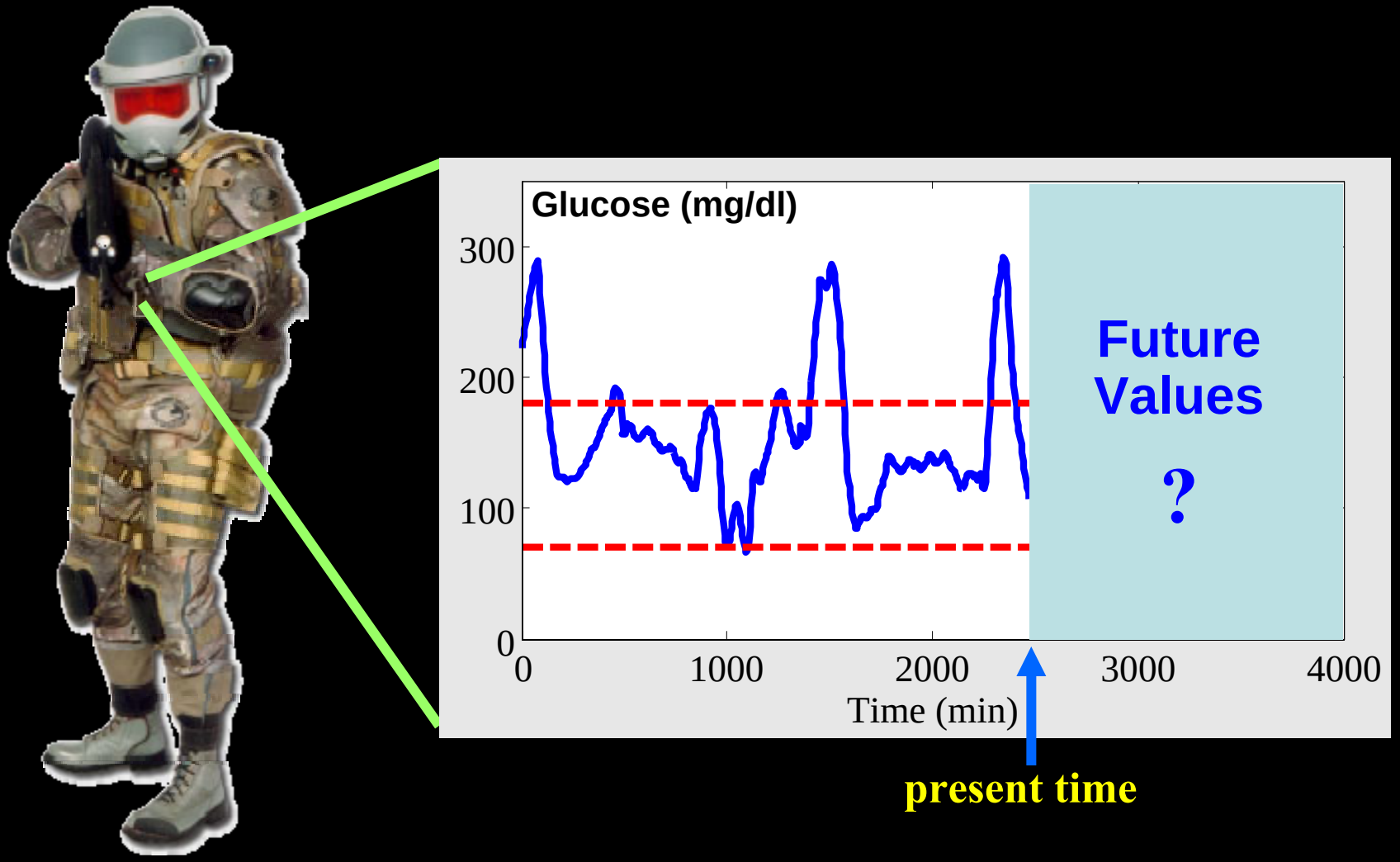
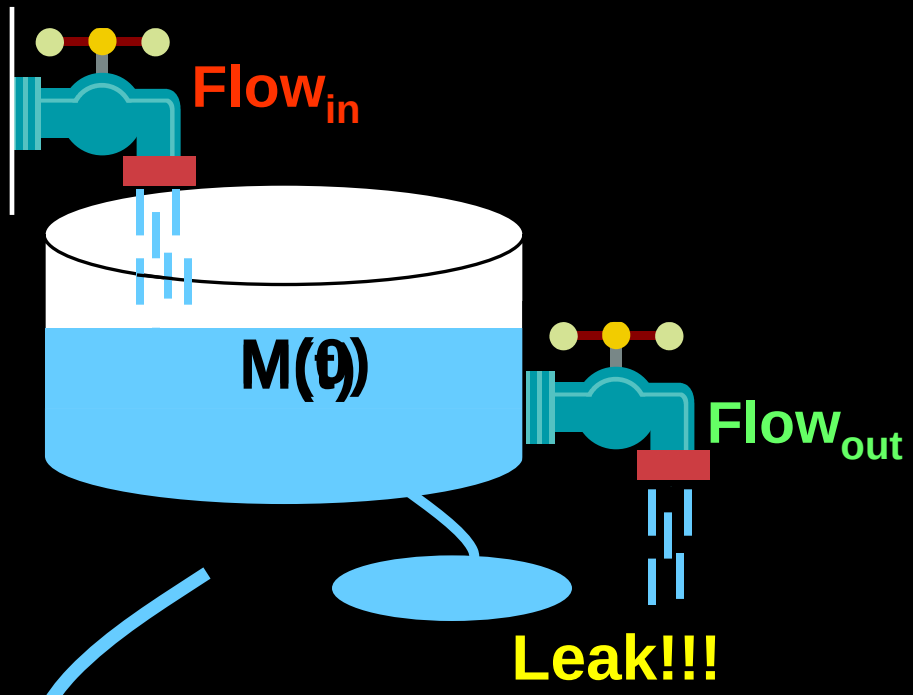
Knowing the Past is Good, but Knowing the Future is even Better: Predictive Models!

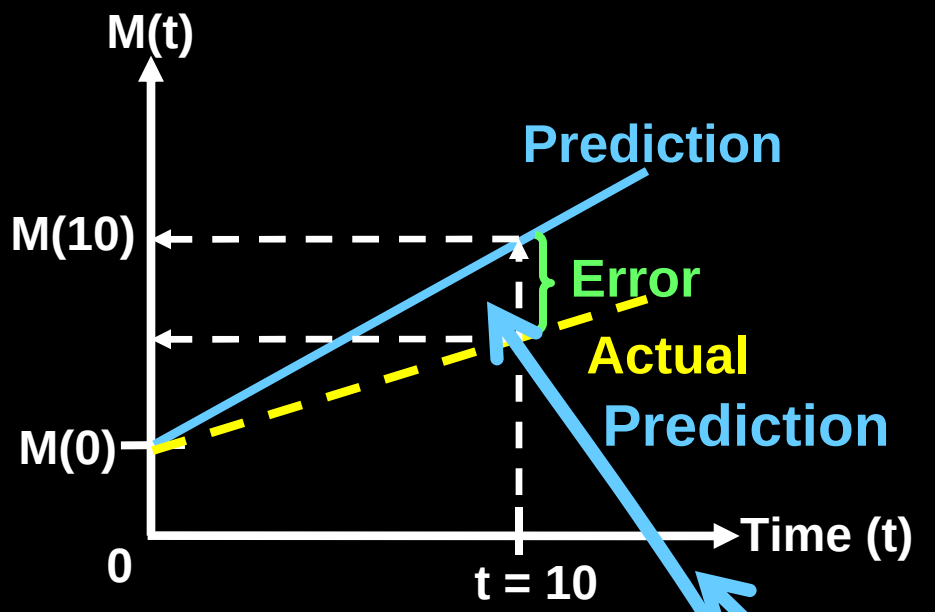


Biomathematical Models

- **First-Principles Models (physiology based)**
- **Data-Driven Models (derived from data)**

First-Principles Model





Model

t

Ordinary Differential Equation

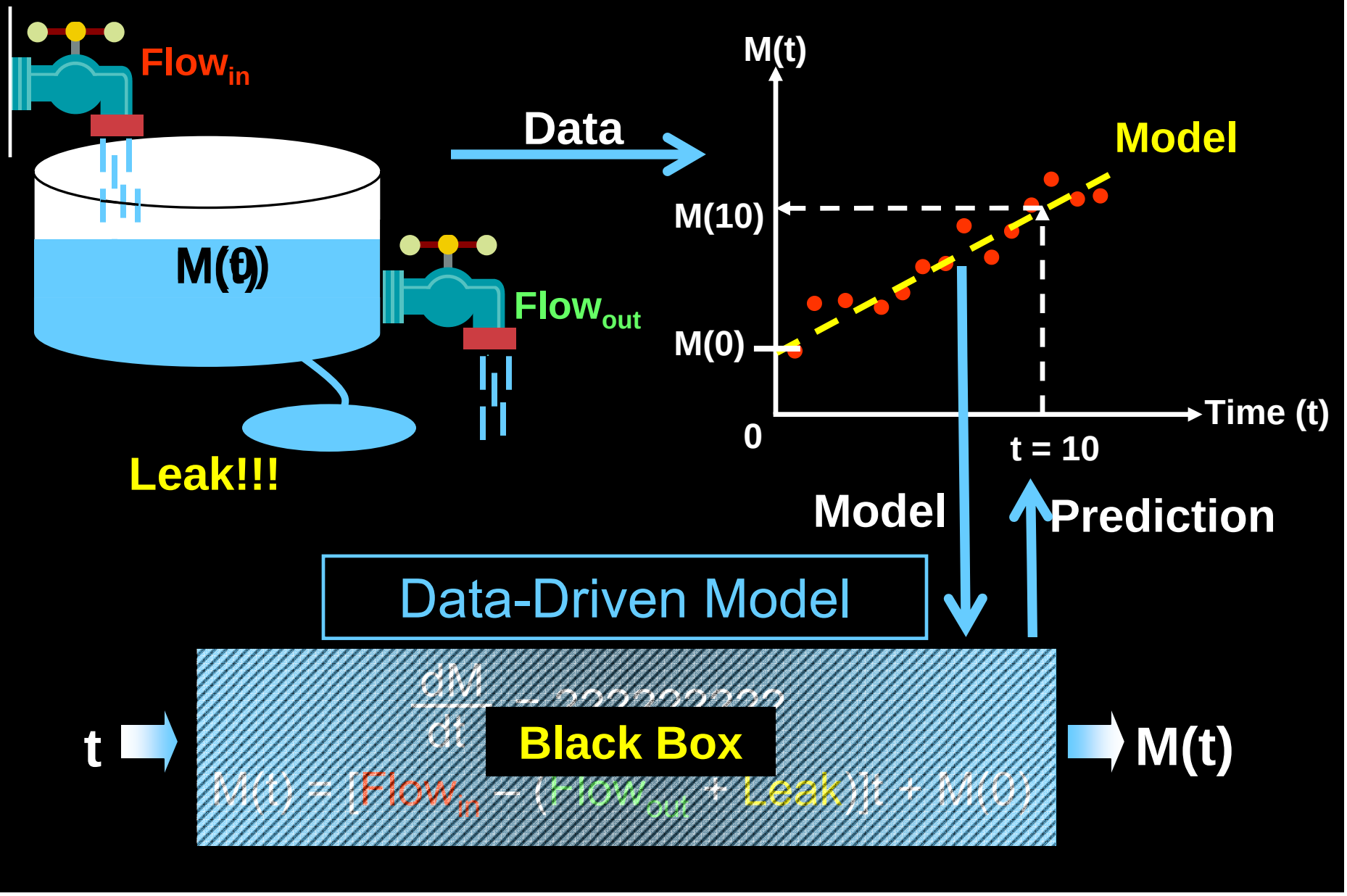
$$\frac{dM}{dt} = Flow_{in} - Flow_{out}$$

$$M(t) = [Flow_{in} - Flow_{out}]\, t + M(0)$$

M(t)

