Computational Psychiatry and Neuroscience: Scientific Gaps and Funding Opportunities

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Agenda

- Explainable Artificial Intelligence for closed-loop behavioral neuromod
- Data-driven validations of RDoC constructs
- Computationally-Defined Behaviors for Back-Translation
- Many FOAs

Explainable Artificial Intelligence for Decoding and Modulating Behaviorally-Activated Brain Circuits

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Explainable Artificial Intelligence for Decoding and Modulating Behaviorally-Activated Brain Circuits

Goal:

To develop eXplainable Artificial Intelligence (XAI) solutions for behavioral neuromod.

XAI approaches combine machine learning with effective explanatory methods to enable a mechanistic understanding of the solutions provided by the computational model.

Approach:

XAI would integrate theory- and data-driven models for precise solutions and causal explanations of closed-loop neuromodulation of brain and behavioral signals (multimodal datasets).

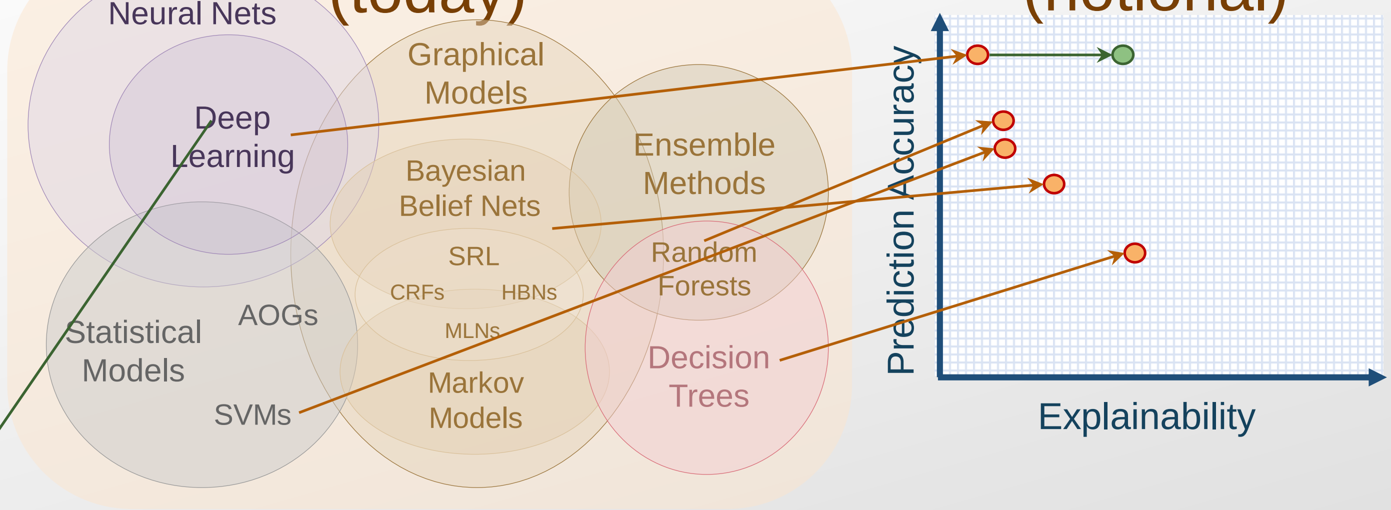
Explainable Artificial Intelligence for Decoding and Modulating Behaviorally-Activated Brain Circuits

