How computational modeling can advance neurorehabilitation: Insights from studies of individuals with chronic stroke

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Acknowledgments

Sensorimotor Learning Group at UD

Bobby Charalambous

CORRT Comprehensive Opportunities in Rehabilitation Research Training

NSF

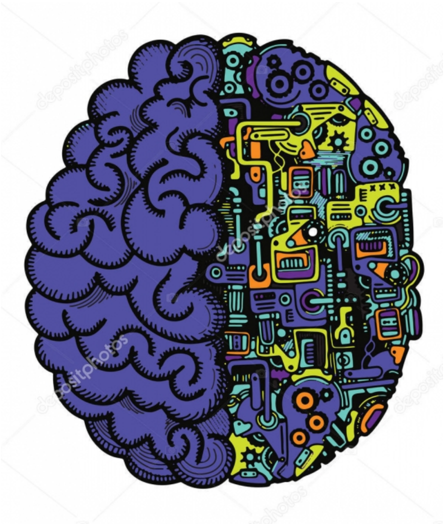
Intro and goals for this talk

- This is not a Research Report
  - Special Report on topic of interest for researchers and clinicians
- Introduce computational approaches to a broad audience
  - Heavy on ideas, light on details
- Discuss specific example of applying computational modeling to study of motor learning in individuals with stroke
- Researchers go back to their labs thinking about incorporating approaches
- Spark interest of clinicians and provide context for computational approaches in literature

What is computational modeling?

- The use of computers to simulate and study the behavior of complex systems using mathematics, physics and computer science (*from* National Institute of Biomedical Imaging and Bioengineering)

- A means of ***formalizing*** intuitions about phenomenon of interest using language of math and implemented with computer code



Brain ➡ biology and machinery

What are the benefits of computational modeling?

A few things ***good*** models can do:

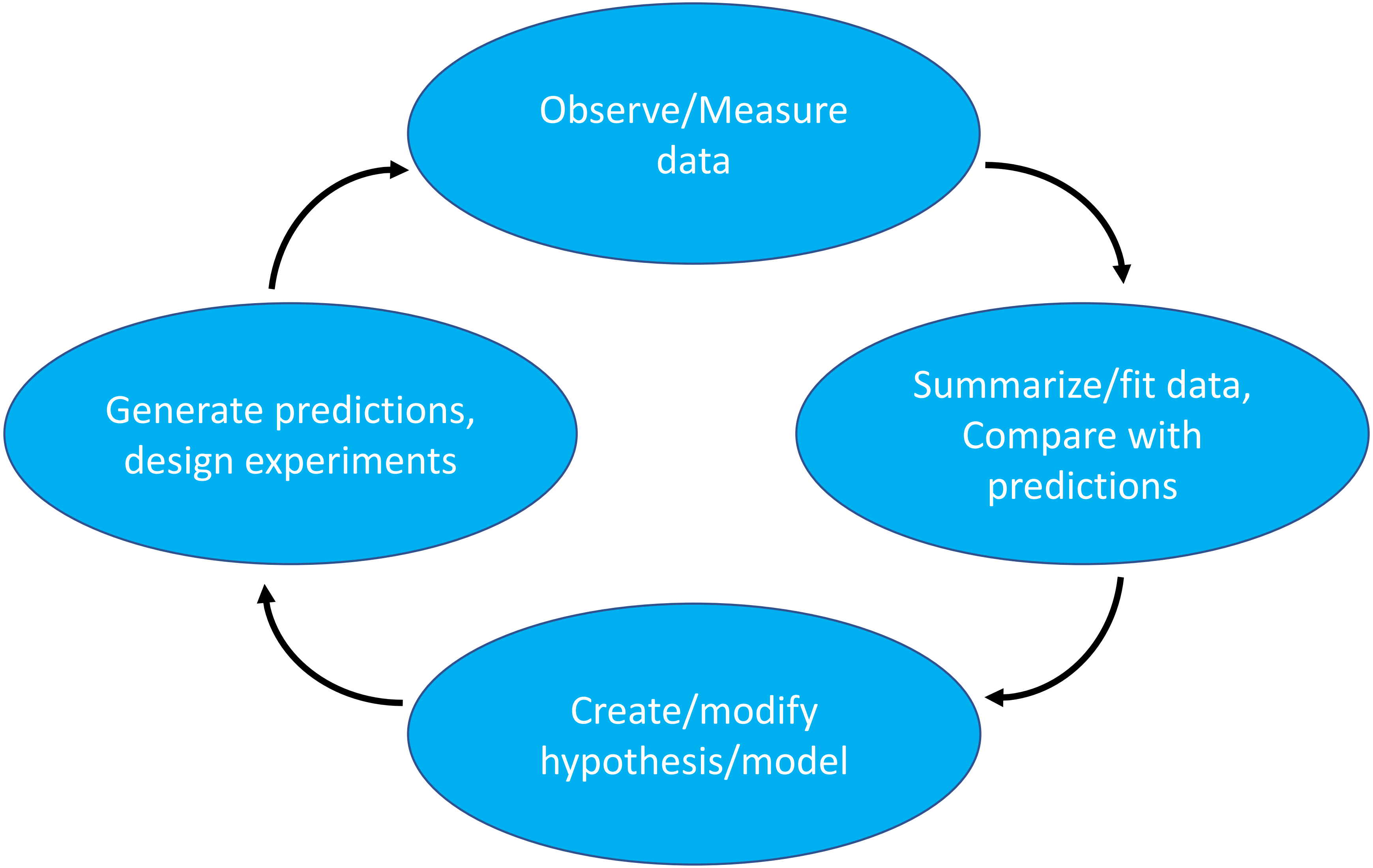
- Capture key components of a complex system/behavior
- Advance our mechanistic understanding
    - Predict variables that cannot be directly measured
- Generate testable (falsifiable) predictions
- Save animal lives; limit number of unnecessary experiments by using simulations

“All models are wrong, but some are useful.”

- George Box

(adapted from 2017 Computational Sensory Motor Neuroscience Summer School:

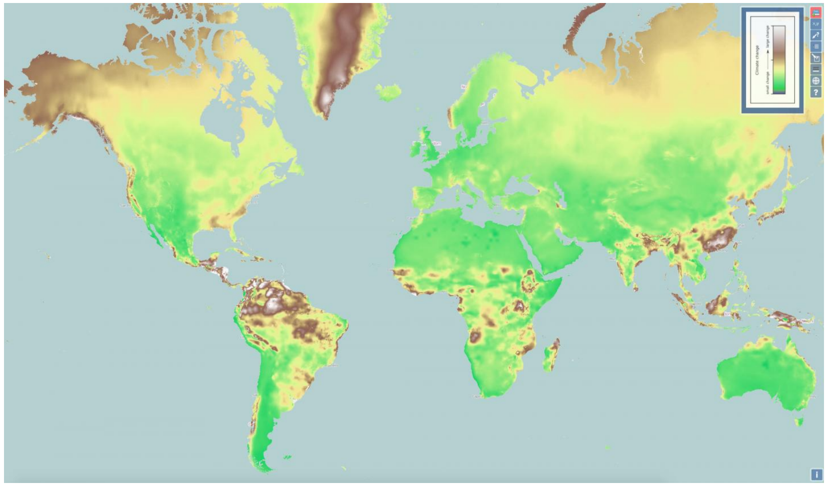
The Scientific Process



Modeling can improve all aspects

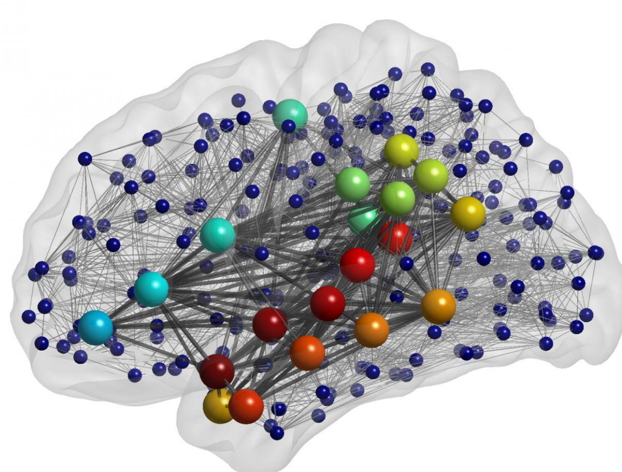
Adapted from [NYU's Math Tools for Neural Science]