Prediction

Data-Driven Model



Model Requirements for Practical Use

- **Highly accurate (for a reasonable horizon)**

  $\Rightarrow$ Individual-specific models

- **Minimum manual tuning**

  $\Rightarrow$ Adaptive first-principles models

  $\Rightarrow$ “Universal” data-driven models

- need to measure “something” from the individual -

Physiologic Variables (or States) We Wish to Predict

1. **Performance impairment due to total sleep loss**

2. **Body core temperature (minimize heat injuries)**

   - Armed forces (2003-2005)[†]: 3617 heat exhaustion injuries

   784 heat stroke injuries

3. **Glucose concentrations (diabetic patients)**

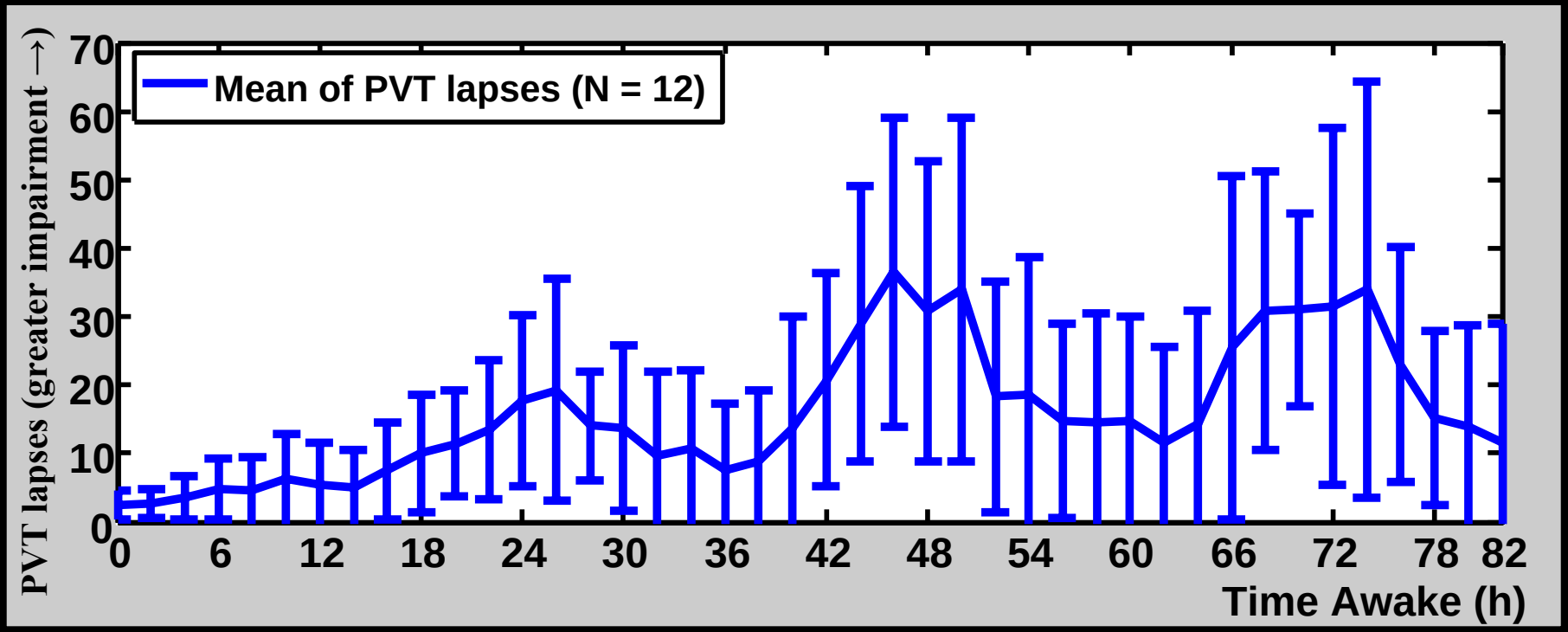
   - $1 in every $10 health care dollars is attributed to diabetes*

[†]chppm-www.apgea.army.mil/heat/ *Hogan et al., *Diabetes Care*, **26**, 917 (2003)

Performance Impairment Prediction

Problem: **Predict performance impairment due to total sleep loss (82-hour study of total sleep deprivation)***

Measure of Performance: **Lapses in a reaction-time test (Psychomotor Vigilance Task – PVT) every two hours**



*Wesensten et al., *J. Sleep Res*, **14**, 255 (2005)

Data from Tom Balkin's group (Walter Reed)

PVT lapses: # of times reaction time > 500 msec over a 10-min test session

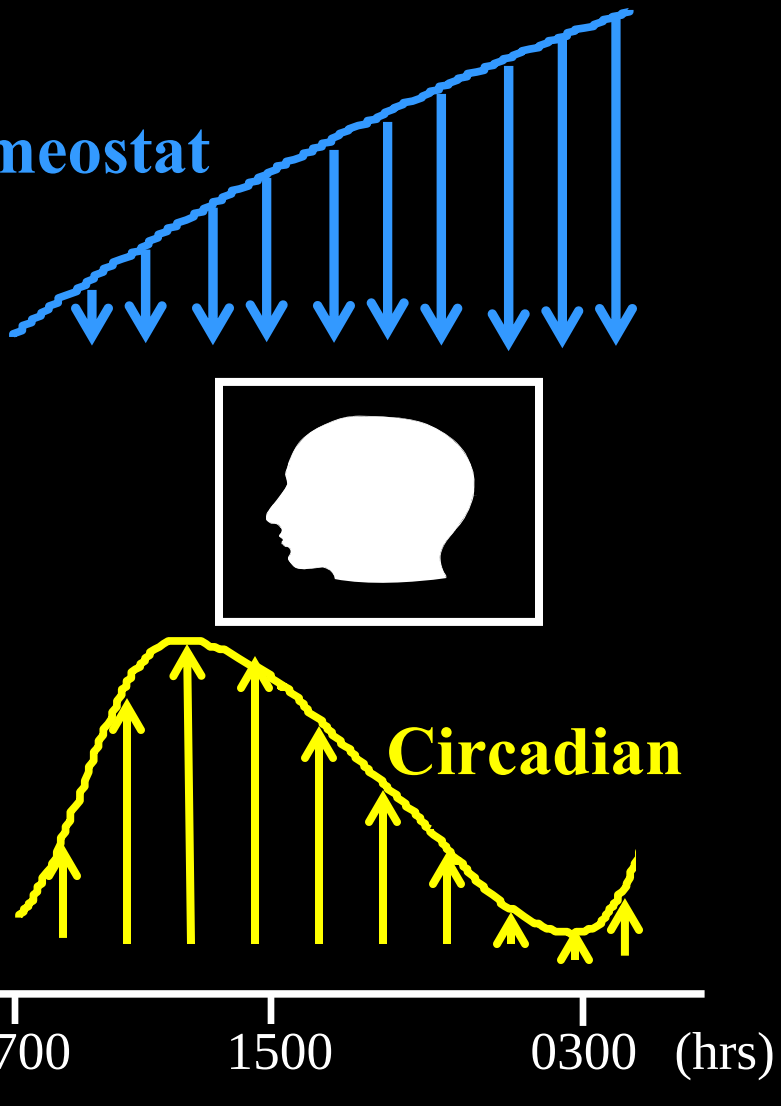
Two-Process Model of Sleep Regulation*

- "state-of-the-art" first-principles model -

Process S

(sleep/wake history)

$$S(t) = 1 - \exp(-\Delta t / \tau_r)(1 - S(t-1))$$



Process C

(biological clock)

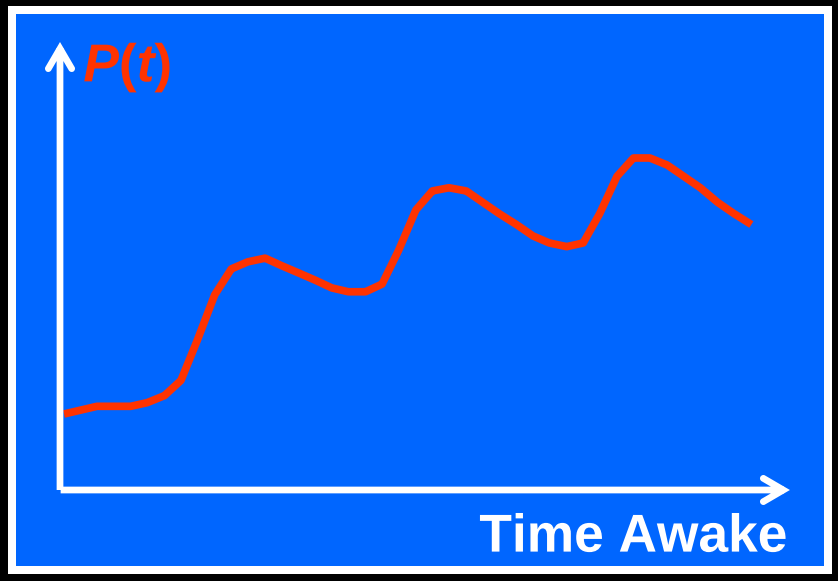
$$C(t) = \sum_{i=1}^{5} a_i \sin\left(\frac{2i\pi}{\tau}(\Delta t(t-1) + \phi)\right)$$

*Borbély, *Human Neurobiol.*, **1**, 195 (1982)

Predicting Performance Using the Two-Process Model

Performance P(t):

$$P(t) = S(t) + C(t)$$

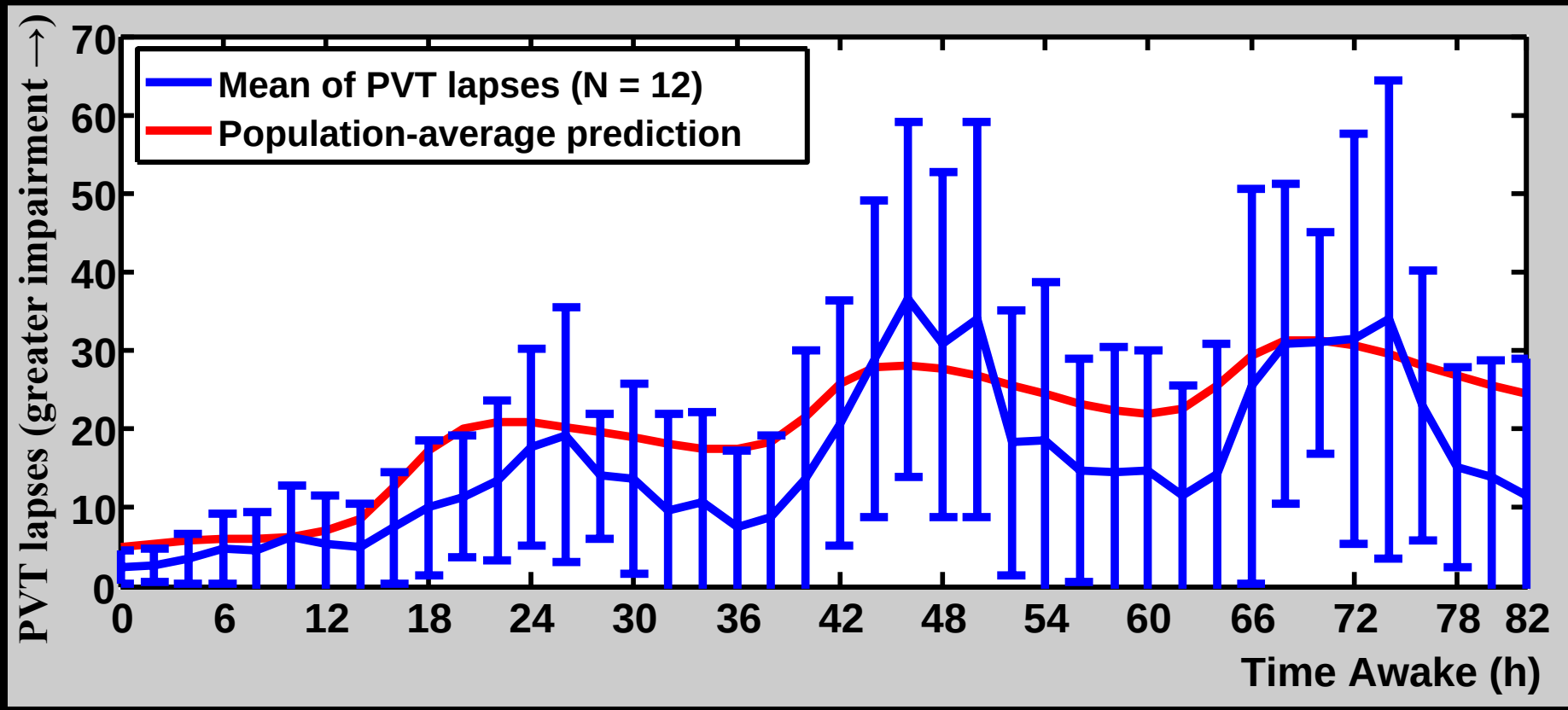


For total sleep deprivation:

$$P(t) = \alpha - \alpha S(0)\,\gamma^{t-1} + \beta \sum_{i=1}^{5} a_i \sin[i\omega((t-1)\Delta t + \phi)]$$