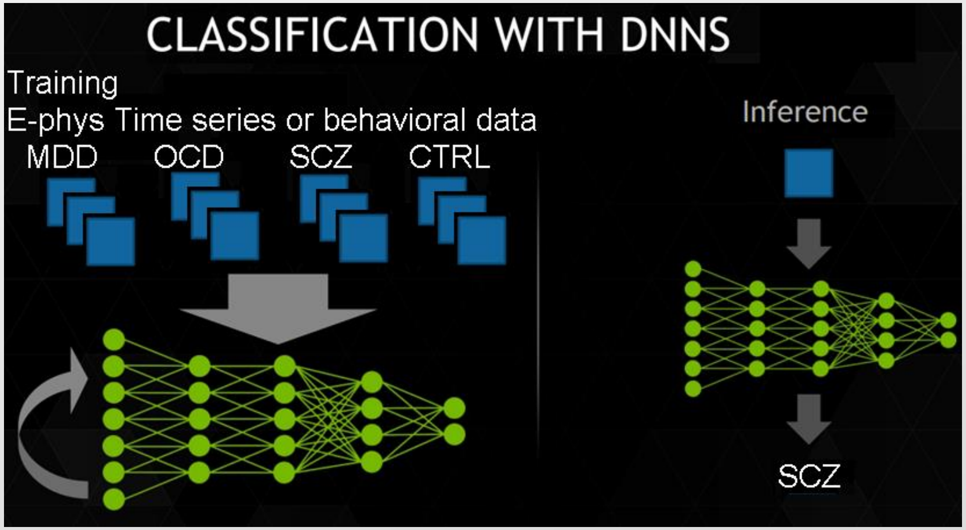
New Approach

Create machine learning techniques that produce more explainable models, while maintaining a high level of learning performance

Learning Techniques (today)

Explainability (notional)





Deep Explanation

Modified deep-learning techniques to learn explainable features from the signals across the nodes of the network:

Hierarchy of physiology

EPSCs → Cell firing → Oscillations → Synchrony between regions

Temporal structure in behavior to identify "atomic" components

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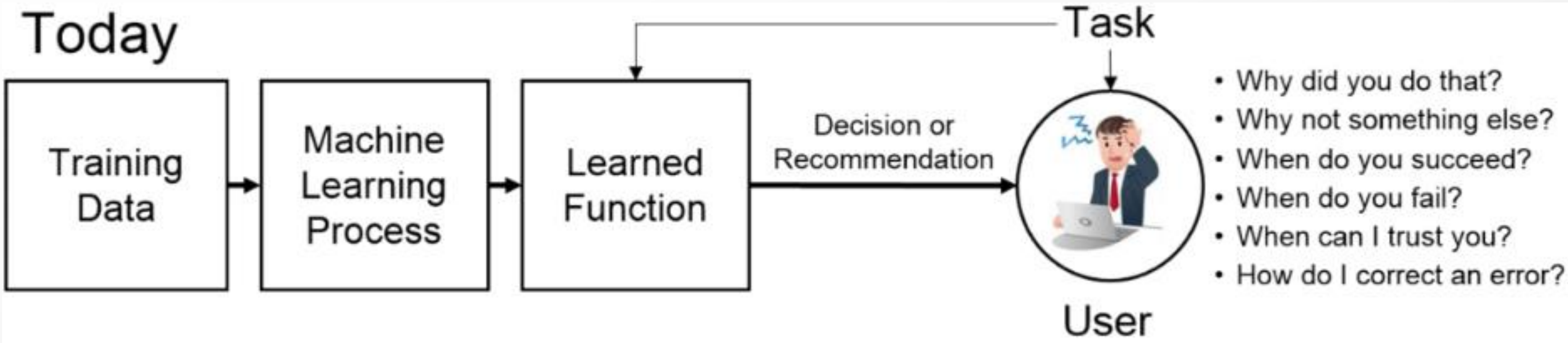
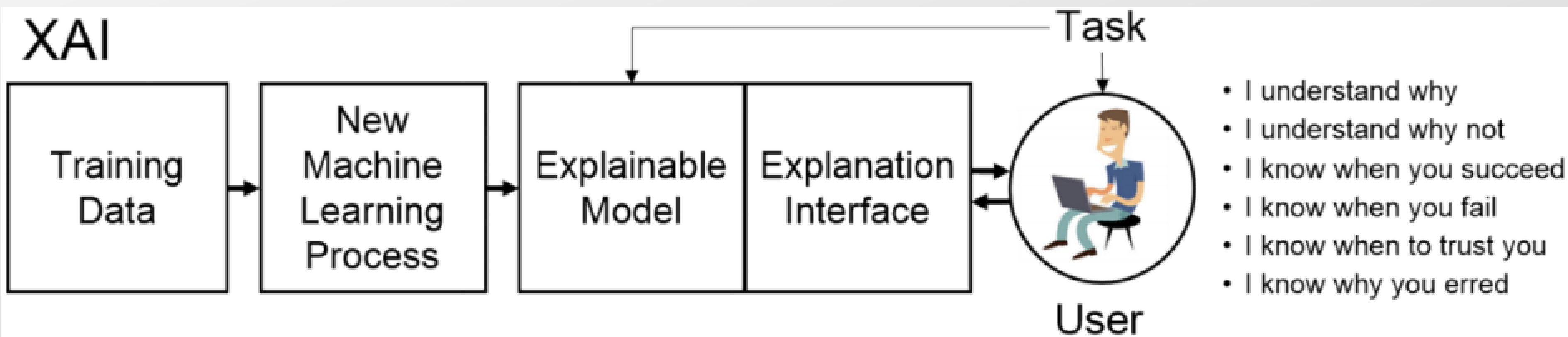
Background: Changing Deep-learning for Mental Health