Computational models are all around us



Models of climate change

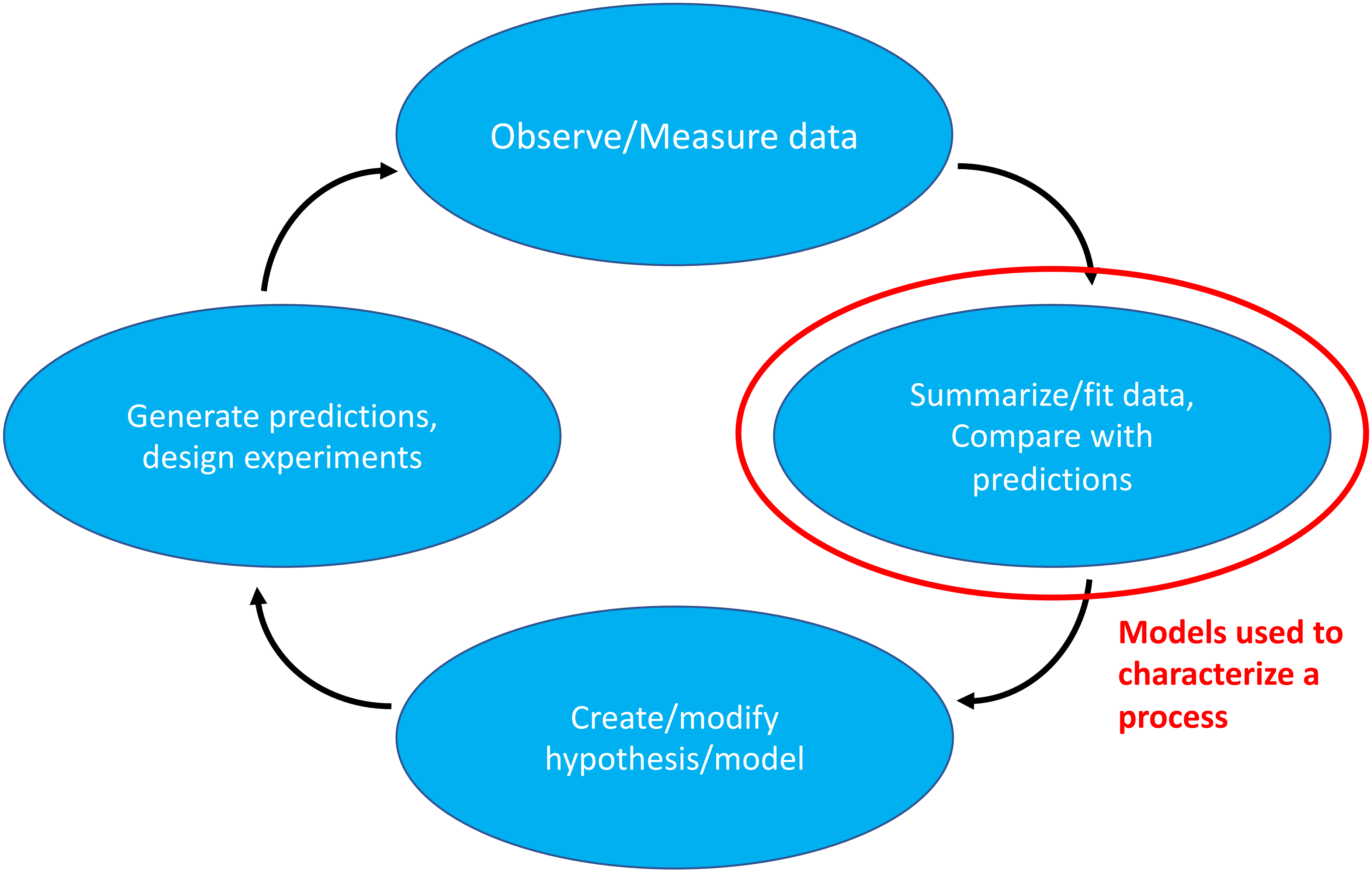
Flight simulators



Neural network models

https://www.eurekalert.org/multimedia/pub/165979.php; https://www.geekwire.com/2019/microsoft-flight-simulator-cloud/;
https://www.eurekalert.org/pub_releases/2018-10/uarl-aus103018.php

The Scientific Process

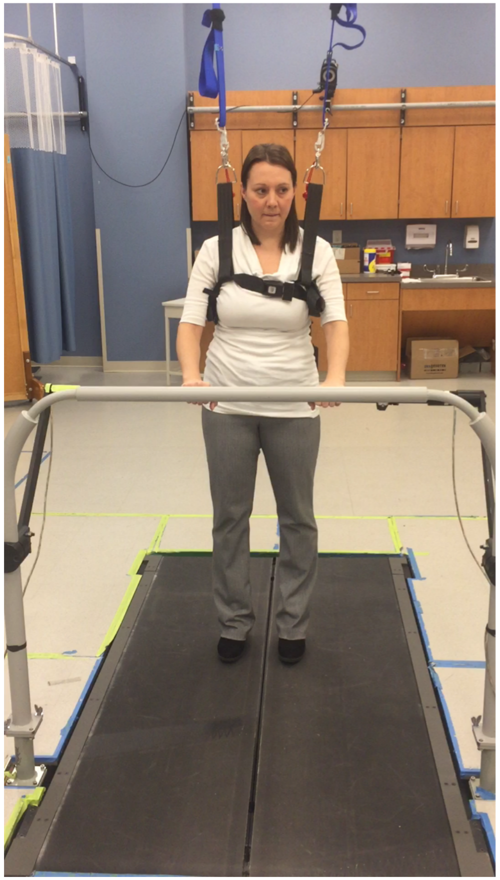


Adapted from [NYU's Math Tools for Neural Science]

Can we apply a computational approach to locomotor learning in individuals with stroke?

- **Modeling goal:** Characterize locomotor adaptation of individuals with stroke across 2 days of training

- **Split-belt paradigm:**
  - Belts split at 2:1 ratio to introduce stepping asymmetry
  - Picked leg that would exaggerate step asymmetry to go on slow belt
  - Adaptation leads to improved step symmetry (Reisman et al 2007)



Charalambous et al (2018)

Can we apply a computational approach to locomotor learning in individuals with stroke?

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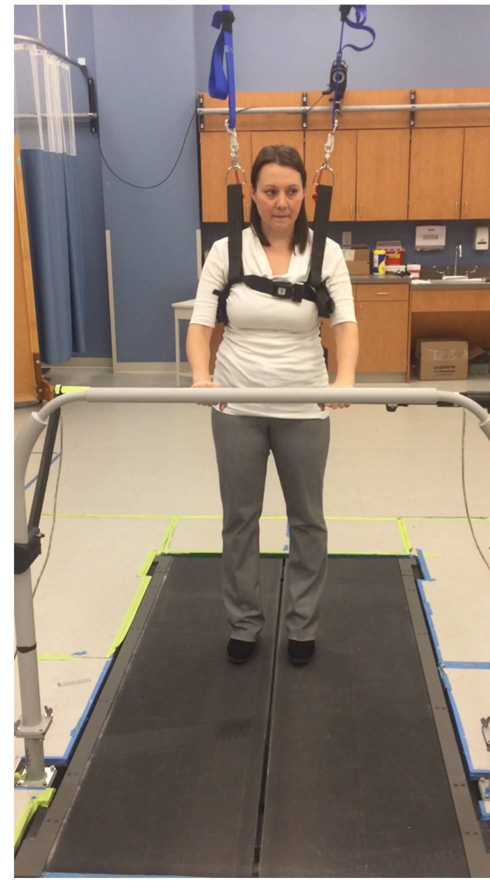
- **Block design:**

Day 1		Day 2
15 minutes split-belt adaptation	24 hours	15 minutes split-belt adaptation



Charalambous et al (2018)

Can we apply a computational approach to locomotor learning in individuals with stroke?