Population-Avg. Solution: Model parameters (τ_r, $S(0)$, α, β, ϕ) are fixed

Population-Avg. Model Not Optimal

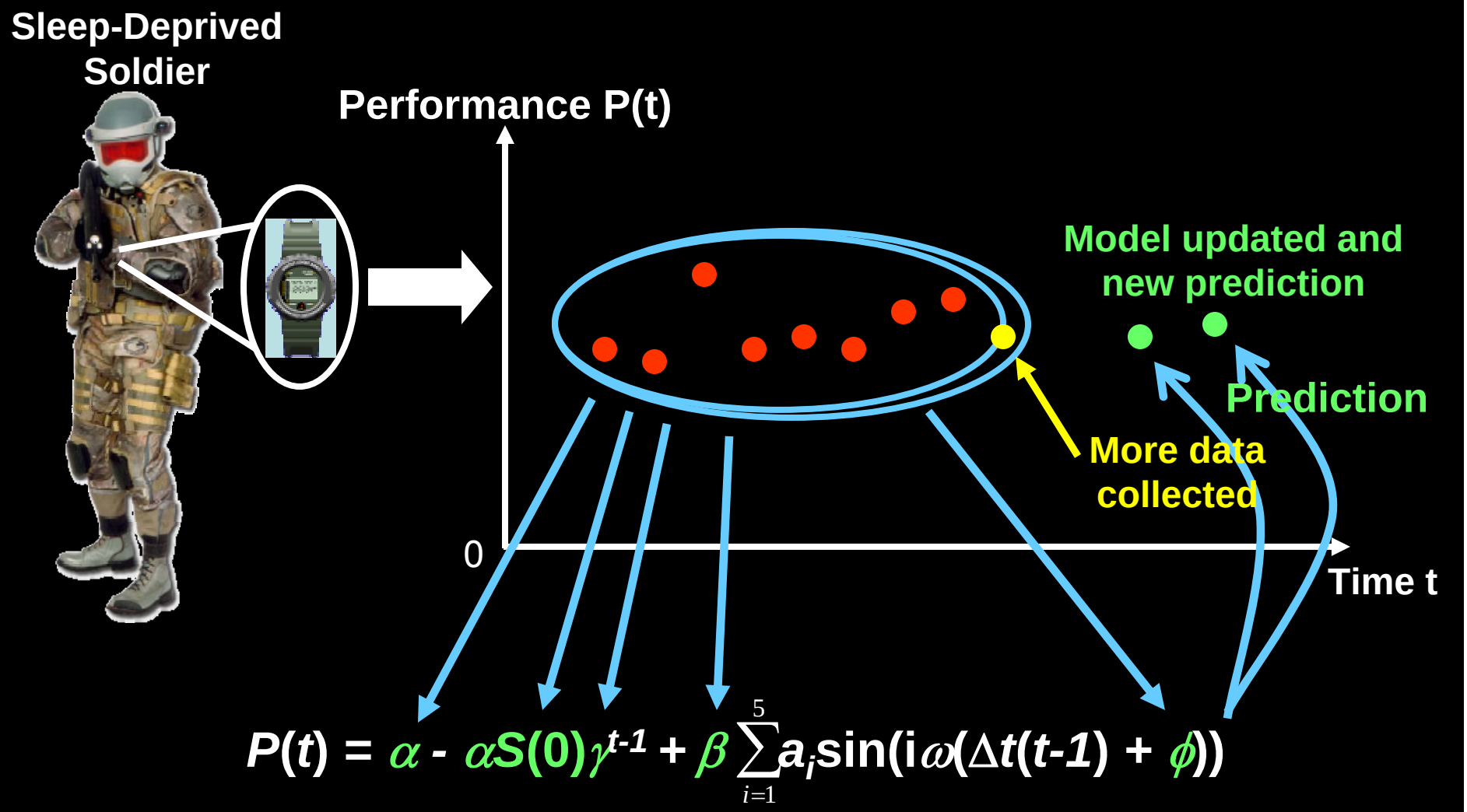


Solution: Individual-specific adaptive models

- Models parameters (τ_r, $S(0)$, α, β, ϕ,) are automatically adjusted, for each individual, after each PVT observation

First-Principles, Two-Process Model

- Adaptive, Individual-Specific Model -

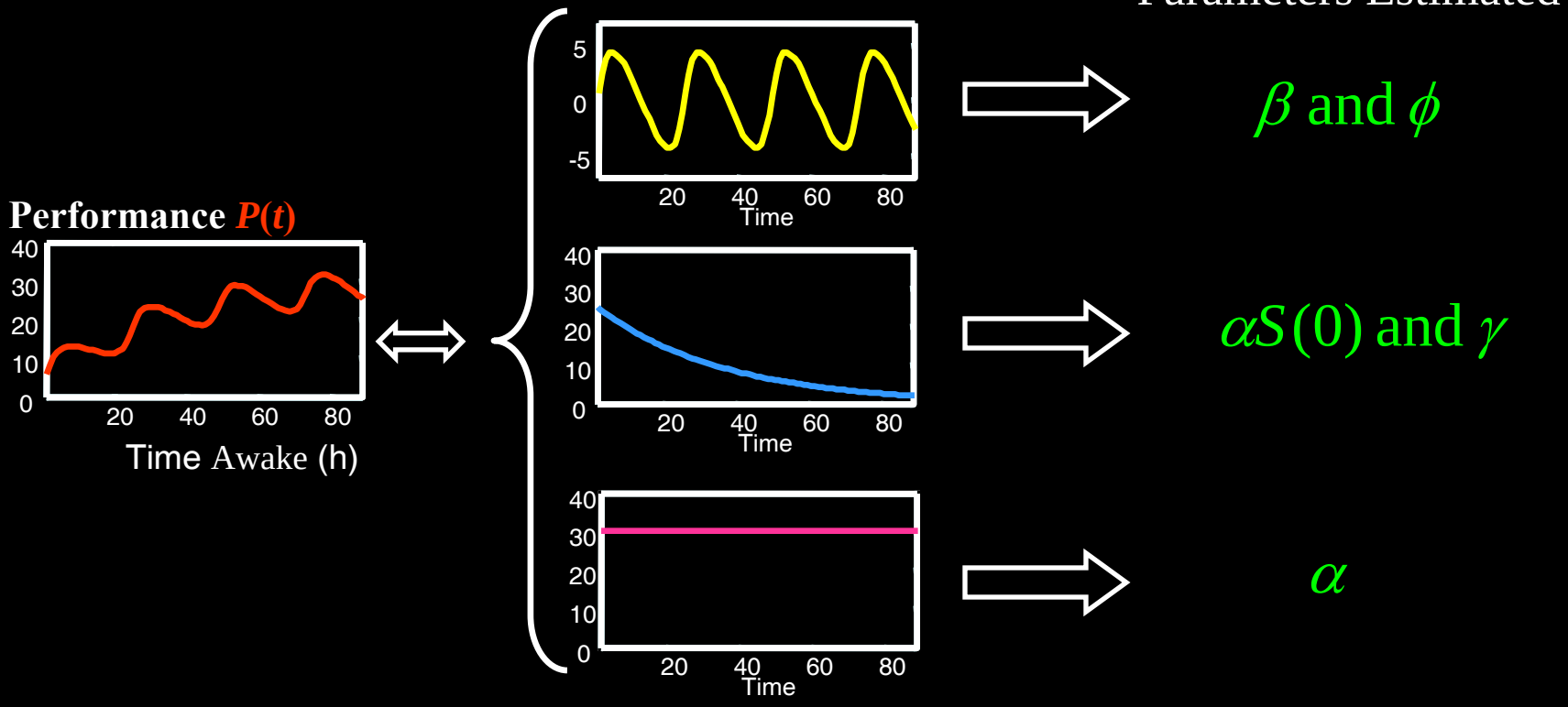


$$P(t) = \alpha - \alpha S(0)\gamma^{t-1} + \beta \sum_{i=1}^{5} a_i \sin(i\omega(\Delta t(t-1) + \phi))$$

Adaptive Individual-Specific Models*

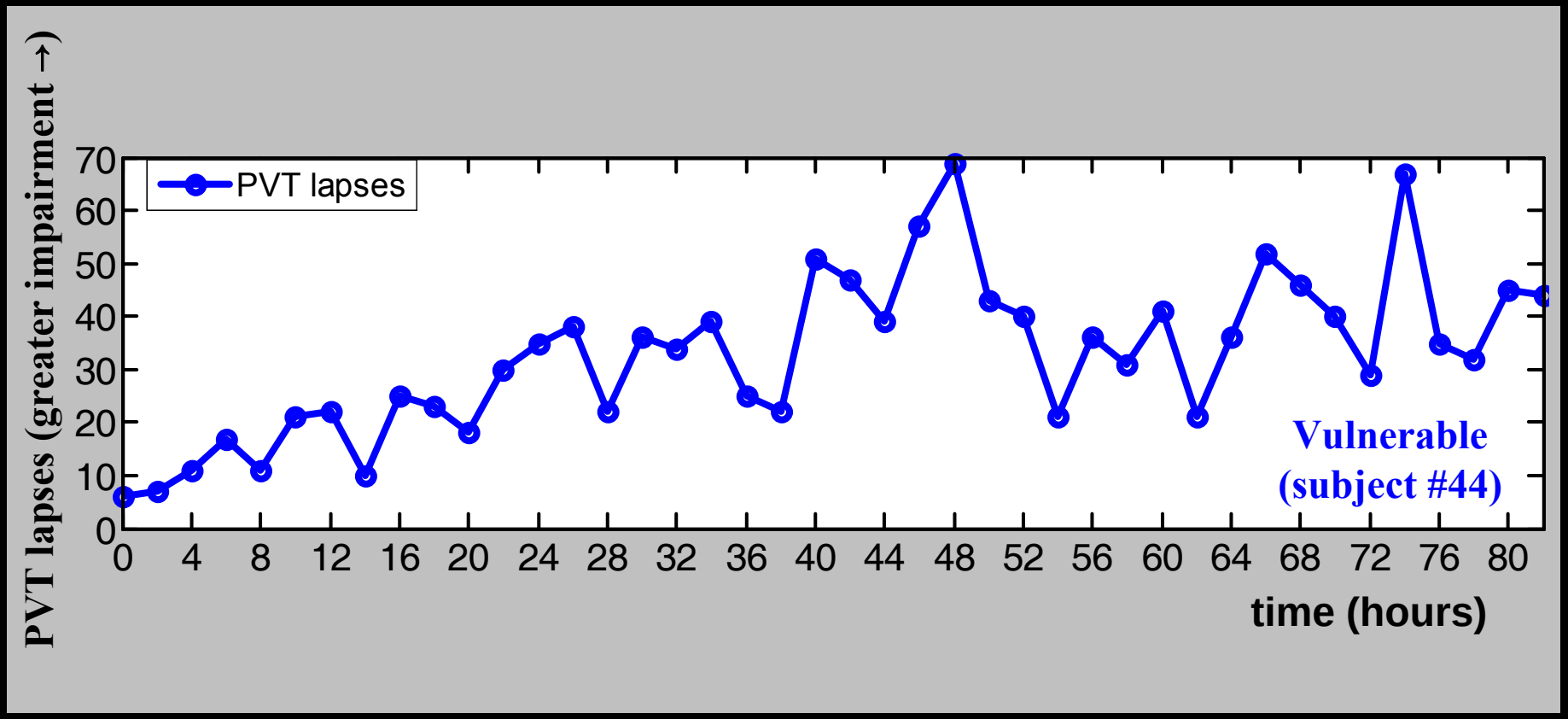
Performance (P):

$$P(t) = \alpha - \alpha S(0)\gamma^{t-1} + \beta \sum_{i=1}^{5} a_i \sin(i\omega(\Delta t(t\text{-}1) + \phi))$$