Deep-learning is great at classifying and predicting but terrible at explaining



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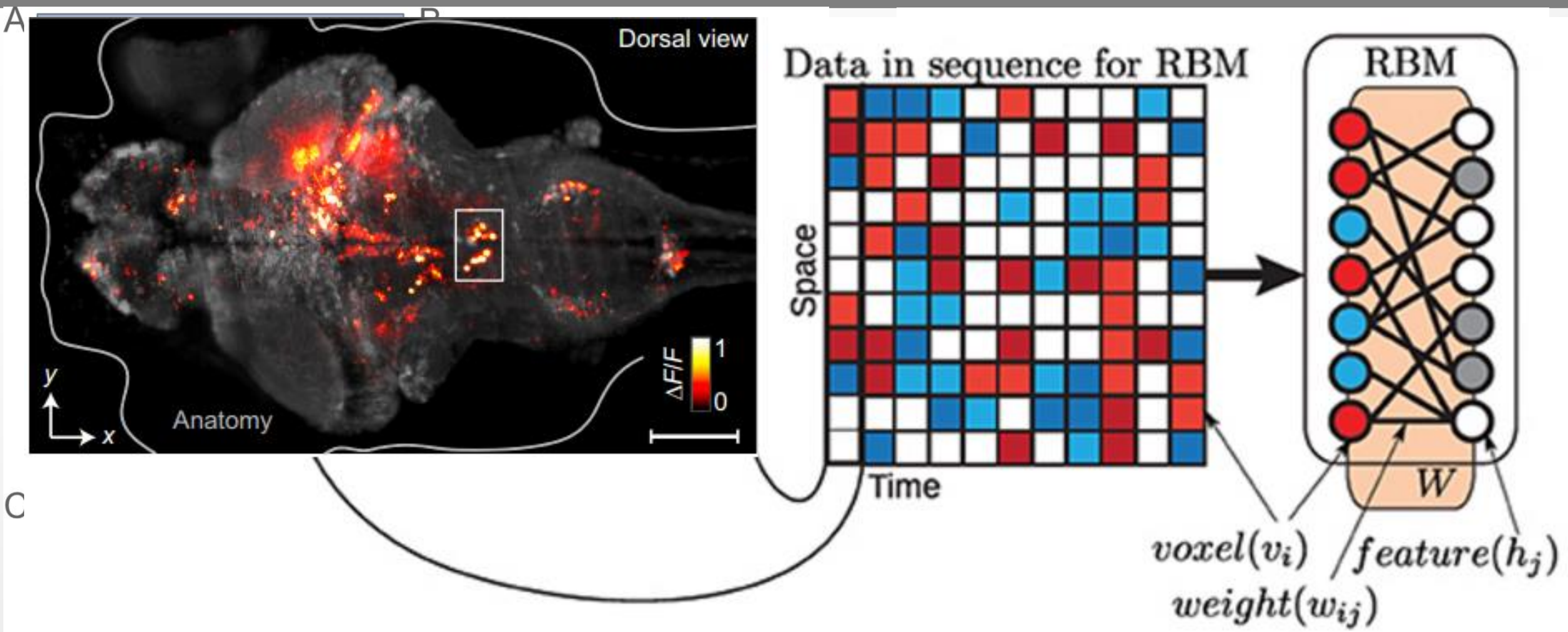
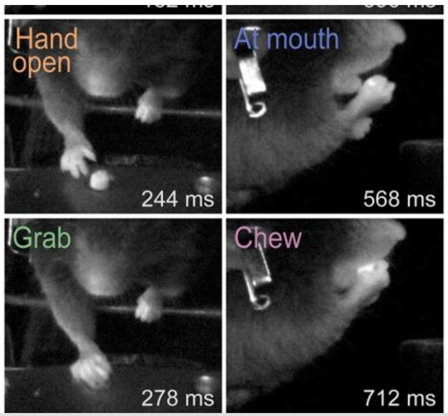
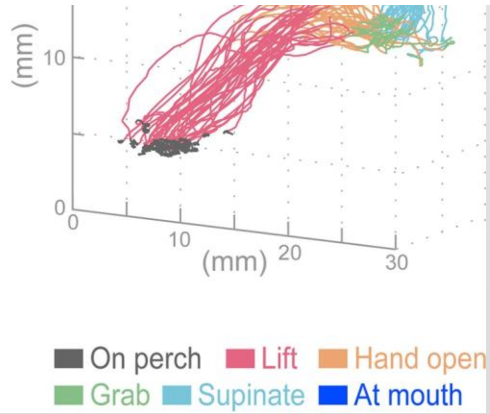
Rationale: Fusing neural and behavioral data for unbiased closed-loop neuromodulation