- **Modeling goal:** Characterize locomotor adaptation of individuals with stroke across 2 days of training

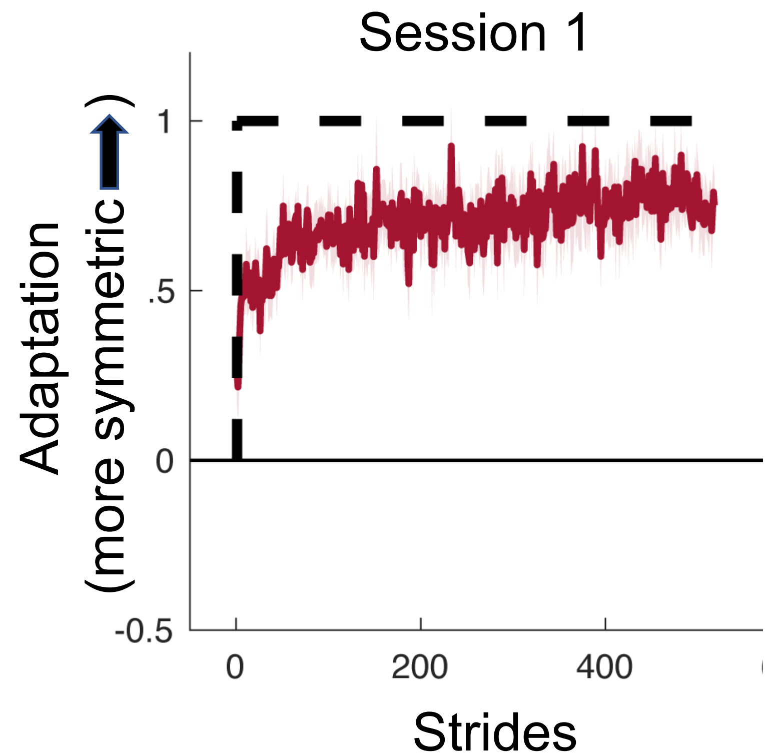
- **Primary dependent variable:**

$$Step\ length\ asymmetry(SLA) = \frac{SL_{slow} - SL_{fast}}{SL_{slow} + SL_{fast}}$$

Maximum step-length asymmetry

$$x(n) = \frac{Perturbation - SLA(n)}{Perturbation}$$

Adaptation metric

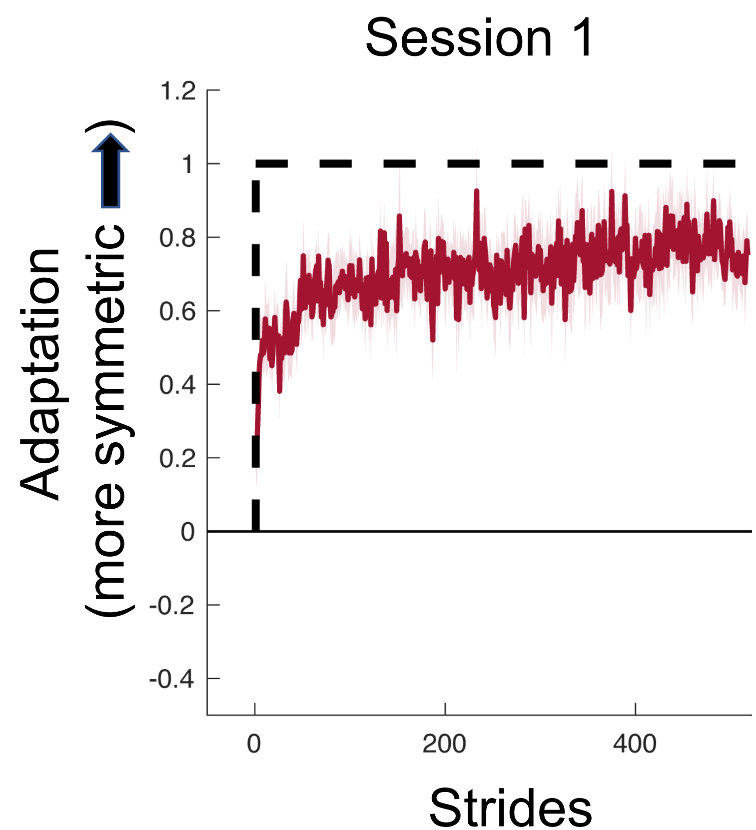


Scales values to be between 0 and 1, with 1 representing baseline symmetry

Charalambous et al (2018)

Multi-rate state-space model of adaptation

- Inspired by basic research showing that different parts of motor system learn on different timescales



Smith et al (2006)

Multi-rate state-space model of adaptation

- **Error signal:**

Baseline symmetry

$$e(n) = 1 - x(n)$$

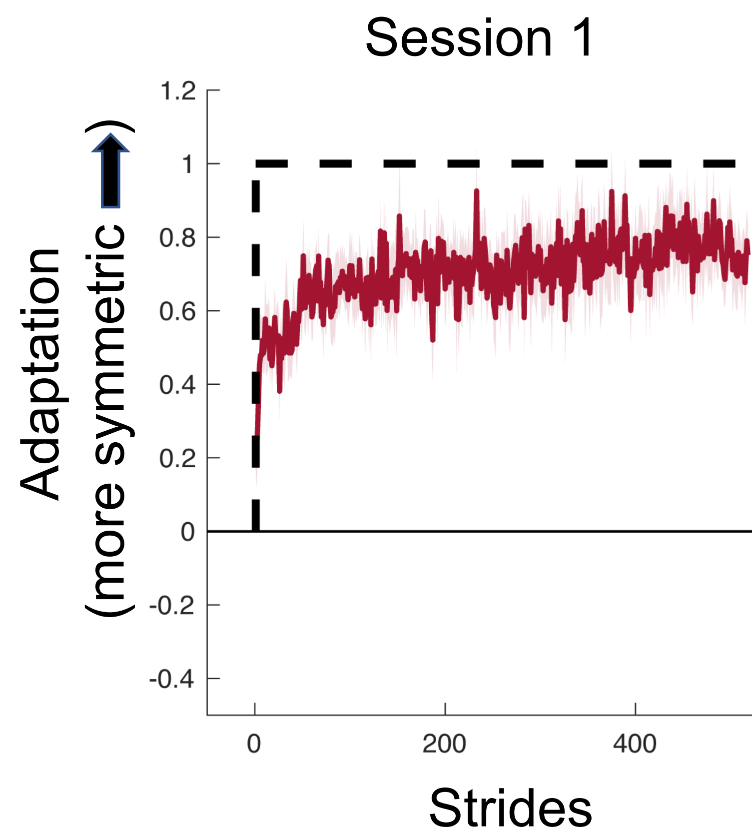
error on stride *n* adaptation

- **Error correction algorithm:**

retention factor learning rate

$$x(n+1) = A \bullet x(n) + B \bullet e(n)$$

The brain tries to minimize this error



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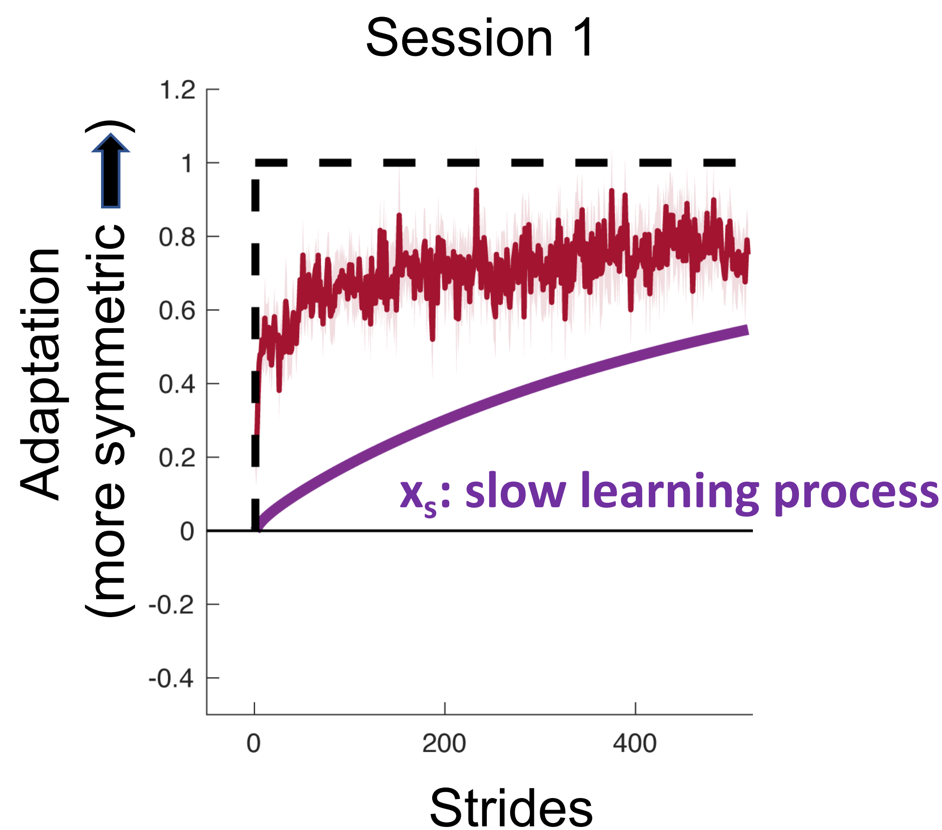
$$x_s(n+1) = A_s \bullet x_s(n) + B_s \bullet e(n)$$



Smith et al (2006)

