Predicting an Individual’s Physiologic State without a Crystal Ball

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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
Predicting an Individual's Physiologic State without a Crystal Ball
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

Ordinary Differential Equation

\[
\frac{dM}{dt} = \text{Flow}_{\text{in}} - \text{Flow}_{\text{out}}
\]

\[
M(t) = [\text{Flow}_{\text{in}} - \text{Flow}_{\text{out}}] t + M(0)
\]

Model

Prediction

Actual

Error

Prediction

M(0)

M(10)

0

Time (t)

M(t)
Data-Driven Model

\[ \frac{dM}{dt} = \text{Flow}_{\text{in}} - (\text{Flow}_{\text{out}} + \text{Leak}) \]

\[ M(t) = [\text{Flow}_{\text{in}} - (\text{Flow}_{\text{out}} + \text{Leak})]t + M(0) \]

Data-Driven Model

Model Prediction

\[ M(0) \]

\[ M(10) \]

0

Time (t)

\[ t = 10 \]

Model

Prediction
Model Requirements for Practical Use

- Highly accurate (for a reasonable horizon)
  ⇒ Individual-specific models

- Minimum manual tuning
  ⇒ Adaptive first-principles models
  ⇒ “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)$^\dagger$: 3617 heat exhaustion injuries
     784 heat stroke injuries

3. Glucose concentrations (diabetic patients)
   - $1 in every $10 health care dollars is attributed to diabetes$^*$

$^\dagger$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

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

Data from Tom Balkin’s group (Walter Reed)
Two-Process Model of Sleep Regulation*  
- “state-of-the-art” first-principles model -

**Process S**
(sleep/wake history)

\[ S(t) = 1 - \exp(-\Delta t / \tau)(1 - S(t - 1)) \]

**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 ($\tau, S(0), \alpha, \beta, \phi$) are fixed
Solution: Individual-specific adaptive models

- Models parameters ($\tau_r, S(0), \alpha, \beta, \phi,$) are automatically adjusted, for each individual, after each PVT observation.
First-Principles, Two-Process Model
- Adaptive, Individual-Specific Model -

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

Sleep-Deprived Soldier

More data collected

Model updated and new prediction

Performance \( P(t) \)

Time \( t \)
Adaptive Individual-Specific Models*

Performance (P):

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

Parameters Estimated

- \( \beta \) and \( \phi \)
- \( \alpha S(0) \) and \( \gamma \)
- \( \alpha \)

Predicting a Vulnerable Subject

Vulnerable (subject #44)
Population-Average Prediction

- Population average (RMSE=18.9)
- Vulnerable (subject #44)
Individualized vs. Population-Average Predictions

Predicting a Resilient Subject

PVT lapses data

Resilient (subject #26)
Population-Average Prediction

PVT lapses (greater impairment $\rightarrow$) over time (hours)

0 4 8 12 16 20 24 28 32 36 40 44 48 52 56 60 64 68 72 76 80

PVT lapses data
Resilient (subject #26)

Population average (RMSE = 23.9)
Individually vs. Population-Average Predictions


PVT lapses (greater impairment $\rightarrow$)

- Population-average (RMSE = 23.9)
- Individualized (RMSE = 6.8)

2-hour ahead prediction

Resilient
(subject #26)
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

Glucose Measurements

Data-Driven, Universal Model (fixed coefficients $b_i$)

Predictions

Glucose

Time (min)
**Problem:** Predict core temperature 20-minutes ahead*

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

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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

Gribok, Buller, Hoyt, and Reifman, under review
Glucose Prediction for Type 1 & 2 Diabetes
- three studies using distinct continuous glucose monitoring (CGM) devices -

<table>
<thead>
<tr>
<th>CGM Device*</th>
<th># of Subjects</th>
<th>Diabetes Type</th>
<th>Sampling Frequency (min)</th>
<th>Collection Time (days)</th>
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<tbody>
<tr>
<td>iSense</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>DexCom</td>
<td>7</td>
<td>2</td>
<td>5</td>
<td>56</td>
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<tr>
<td>Guardian RT</td>
<td>18</td>
<td>1</td>
<td>5</td>
<td>6</td>
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</tbody>
</table>

*Data provided by Ken Ward (iSense), Robert Vigersky (DexCom), Dircenct (Guardian RT)
Glucose Prediction for iSense Subject #7

- **30-min ahead (RMSE=2.3 mg/dl, lag=0 min)**
- **60-min ahead (RMSE=13.9 mg/dl, lag=12 min)**
- **90-min ahead (RMSE=29.5 mg/dl, lag=38 min)**

Model Coefficients: physiologic
Model Stability: stable
Prediction Error: small
Prediction Time Lag: small

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

- 30-min ahead, iSense #8 model (RMSE=3.1 mg/dl, lag=0 min)
- 30-min ahead, Guardian RT #13 model (RMSE=2.9 mg/dl, lag=0 min)
- 30-min ahead, DexCom #4 model (RMSE=3.3 mg/dl, lag=0 min)
# Universal Model

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

<table>
<thead>
<tr>
<th>Subject #</th>
<th>iSense Model (Avg. 8)</th>
<th>Guardian RT Model (Avg. 18)</th>
<th>DexCom Model (Avg. 7)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>RMSE (mg/dl)</td>
<td>Lag (min)</td>
<td>RMSE (mg/dl)</td>
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<tr>
<td>1</td>
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<td>2.2</td>
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<tr>
<td>Average</td>
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<td>3.1</td>
</tr>
</tbody>
</table>

Gani et al., in preparation
What’s Next? Field Testing of Universal Model

Real-Time Body Core Temperature Prediction

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

Joint effort with Reed Hoyt’s group (USARIEM)
“All models are wrong, some are useful.”

George Box
QUESTIONS?

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