Multiple trials to identify the activity patterns characterizing right and wrong responses.

Optimizing behavioral outcome by adaptively biasing the neural signal?

Research Objectives: Intelligently Altering Function in Neural Circuits to Affect Behavior

How to implement XAI solutions:

- Integrate data-driven and theory-driven models (e.g., Connect DL with biophysically informed models)
- Label model's features with semantic info (e.g., peak theta oscill.)
- Design models with the sole purpose of explanation

Workshop informing this FOA: SfN satellite on XAI (Nov 2017)
Feasibility: DARPA has a program in XAI

These approaches may provide:

- **Solutions**: Where, when, and how to stimulate to change behaviors.
- **Explanations**: Why this stimulation works and others won't.

Enabling a greater understanding of the circuit-level determinants of behaviors by creating new breakthroughs in multimodal data analytics and the generation of new unbiased brain theories.

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Computational Approaches for Validating Dimensional Constructs of Relevance to Psychopathology

RFA-MH-19-242

Application Due Date(s): December 3, 2018
October 20, 2019, 2020

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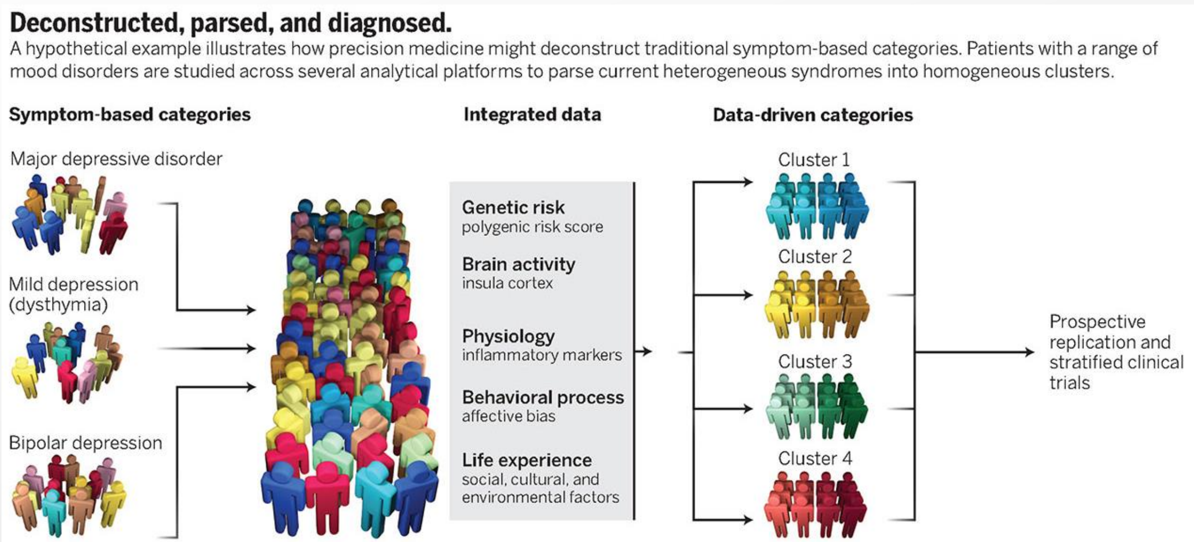
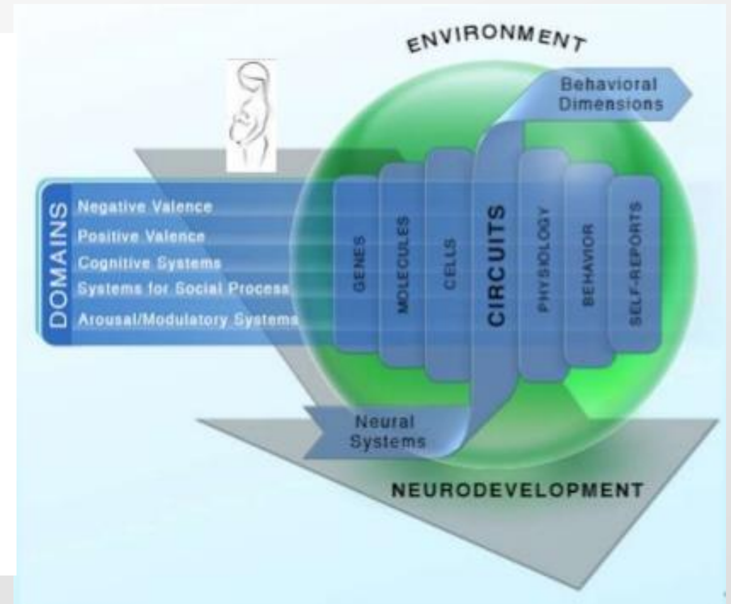
Data-driven validations of RDoC





NIMH is interested in:

1. Fostering **collaborations between clinical researchers & computational neuroscientists** using theory-driven and/or data-driven models
2. Must include at least:
    a) **Two constructs**; these may be existing RDoC constructs or constructs that do not appear in the matrix but meet the criteria provided above.
    b) **At least two levels of analysis** (brain-based measure & behavior)