Multi-rate state-space model of adaptation

- **Error signal:**

Baseline symmetry

$$e(n) = 1 - x(n)$$

error on stride *n* adaptation

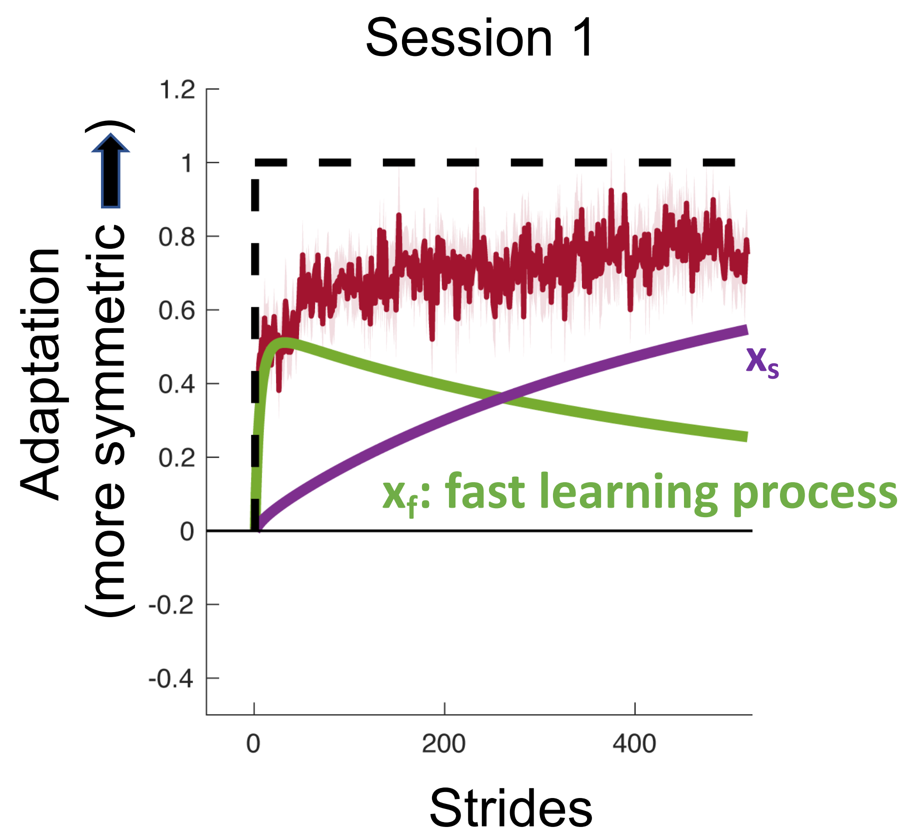
Motor system tries to minimize this error

- **Error correction algorithm:**

retention factor learning rate

$$x_s(n+1) = A_s \bullet x_s(n) + B_s \bullet e(n)$$

$$x_f(n+1) = A_f \bullet x_f(n) + B_f \bullet e(n)$$



Smith et al (2006)

Multi-rate state-space model of adaptation

- **Error signal:**

Baseline symmetry

$$e(n) = 1 - x(n)$$

error on stride *n* adaptation

Motor system tries to minimize this error

- **Error correction algorithm:**

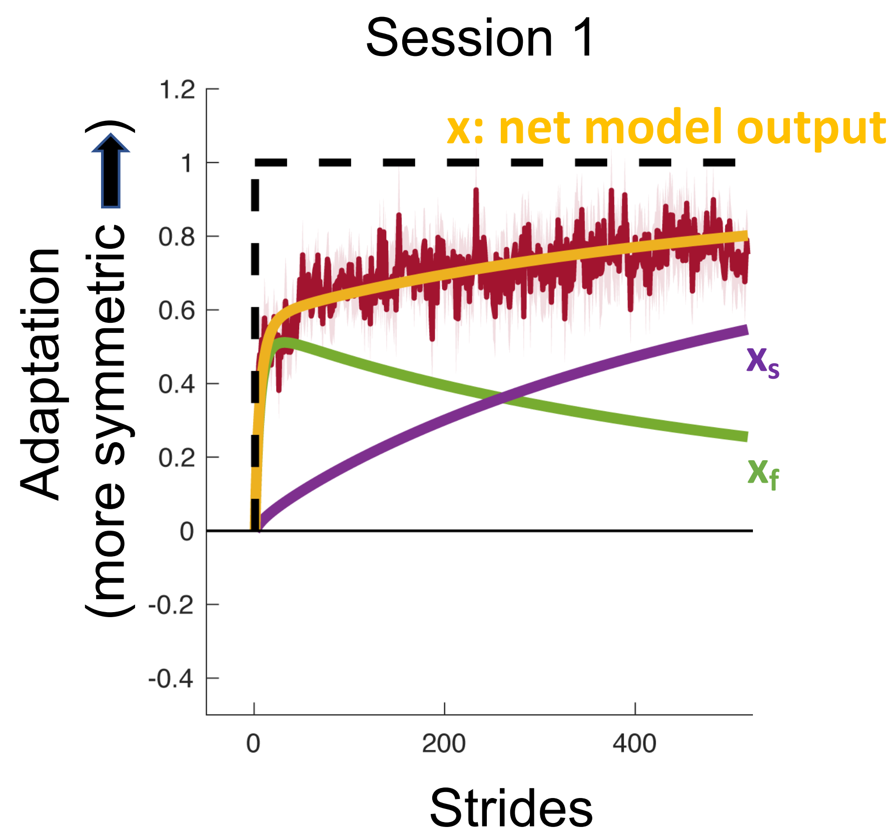
retention factor learning rate

$$x_s(n+1) = A_s \bullet x_s(n) + B_s \bullet e(n)$$

$$x_f(n+1) = A_f \bullet x_f(n) + B_f \bullet e(n)$$

$$A_s > A_f,\ B_f > B_s$$

$$x(n) = x_s(n) + x_f(n)$$



Smith et al (2006)

Predicting 24-hour retention using model

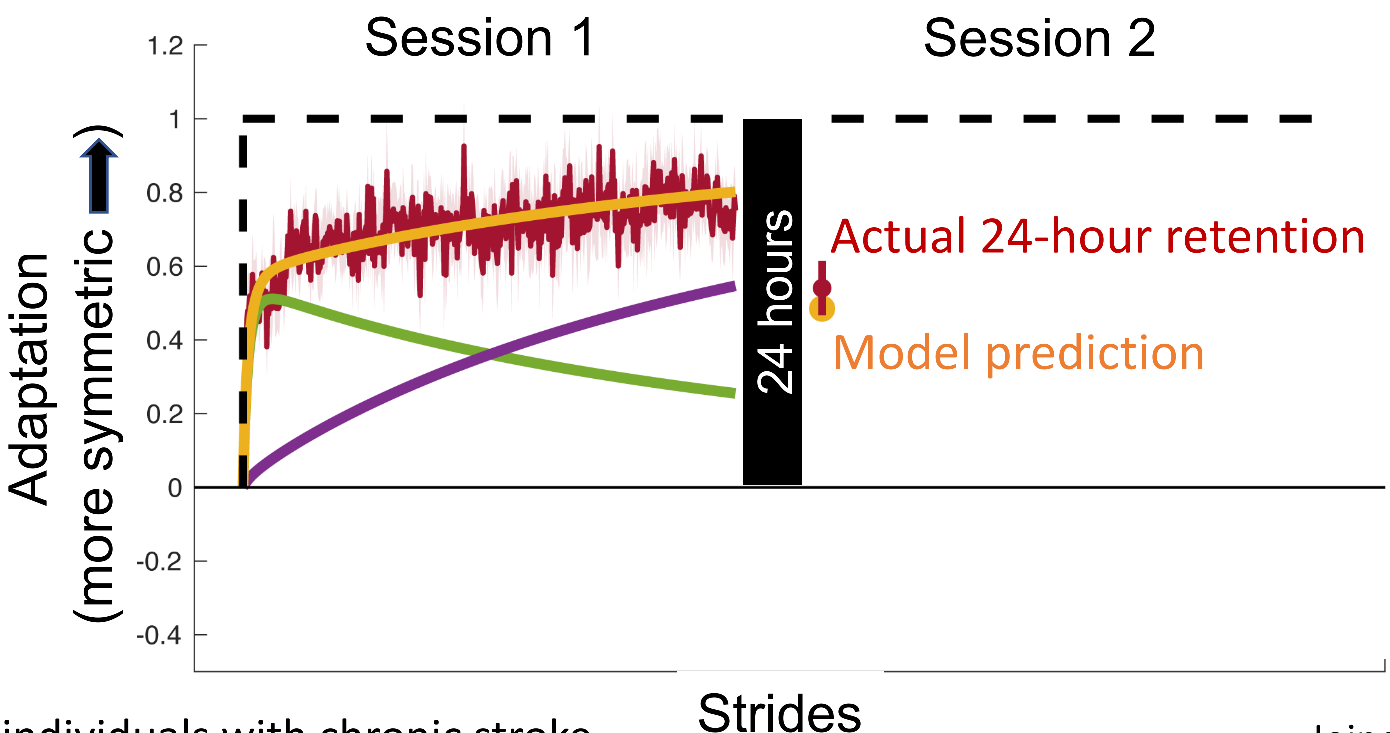
- Taking one step further: Can we also explain 24-hour retention?