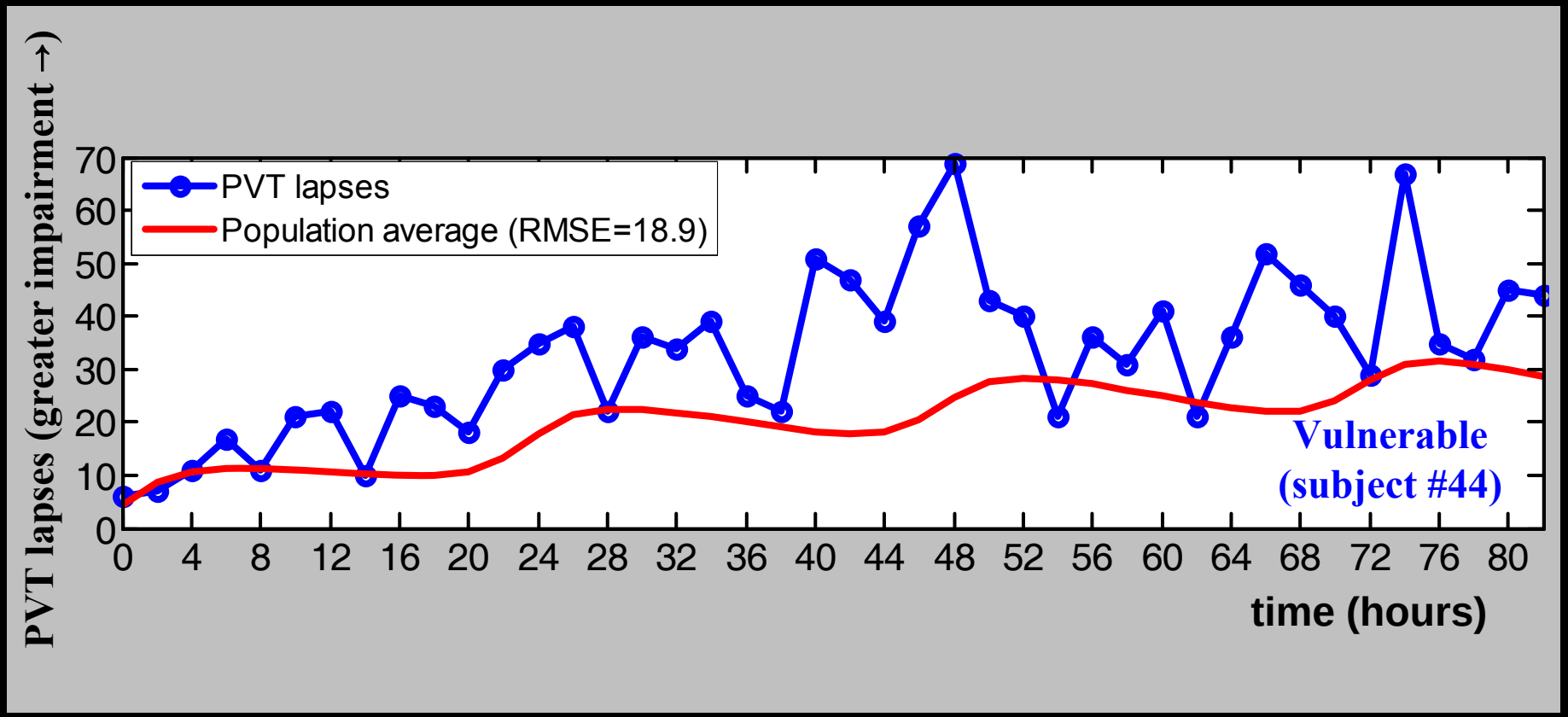


* Rajaraman et al., *J Appl Physiol*., **104**, 459 (2008)