    c) **Multiple behavioral tasks per construct**, for convergent validity. Using distinct tasks will enable a broader, more dynamic, and complex definition of each construct.
3. Utilizing **accelerated longitudinal studies** (focusing on childhood & adolescence) to predict optimal neurodevelopmental stage for interventions
4. Explicating the dimensions and constructs of interest through the inclusion of **healthy subjects & patients from multiple diagnostic groups.**

Goal: Perform unbiased data-driven validation of existing constructs that may involve **finding continua**, **merging**, **subdividing**, or **hierarchically organizing** constructs by integrating data between and within constructs.

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Research Objectives

1. Data-driven updates into the RDoC matrix for dimensional psychopathology
2. New computational psychiatry platforms to study large cohorts (e.g., All-Of-Us/Precision Medicine Initiative)
3. New neuro-behavioral markers in heterogeneous populations that can be used for targeted treatments and to better predict who will respond

Computationally-Defined Behaviors in Psychiatry

RFA-MH-19-240

Application Due Date(s): November 20, 2018
2019
2020

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Computationally-defined behaviors

- Translational research requires the ability to investigate mental-health relevant questions and neurobiological mechanisms in both humans & animals (e.g., rodents).

- Rigorous research requires assays that capture behavioral complexity by defining sub-components (*parameters),* specifying the relationships between these parameters, and applying sensitive, quantitative measurement techniques.

- **Goal**: To apply computational approaches to highly parameterizable and back-translatable behavioral assays across mental-health relevant domains of function.