$$\textit{24-hour retention} = \alpha \bullet x_f(n) + \beta \bullet x_s(n)$$

Proportion of adaptation retained from end of day 1 to start of day 2

final stride of Day 1

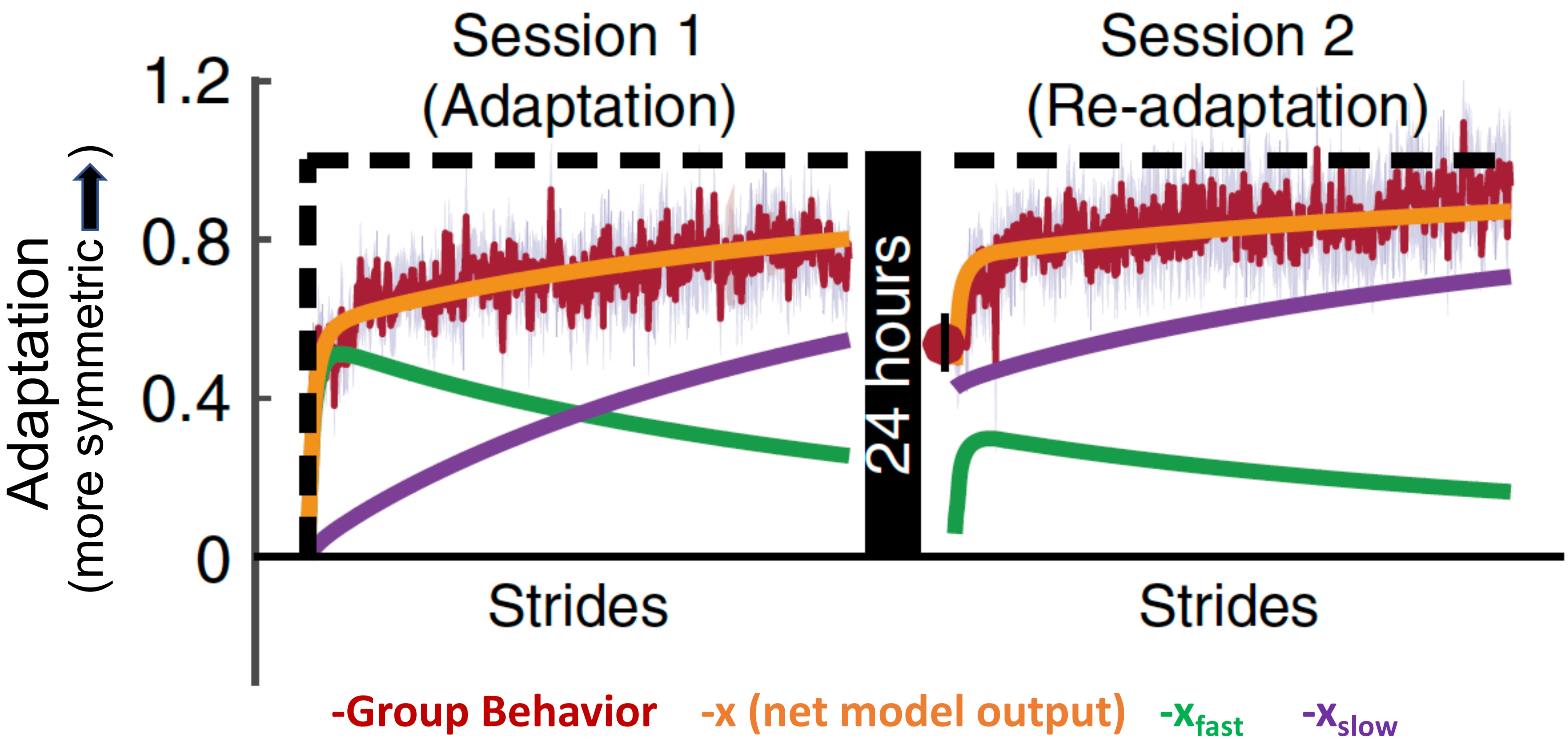
α, β are weights on x_f and x_s



N = 13 individuals with chronic stroke

Joiner and Smith (2008)

Computational models capture locomotor learning and 24-retention in stroke-affected individuals



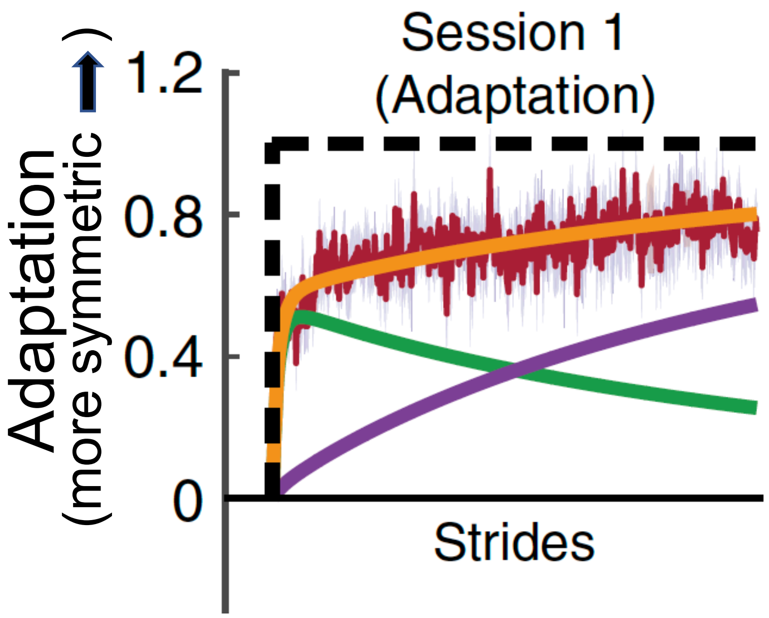
Models accurately characterize adaptation on Days 1 and 2, and 24-hour retention

N = 13 individuals with chronic stroke

Charalambous et al (2018)

What did we learn from modeling?

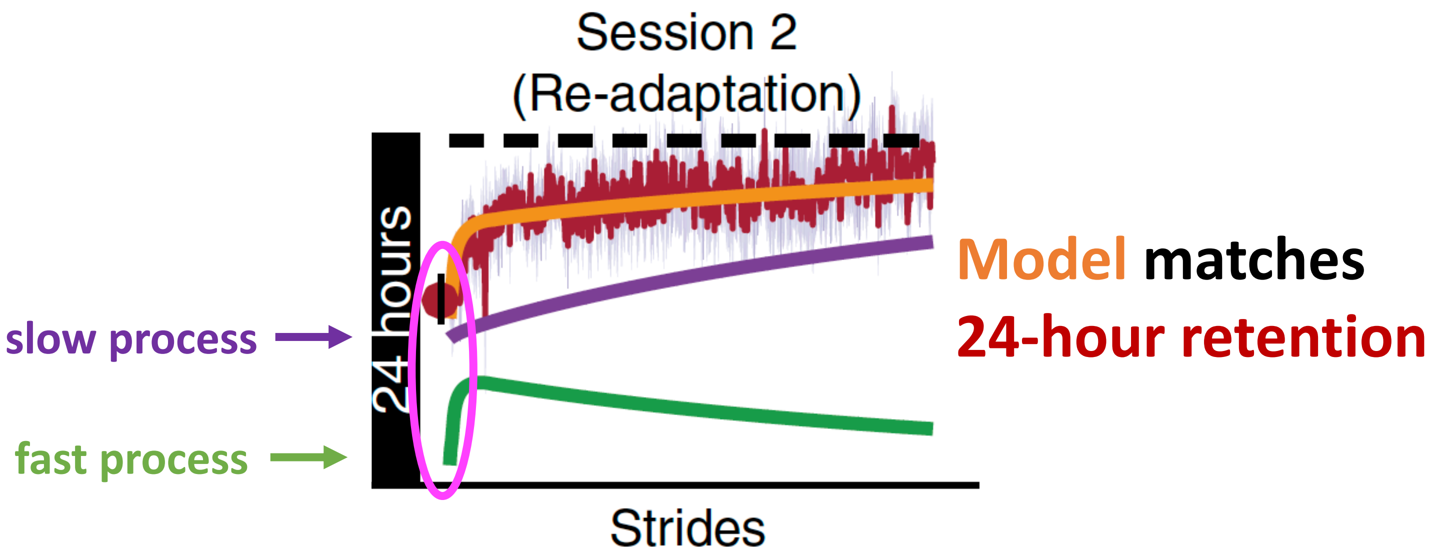
- Strong evidence of learning at two different time-scales