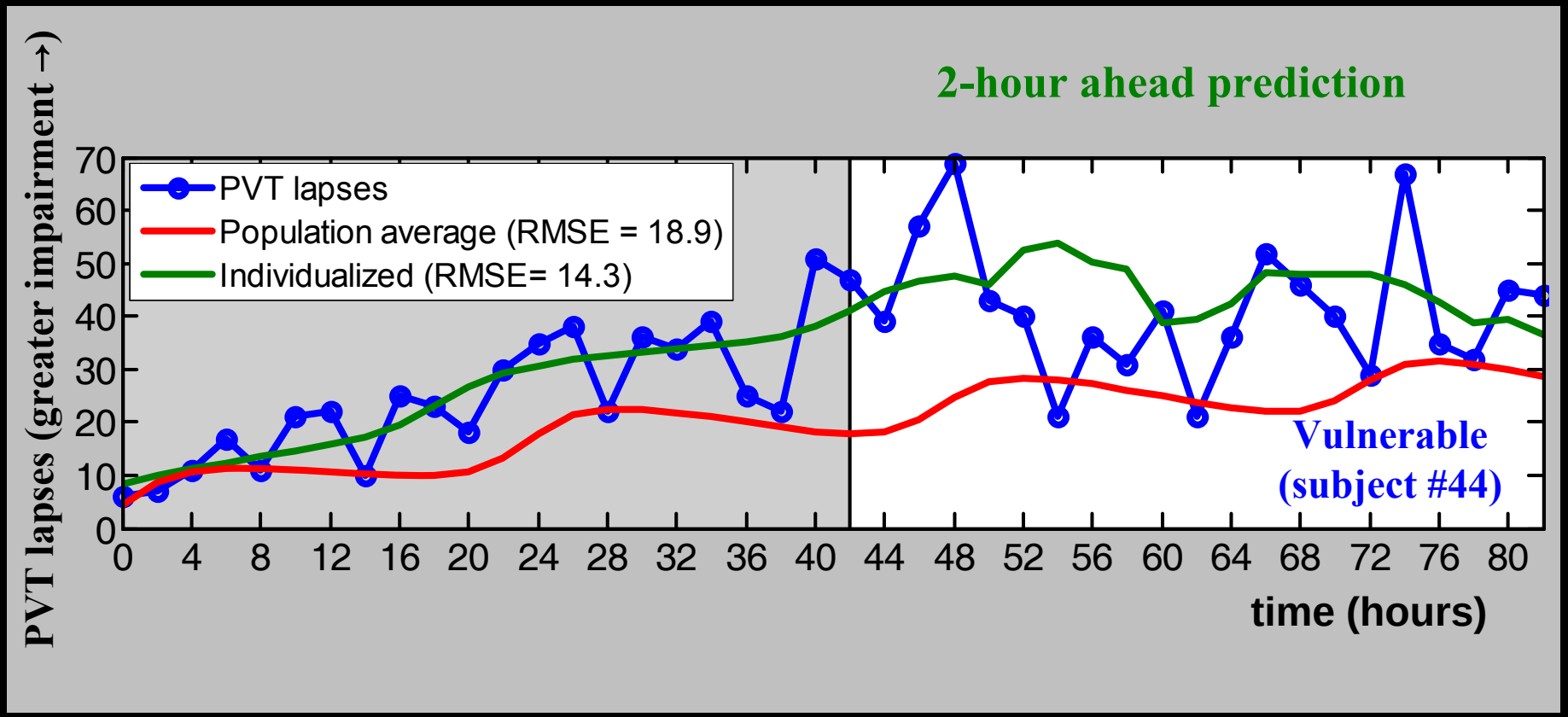
Predicting a Vulnerable Subject



Population-Average Prediction

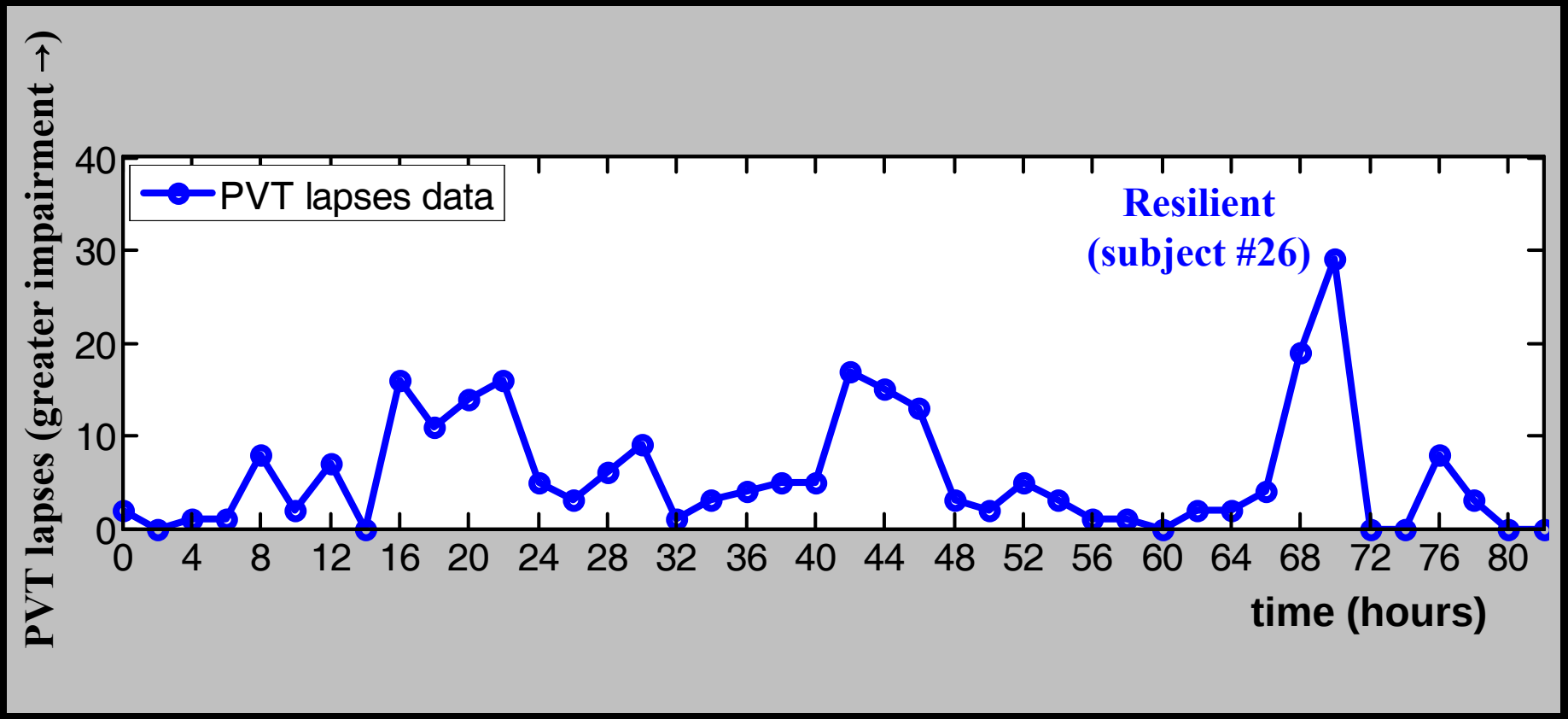


Individualized vs. Population-Average Predictions

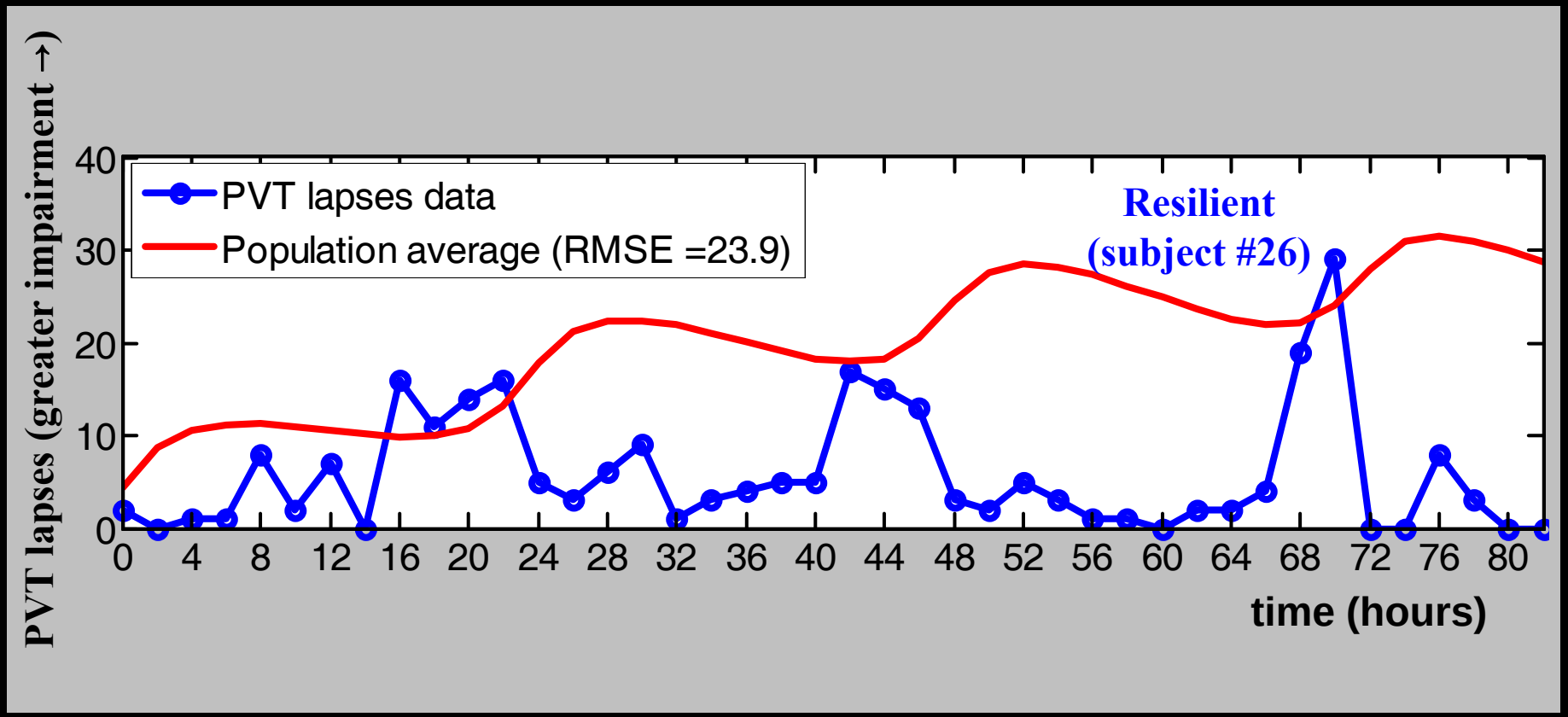


Rajaraman et al., *J Appl Physiol*., **104**, 459 (2008)

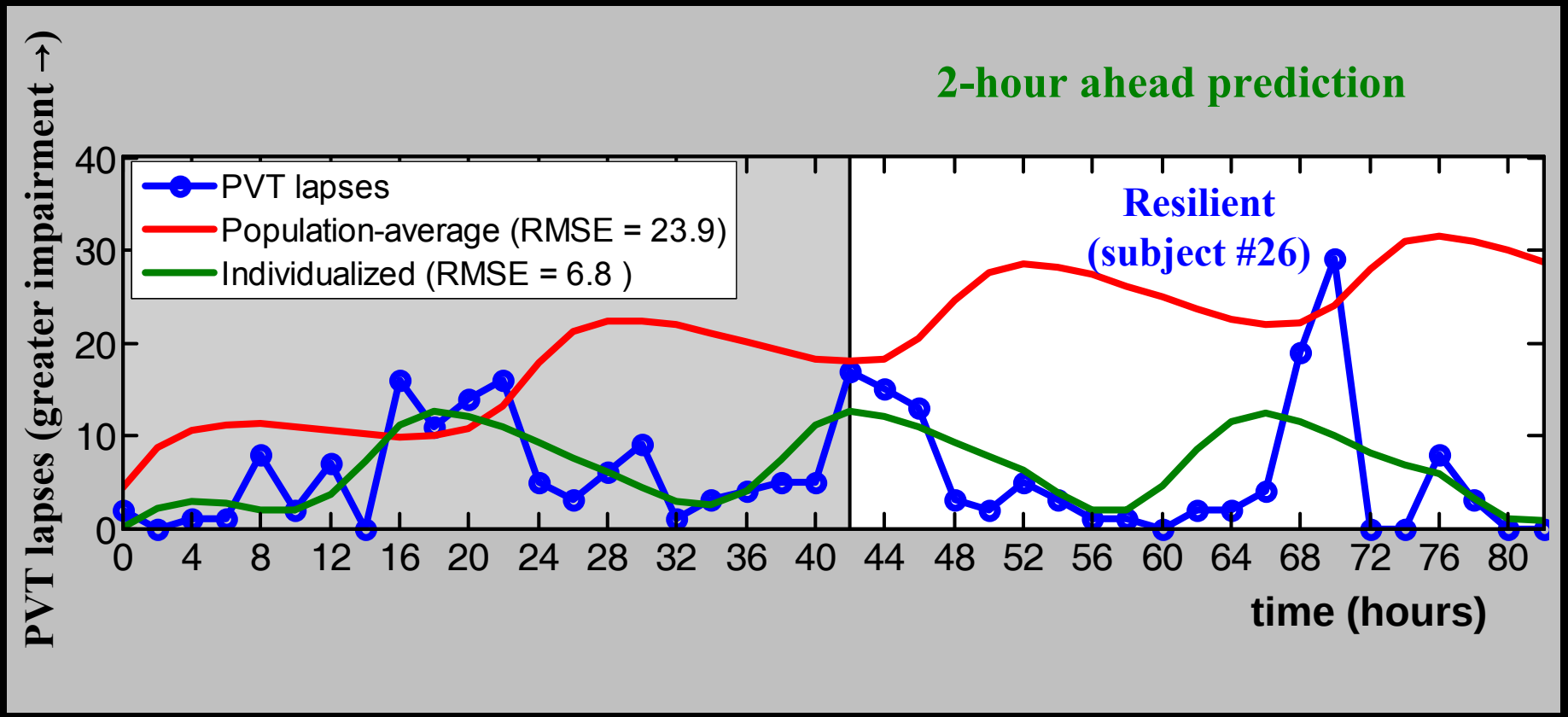
Predicting a Resilient Subject



Population-Average Prediction



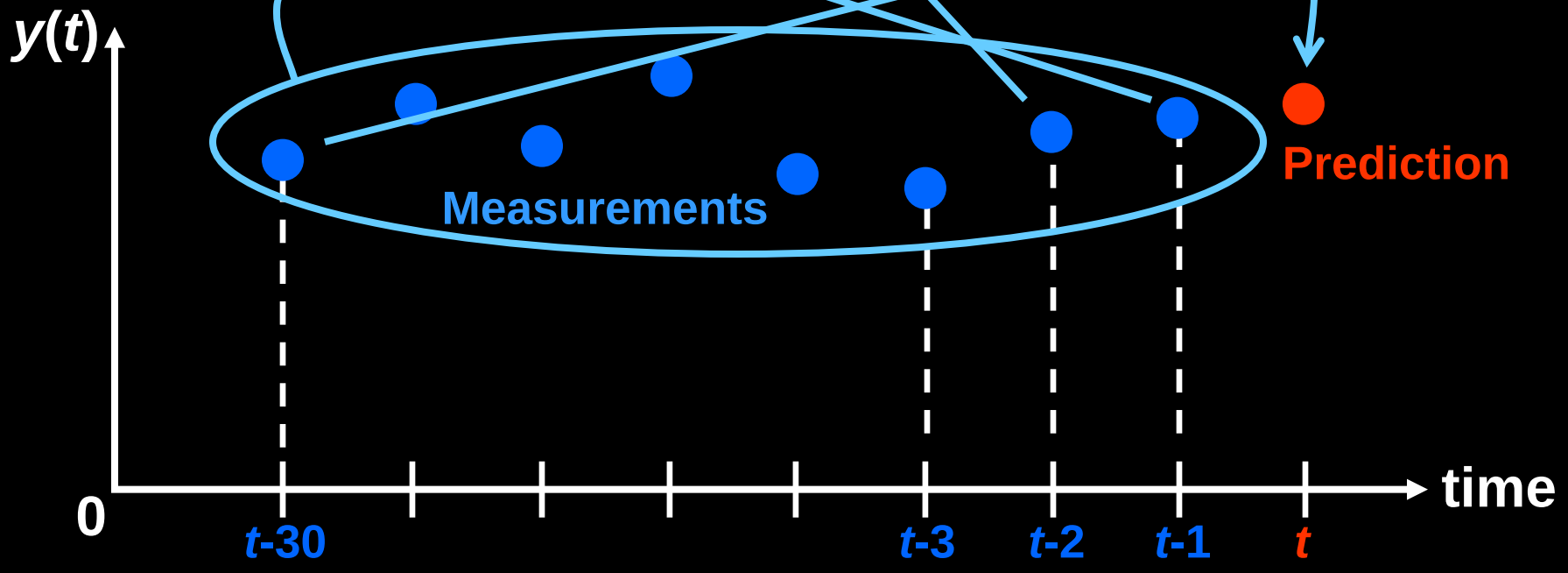
Individualized vs. Population-Average Predictions



Rajaraman et al., *J Appl Physiol*., **104**, 459 (2008)

Autoregressive (AR), Data-Driven Model

$$y(t) = b_1 y(t - 1) + b_2 y(t - 2) + \ldots + b_{30} y(t - 30)$$



$y(t)$: measurement/prediction at time t

b_i: model coefficients (unknown)

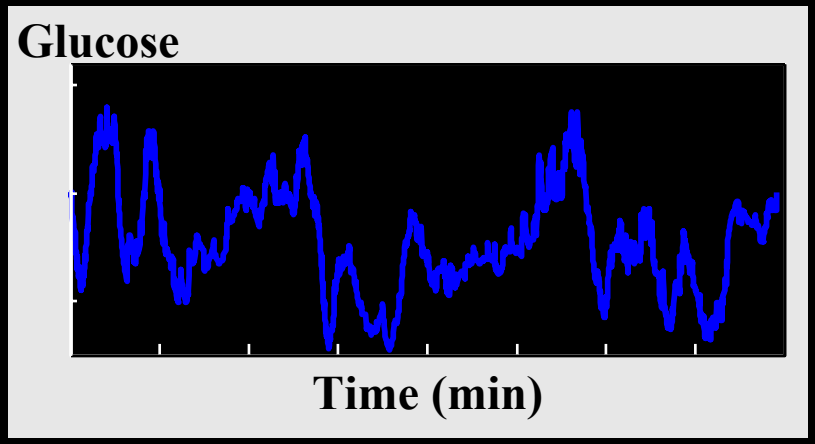
30: number of previous measurements

Found to be individual independent!!!