Longer Term Goals

Back-Translation:

- Testing and validation in animals.
- Integration with causal neurobiological experimental designs to expand mechanistic understanding.
- Integration into pre-clinical study designs for more predictive, translatable therapeutic discovery in animals.

Clinical Applications:

- Classification and quantification of behavioral heterogeneity in humans.
- Integration with neurobiological measures to expand understanding of underlying pathophysiology.
- Determination of therapeutic strategies and stratification of patients for treatment decisions.

Computationally Informed Behavioral Assay Development

A theoretical model of a behavioral phenotype can be achieved by:

- **Breaking down the behavior into fine-grained parameters** that can be mathematically described.
- **Integrating the behavioral parameters in an experimentally-grounded mathematical formalism (i.e., a new behavioral theory).** The model should integrate prior experimental findings, allow the tracking of all parameters, and predict behavioral outcomes.
- **Experimentally validating and optimizing these theory-driven models.** Rigorous determination of the relationships between all the behavioral parameters and the behavioral outcomes. Demonstration that the model can make behaviorally accurate predictions for a new experiment or dataset.

Example: A computational model for social interactions

The probability to engage in a given social interaction depends upon a set of parameters:

- Individual social traits at baseline (w_0)
- Value of social reward (SR)
- Value of non-social rewards (NSR)
- Social Prediction Error (SPE)
- SR received by you (Uj) exceeds the SR received by the other (Oj)
- SR received by Oj exceeds Uj
- Forgetting factor (γ)

$$SI_{(t)} = w_0 + w_1 \sum_{j=1}^{t} \gamma^{t-j}\, SR_j \; - w_2 \sum_{j=1}^{t} \gamma^{-j}\, NSR_j \; + w_3 \sum_{j=1}^{t} \gamma^{t-j}\, SPE_j$$

$$+ w_4 \sum_{y=1}^{t} y^{t-j} \max(U_j - O_j, 0) \; + w_5 \sum_{y=1}^{t} y^{t-j} \max(O_j - U_j, 0)$$

Thank you!

Q&A time

Relevant FOAs

- Collaborative Research in Computational Neuroscience (R01) US-France-Israel-Japan-Germany-Spain
- Temporal Dynamics of Neurophysiological Patterns as Potential Targets for Treating Cognitive Deficits in Brain Disorders (R01).
- Predictive Multiscale Models for Biomedical, Biological, Behavioral, Environmental and Clinical Research (U01).
- BRAIN Initiative: Theories, Models and Methods for Analysis of Complex Data from the Brain (R01).
- Administrative Supplements for Advancing Computational Modeling and Data Analytics Relevant to Mental Health, $100K for 1 year, ongoing, April 1st deadline.

For Centers

- P50 Conte Center
- U19 BRAIN Initiative: Team-Research BRAIN Circuit Programs – TeamBCP