- Modeling reveals two unobserved processes that constitute overall adaptation – impossible to know without modeling
- *How can this advance neurorehab?*
  - *Provides more well-defined targets for intervention*
  - *Different learning processes may respond better or worse to different forms of intervention*

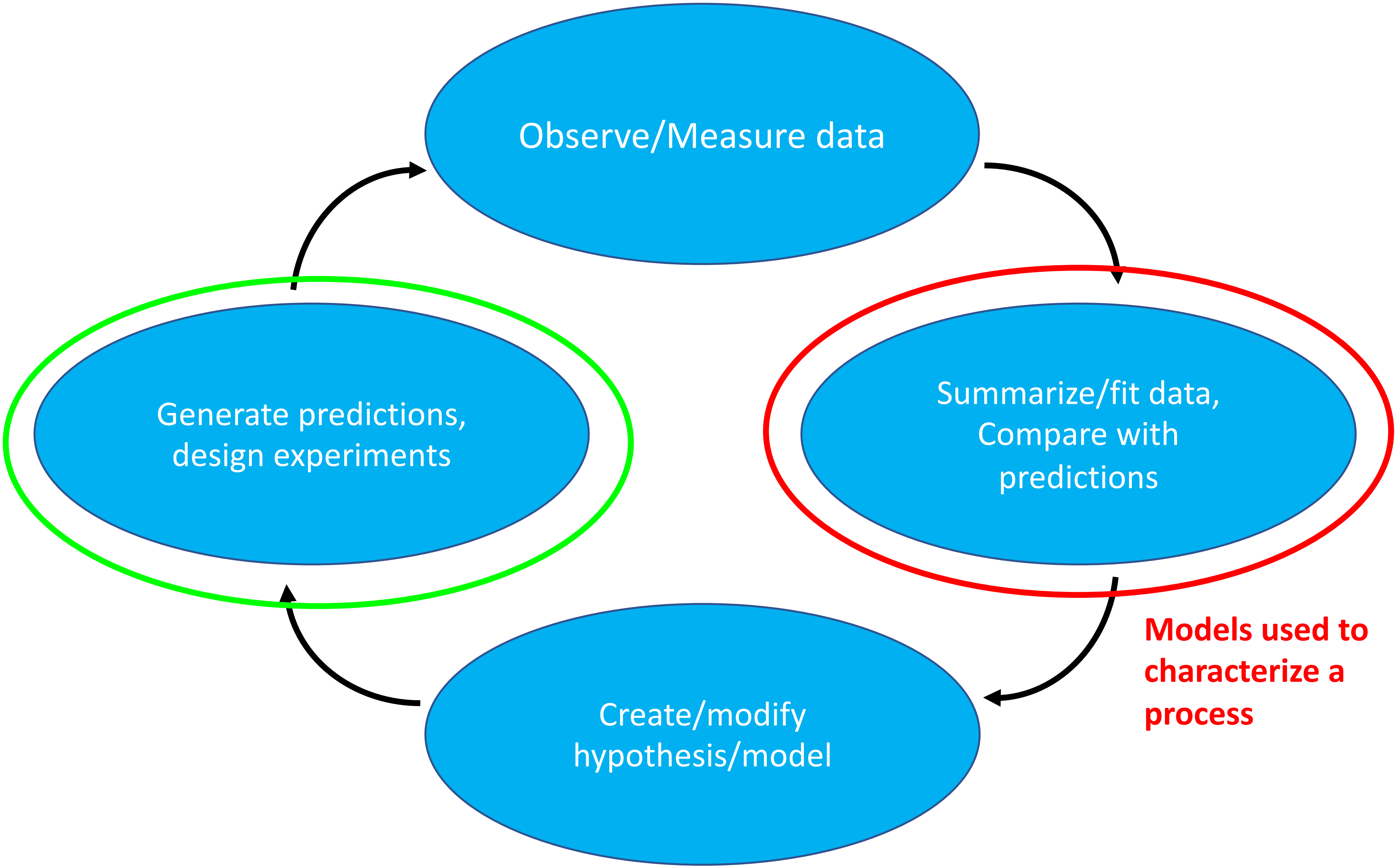
What did we learn from modeling?

- 24-hour retention was mostly due to slow learning process



- *How can this advance neurorehab?*
  - *Provides rationale for extensive training on interventions that target slow adaptation process (e.g., more implicit forms of learning like split-belt adaptation)*

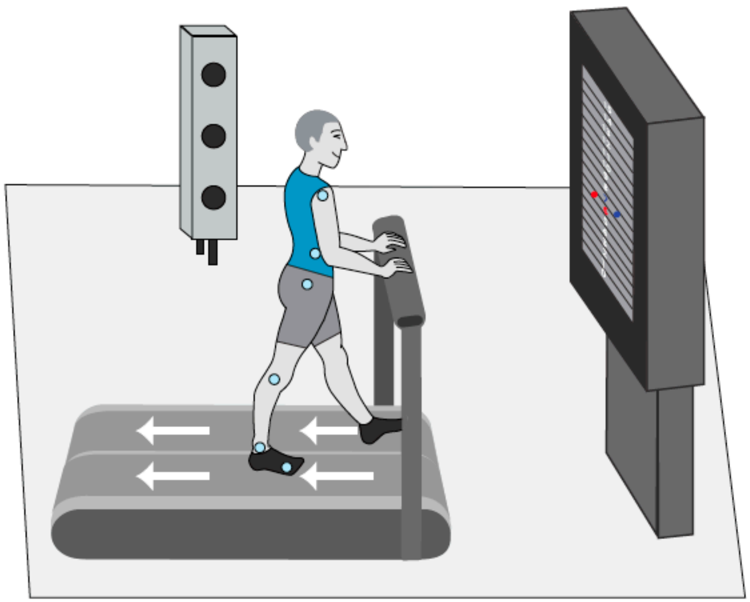
Models can be used to design future experiments

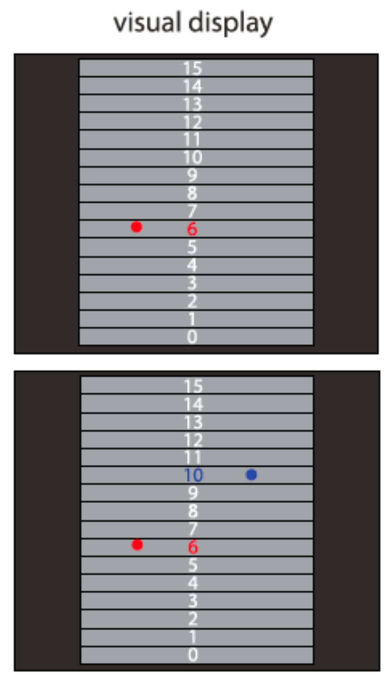


Adapted from NYU's Math Tools for Neural Science

Future directions: How are strategic motor learning processes impacted by stroke?

- Modeling contributions of explicit strategies to stroke-affected locomotor adaptation





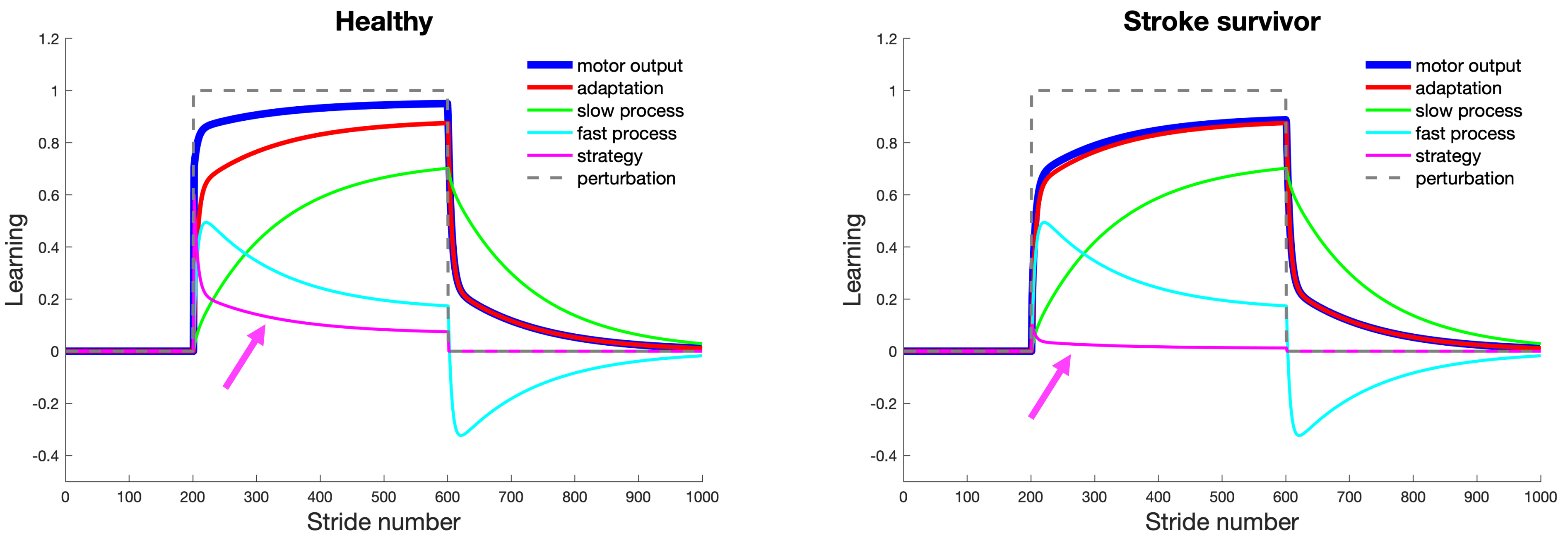
Split-belt adaptation with visual feedback of step asymmetry