Autoregressive (AR), Data-Driven Model

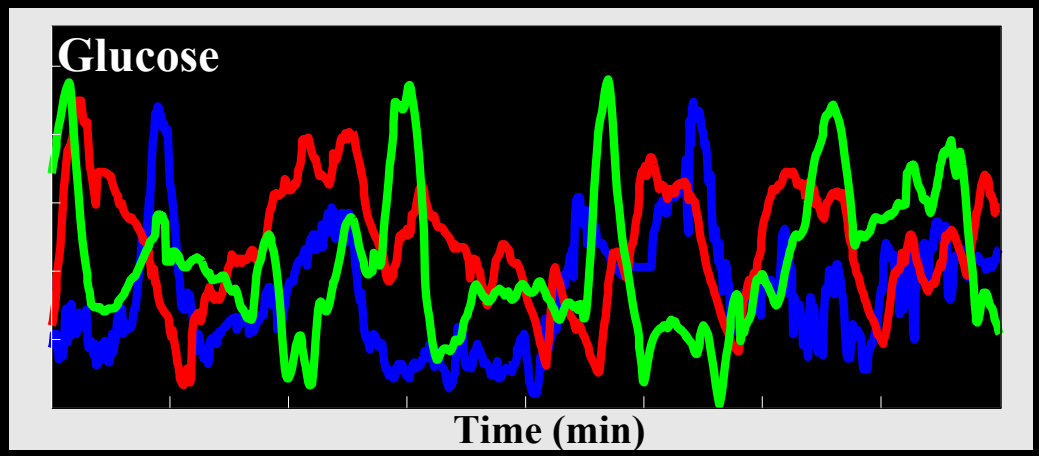
- "Universal," Individual-Independent Model -

Continuous Glucose Monitor



Predictions

Data-Driven, Universal Model (fixed coefficients b_i)

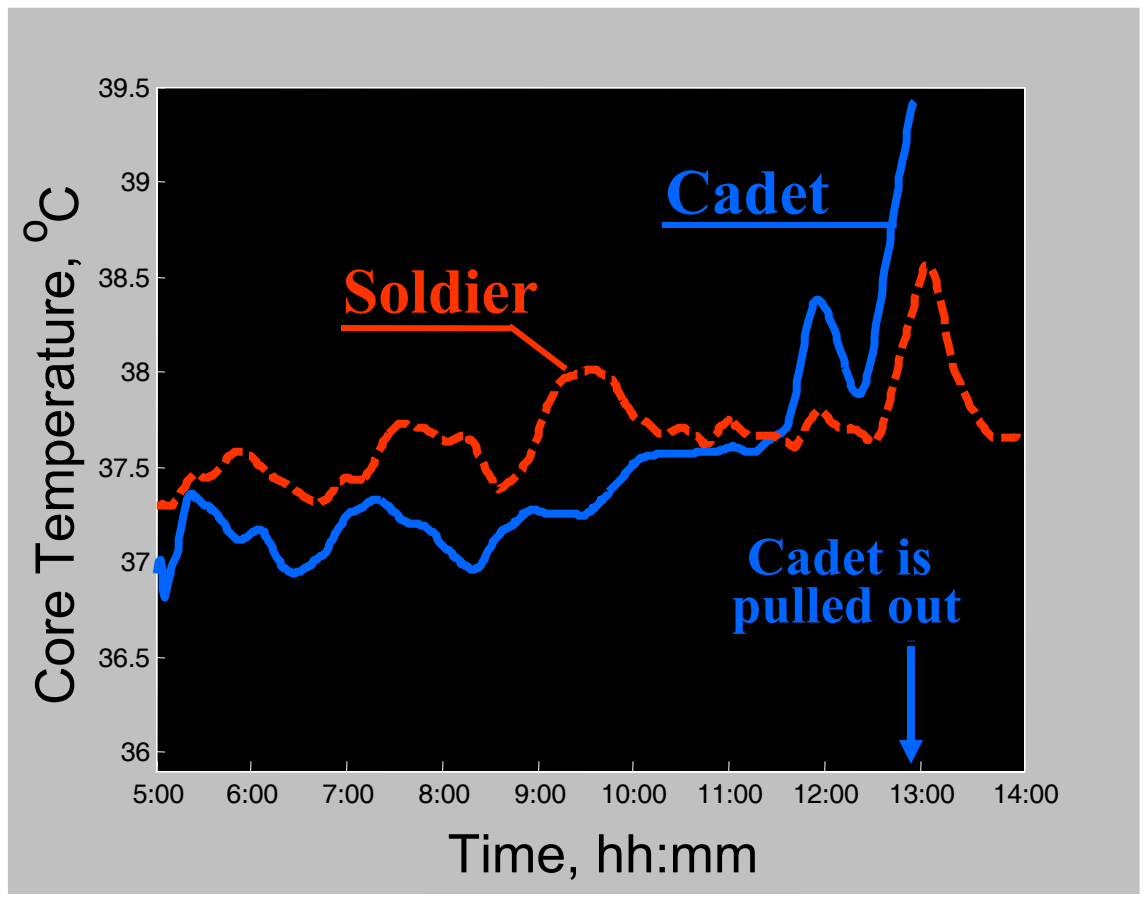


Glucose Measurements

Body Core Temperature Prediction

Problem: **Predict core temperature 20-minutes ahead***

Measurement: **Temperature pill (1-minute data)**

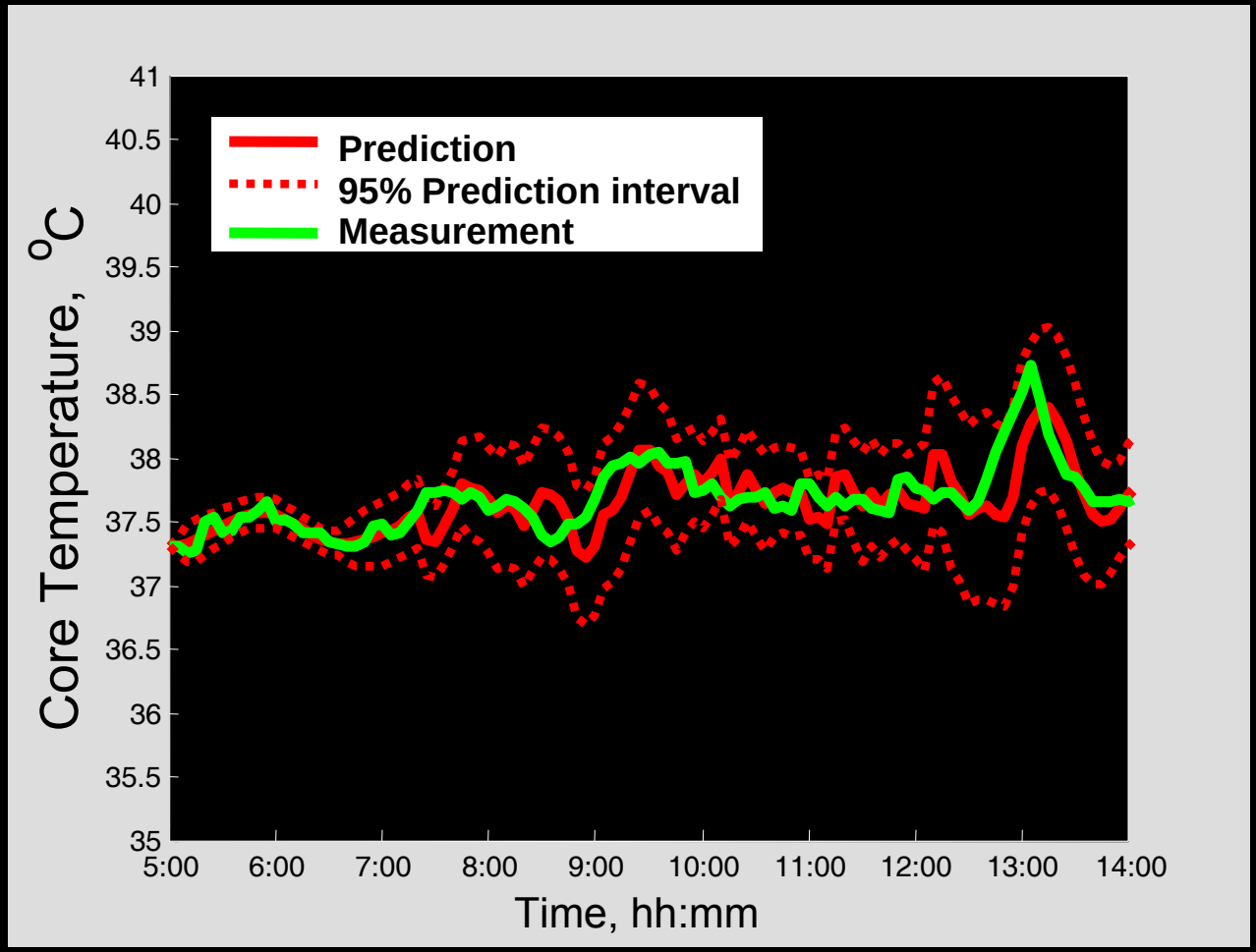


Joint Readiness Training Center, Ft. Polk, LA, Aug/01

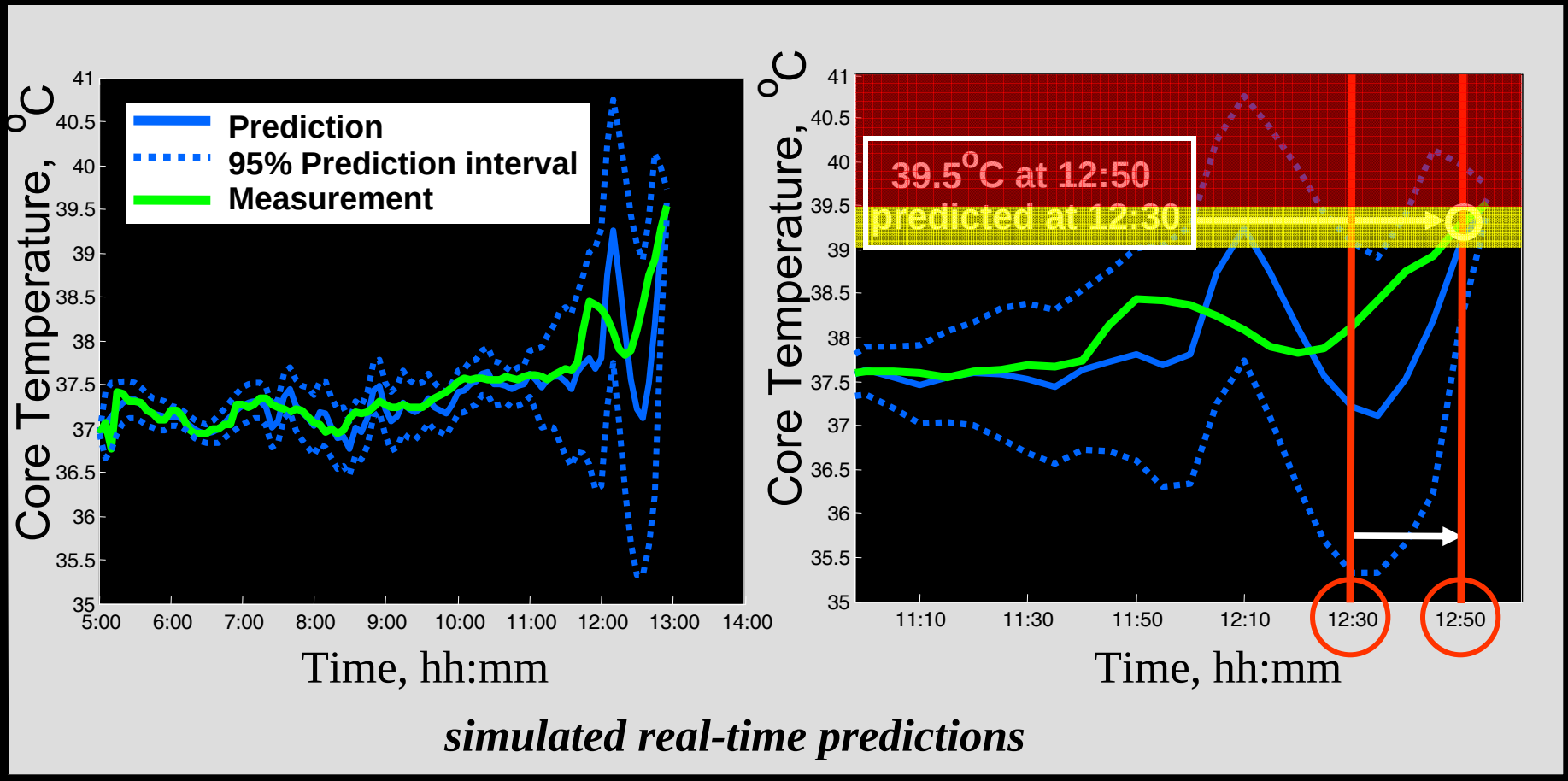
- **West Point Cadet and Soldier from 509th Infantry Regiment**
- **Soldier was very fit and heat acclimated**
- **Cadet was not as fit, not heat acclimated and was carrying a heavier load**
- **Soldier's model used to predict Cadet's temperature and vice versa**

Data from Reed Hoyt's group, U.S. Army Research Institute of Environmental Medicine (USARIEM)

Cadet's Model Used to Predict Soldier's Core Temperature 20-min Ahead



Soldier's Model Used to Predict Cadet's Core Temperature 20-min Ahead



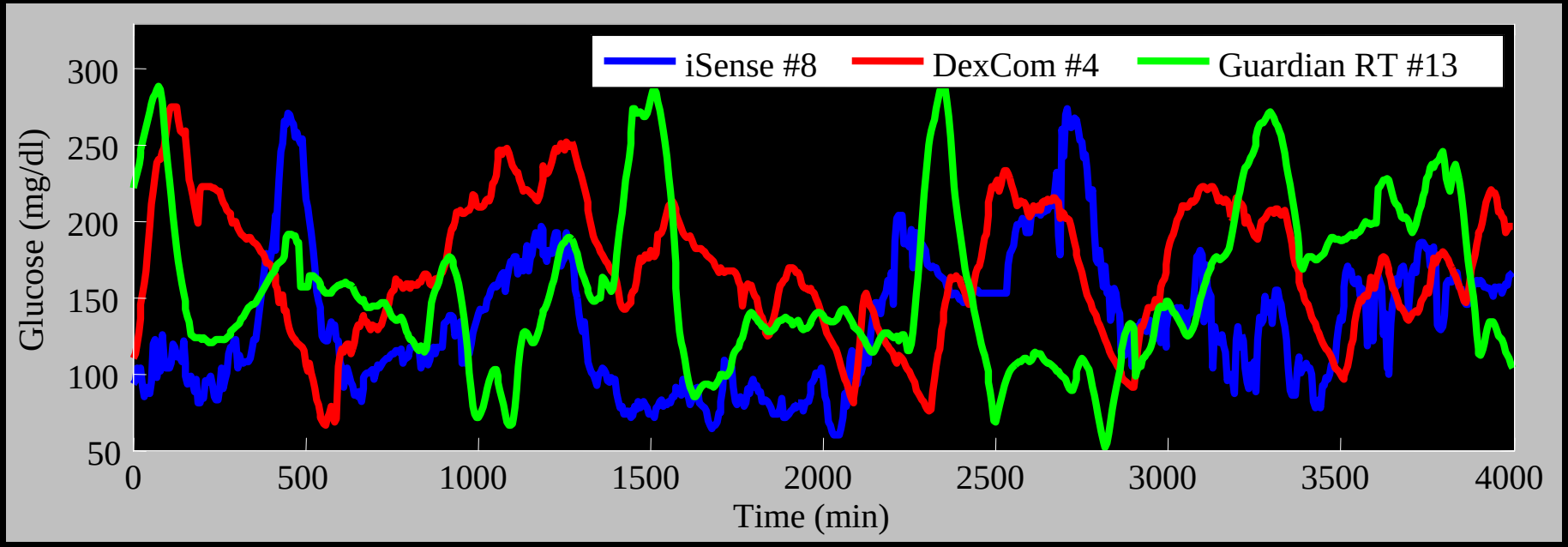
simulated real-time predictions

Gribok, Buller, and Reifman, *IEEE Trans. Biomed. Eng.*, in press
Gribok, Buller, Hoyt, and Reifman, under review

Glucose Prediction for Type 1 & 2 Diabetes

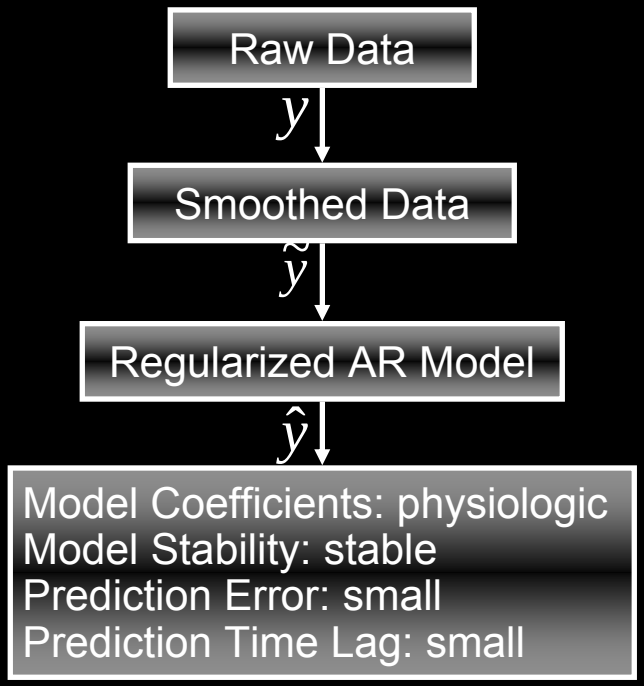
- three studies using distinct continuous glucose monitoring (CGM) devices -

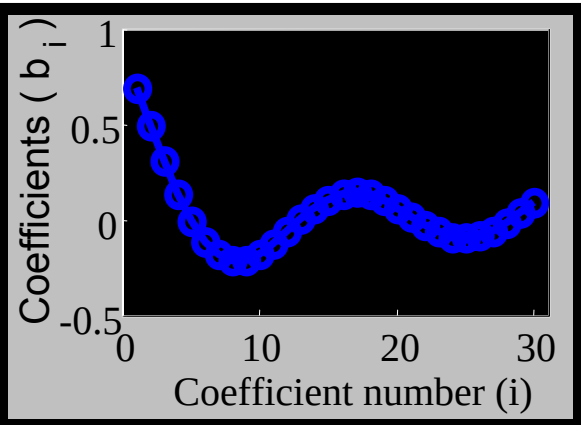
CGM Device*	# of Subjects	Diabetes Type	Sampling Frequency (min)	Collection Time (days)
iSense	9	1	1	5
DexCom	7	2	5	56
Guardian RT	18	1	5	6

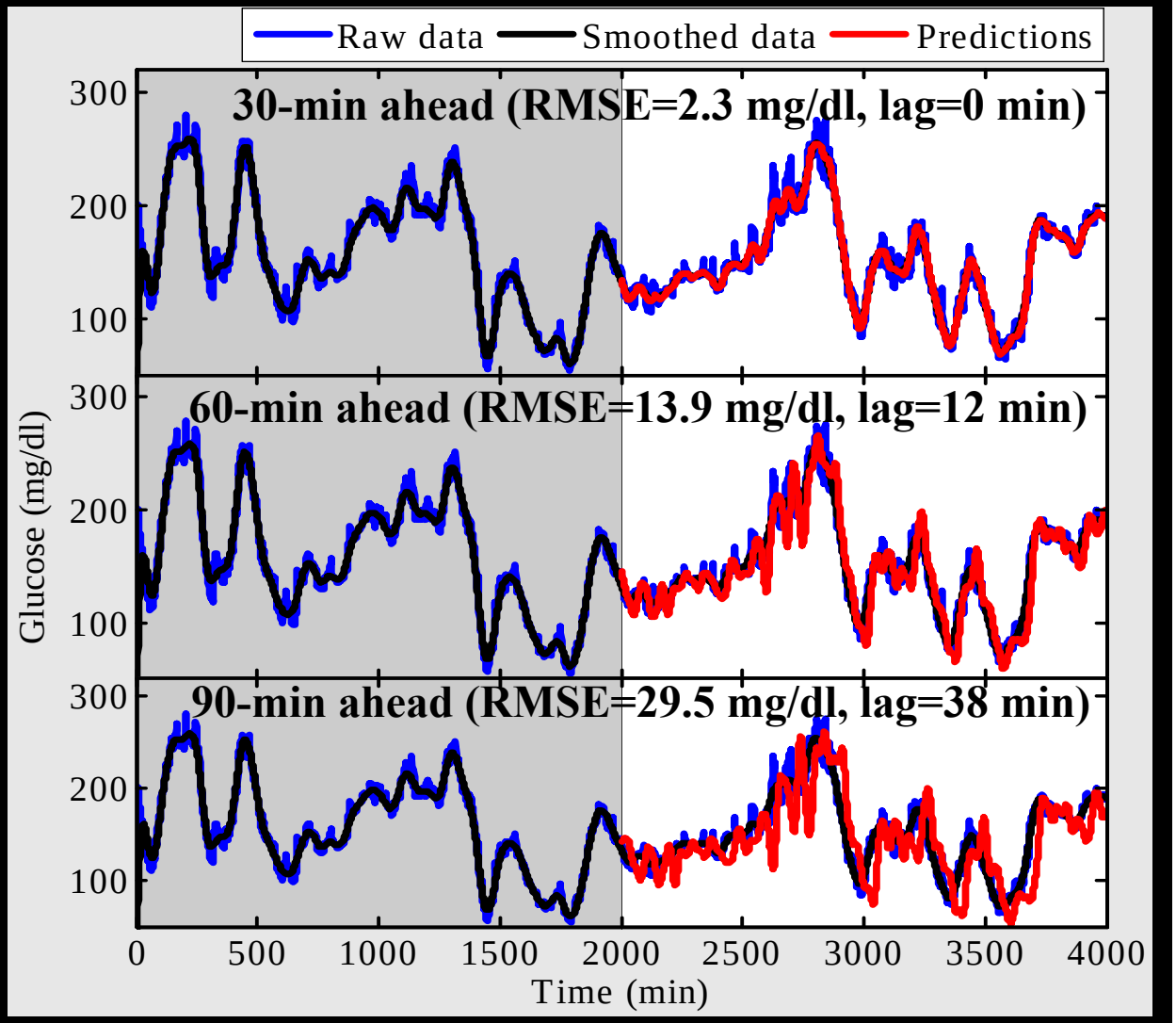


*Data provided by Ken Ward (iSense), Robert Vigersky (DexCom), Direcnet (Guardian RT)