Visual feedback drives explicit learning

Roemmich et al (2016)

Simulating predicted outcomes on task

- Prediction:



Remember that we can only directly observe the blue function (sum of all the other curves)

Differences in performance determined by relative contributions of **explicit strategies**

What are the benefits of computational modeling?

A few things ***good*** models can do:

- Capture key components of a complex system/behavior ✓
- Advance our mechanistic understanding ✓
  - Predict variables that cannot be directly measured ✓
- Generate testable (falsifiable) predictions ✓

(adapted from 2017 Computational Sensory Motor Neuroscience Summer School:
http://compneurosci.com/wiki/index.php/CoSMo_2017)

Thank you!

You can download slides and simulation code here:
https://github.com/hyosubkim/CSM2020

What are the benefits of computational *thinking*?

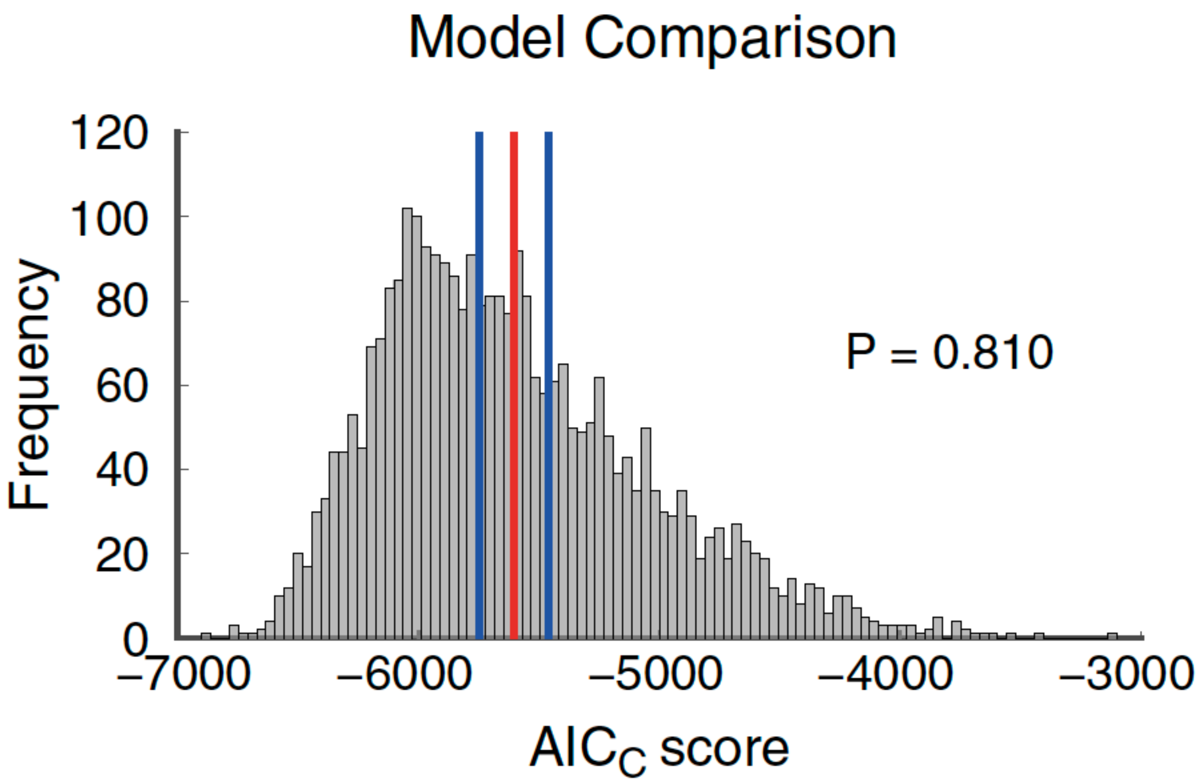
"I've noticed an interesting trend. Pick any field X, from archeology to zoology. There either is now a 'computational X' or there soon will be. And it's widely viewed as the future of the field…doing [computational thinking] well is going to be a key to success in almost all future careers."

-Stephen Wolfram

(Founder & CEO of Wolfram Research; creator of Mathematica, Wolfram|Alpha)

What did we learn from modeling?

- Trial-by-trial learning and retention did not improve on Day 2



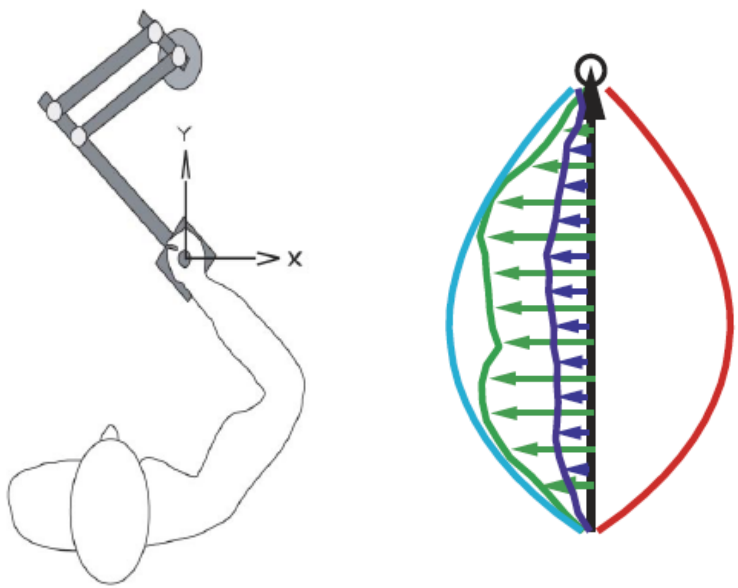
Fitting day 2 data with different parameter values did not improve objective model selection scores

Charalambous et al (2018)

- Does exercise priming improve locomotor adaptation?
  - What could we get from modeling that we can't from standard approaches?
  - Standard approach: Examine behavioral measures and compare across groups
  - Computational approach: Formalize intuitions about underlying processes; Identify key factors/components of the system
  - Is one of these processes related more to 24 hour retention?

Computational models have advanced understanding of error-based learning/sensorimotor adaptation…

Force-field adaptation:



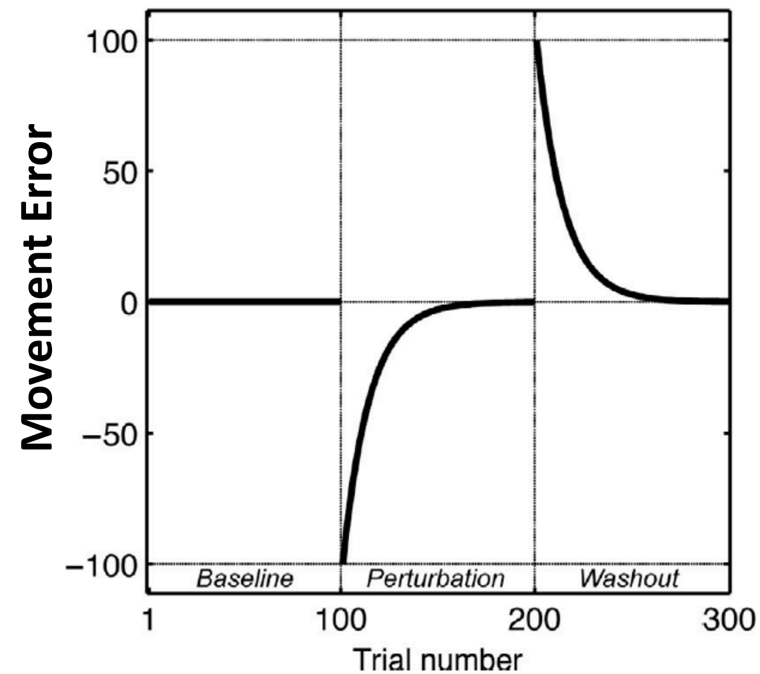
Robot-applied forces

Ideal compensatory forces

Force patterns produced early

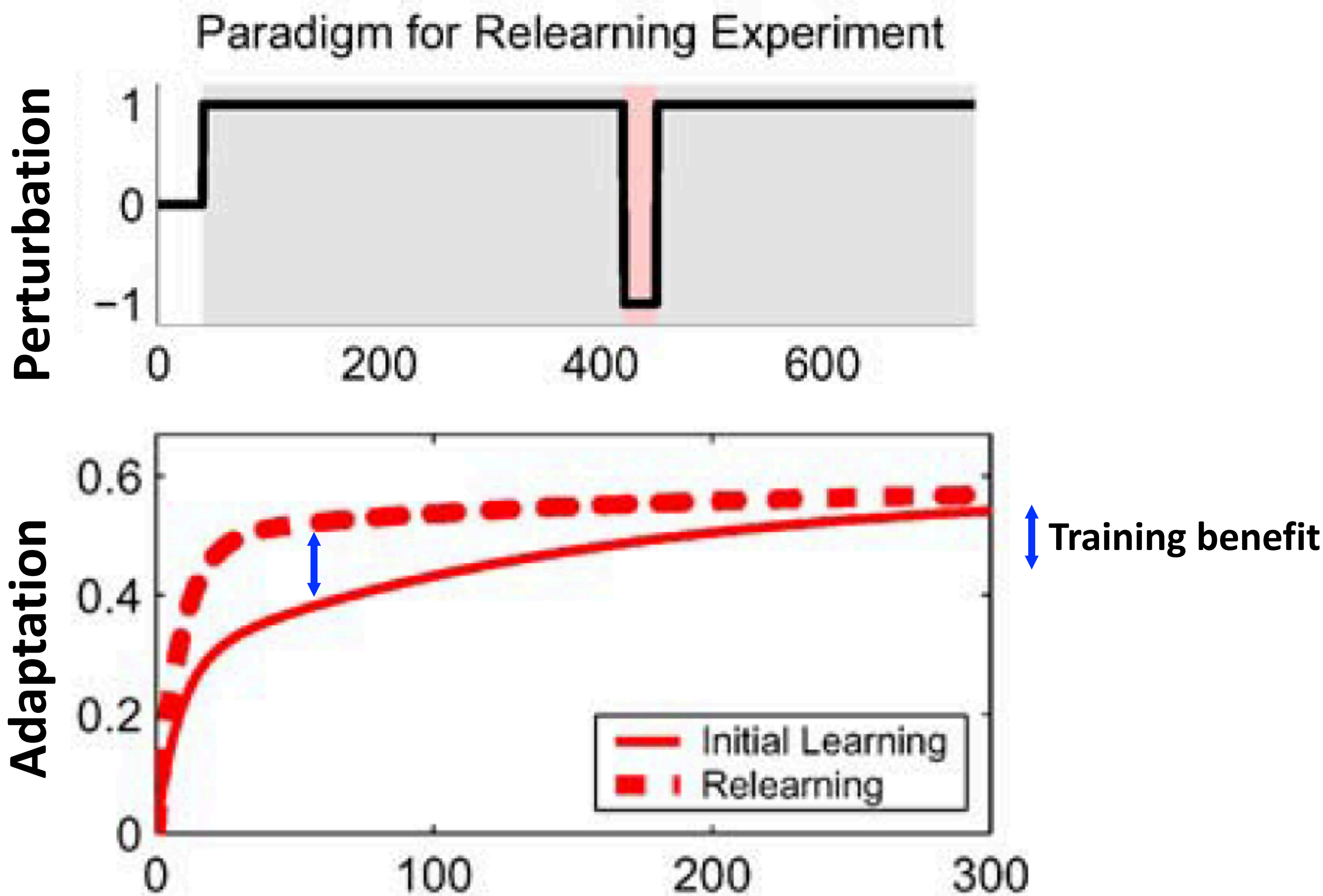
Force patterns produced late

Typical sensorimotor adaptation function



Joiner and Smith (2008); Taylor and Ivry (2014)

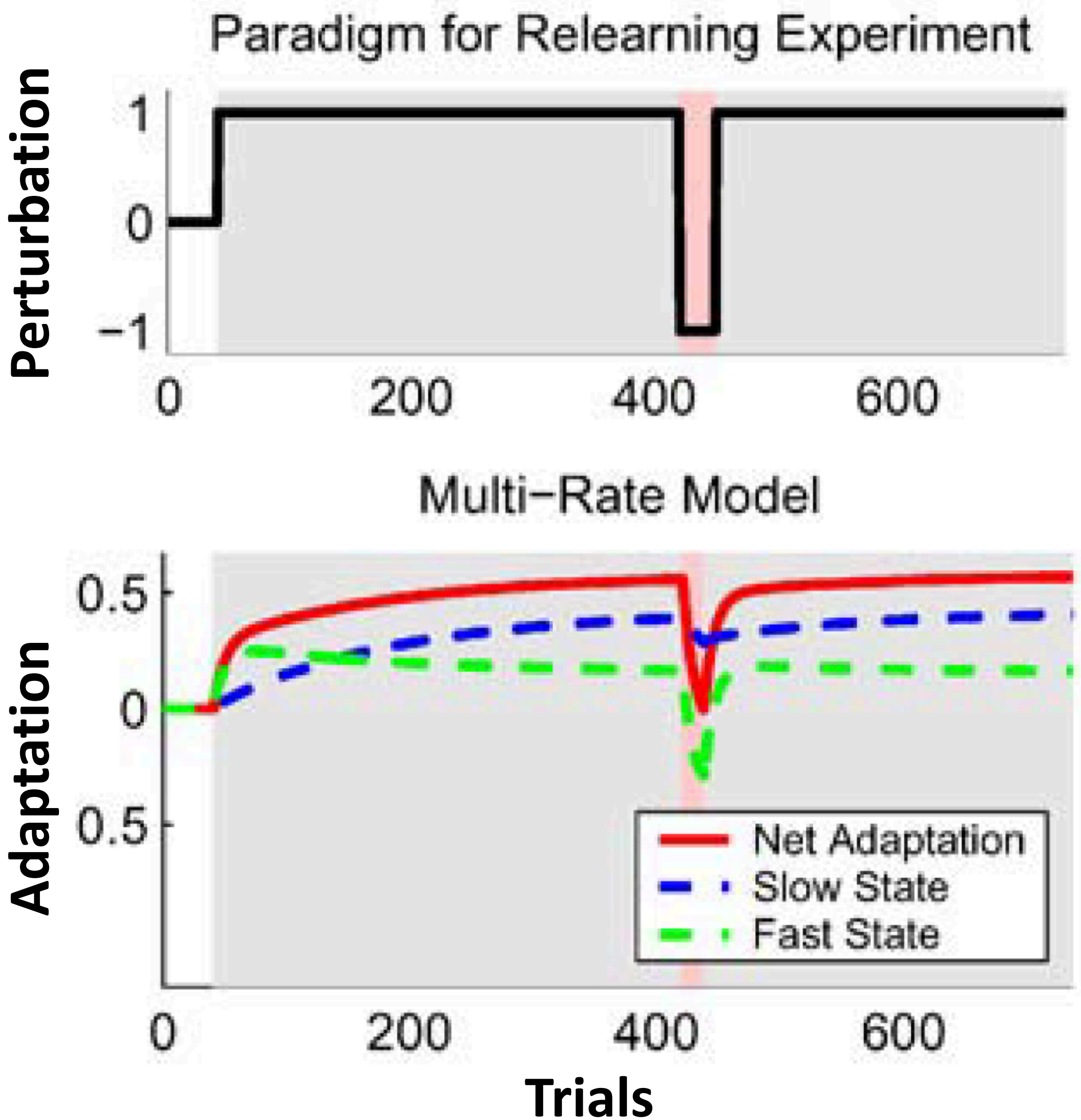
…as well as "savings" (faster relearning)



Understanding necessary components for savings and retention is first step in designing more effective therapies.

Smith et al (2006)

Model explains savings as result of interacting adaptive processes acting on different time scales



Slow and **fast** states cannot be measured directly

Smith et al (2006)