Glucose Prediction for iSense Subject #7

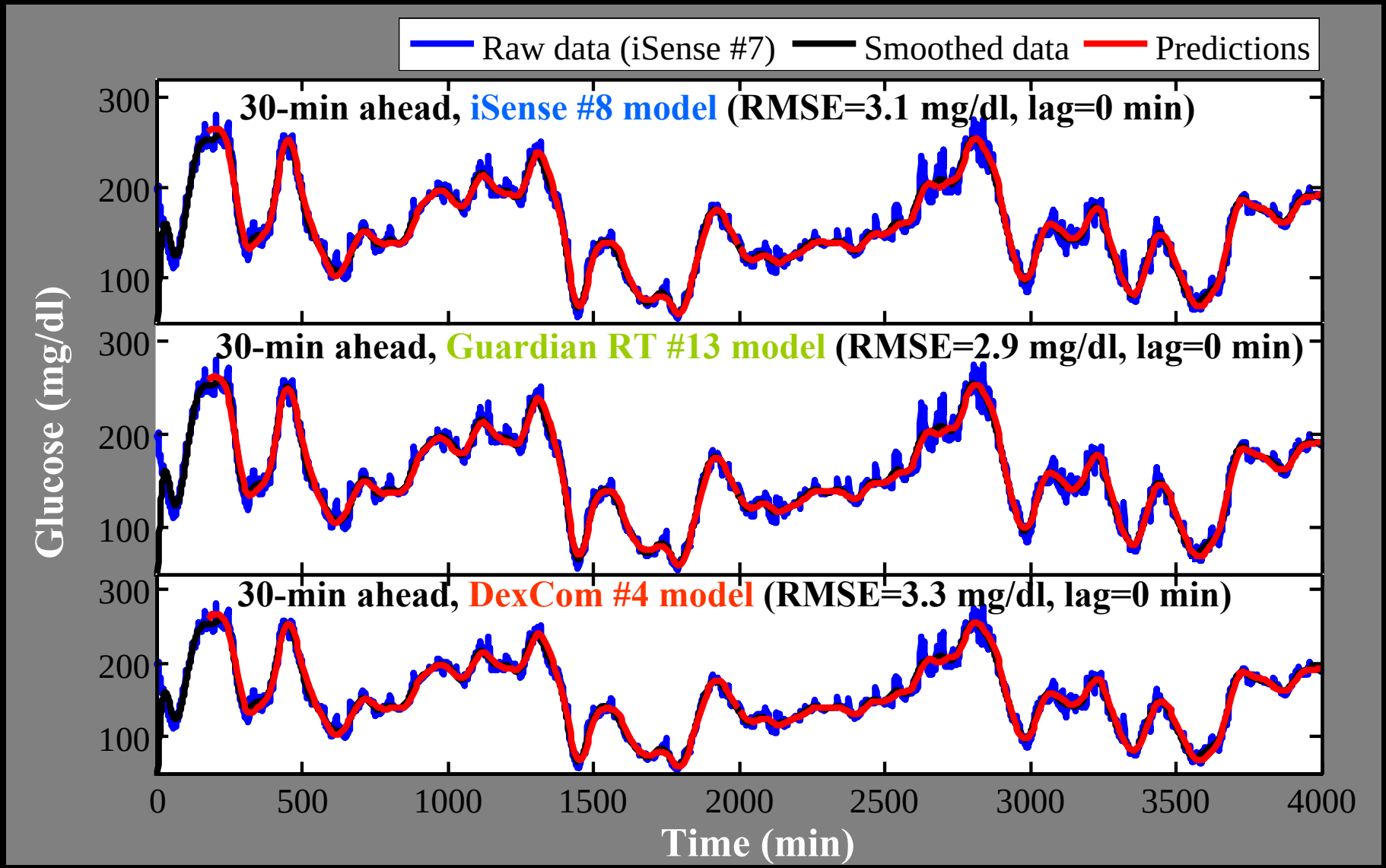






Reifman et al., *Diabetes Science & Technology*, **1**, 478 (2007)
Gani et al., under review

Models from 3 Different Subjects Used for Glucose Prediction of iSense Subject #7



Universal Model

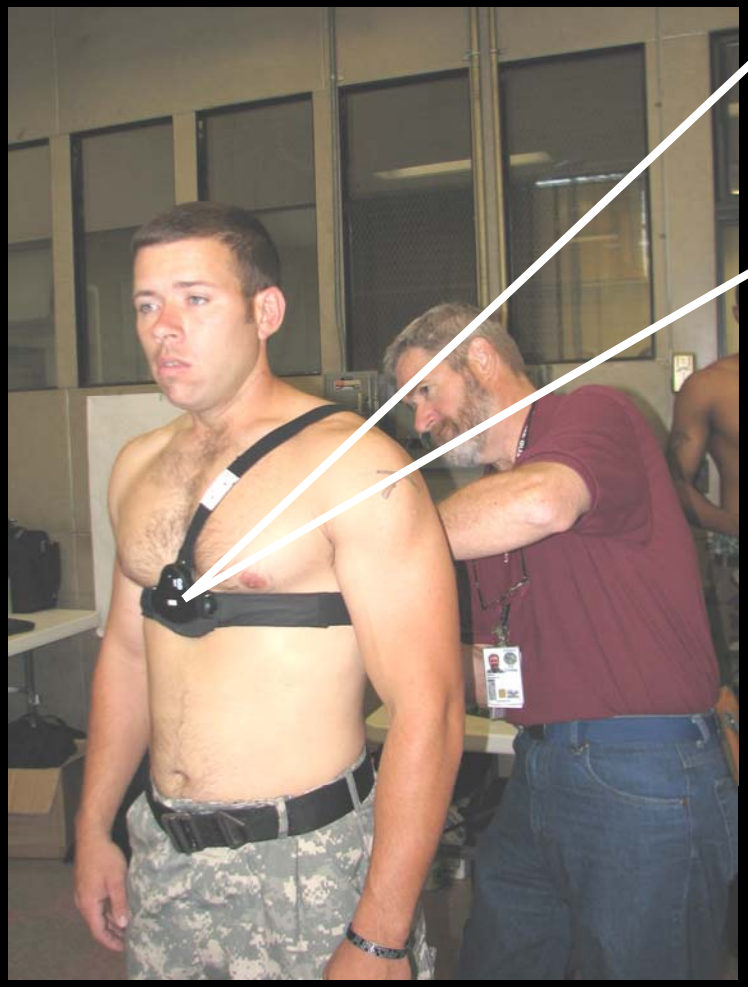
- predictions across different subjects, devices, types of diabetes -

iSense Testing Subject #	30-min Prediction Horizon (models based on different subjects/devices)					
	iSense Model (Avg. 8)		Guardian RT Model (Avg. 18)		DexCom Model (Avg. 7)	
	RMSE (mg/dl)	Lag (min)	RMSE (mg/dl)	Lag (min)	RMSE (mg/dl)	Lag (min)
1	**2.3**	**1.3**	**2.2**	**0.8**	**2.2**	**2.1**
2	**3.4**	**0.0**	**3.1**	**0.0**	**3.3**	**0.0**
3	**3.7**	**0.0**	**3.5**	**0.0**	**3.7**	**0.0**
4	**3.2**	**1.3**	**3.0**	**1.7**	**3.2**	**5.0**
5	**4.1**	**0.0**	**3.9**	**0.0**	**3.9**	**0.0**
6	**3.8**	**0.0**	**3.6**	**0.0**	**3.8**	**0.0**
7	**3.0**	**0.0**	**2.9**	**0.0**	**3.0**	**0.0**
8	**3.3**	**0.0**	**3.2**	**0.0**	**3.2**	**0.0**
9	**2.5**	**0.0**	**2.5**	**0.0**	**2.5**	**0.0**
Average	**3.3**	**0.3**	**3.1**	**0.3**	**3.2**	**0.8**

Gani et al., in preparation

What's Next? Field Testing of Universal Model

$$y(t) = b_1 y(t - 1) + b_2 y(t - 2) + \ldots + b_{30} y(t - 30)$$



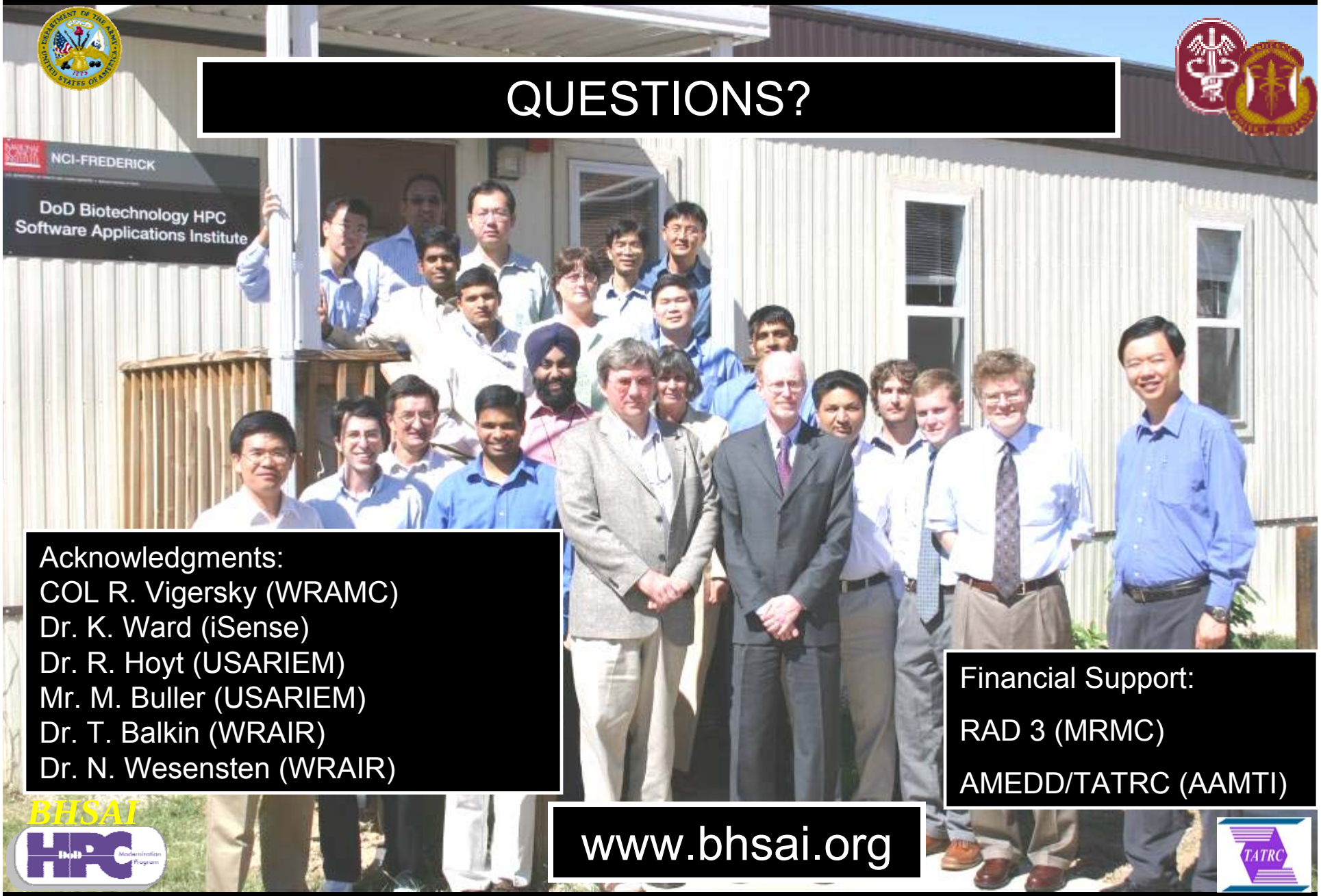
Real-Time Body Core Temperature Prediction

Joint effort with Reed Hoyt's group (USARIEM)

"All models are wrong,
some are useful."

George Box

QUESTIONS?



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