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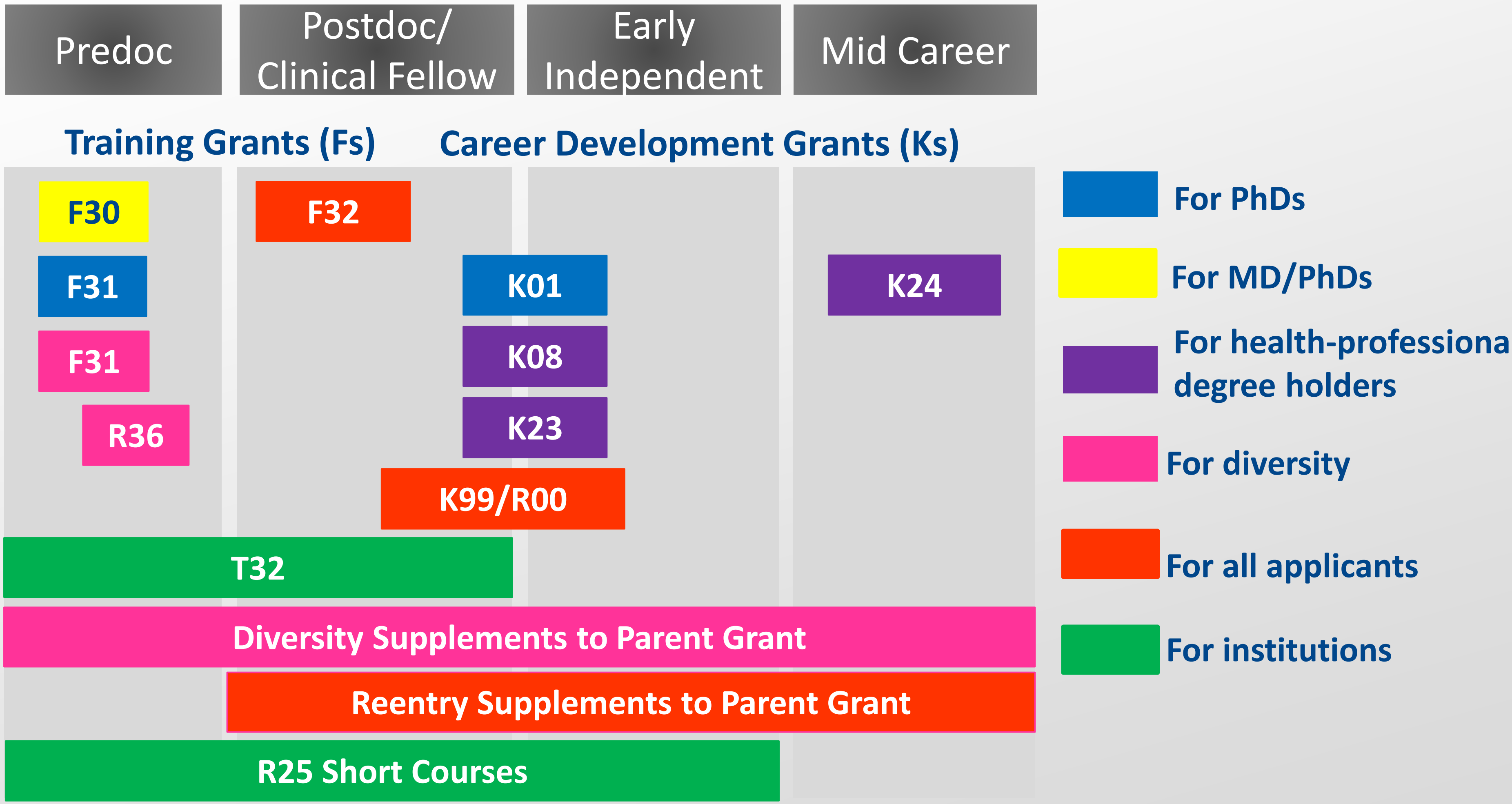
NIMH Training and Career Development Awards



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National Institute of Mental Health Data Archive (NDA)

1. Makes available **human subjects data** collected from hundreds of research projects across many scientific domains.
2. Provides infrastructure for **sharing research data**, **tools**, **methods**, and **analyses** enabling collaborative science and discovery.
3. **De-identified human subjects data, harmonized to a common standard**, are available **to qualified researchers**. **Summary data is available to all**.
4. Mission: accelerate scientific research and discovery through data sharing, data harmonization, and the reporting of research results.
5. **Repositories:**
    1. **NDAR (National DB for Autism Research)**
    2. **NDCT (National DB for Clinical Trials Related to Mental Illness)**
    3. **RDoCdb (Research Domain Criteria DB)**
    4. **ABCD (Adolescent Brain Cognitive Development Study)**
    5. **CCF (The Connectome Coordination Facility)**

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Responsive Projects

- Identify a well-defined question in behavioral science relevant to psychiatry.
- The behavioral targets, models, and parameters should to reflect a dimensional process linked to a specific domain of function.
- Focus on highly-parameterizable behaviors that:
  - Have the potential for back-translation from humans to animals (e.g., rodents).
  - Lend themselves to computational analysis, predictions, & explanations
  - Have not been extensively mathematically modeled (e.g., learning theory)
- Experimentally validate computationally-informed behavioral assay(s) in large "unselected" human populations (mturk, apps, web etc.,).
  - To avoid constricting the range of functioning in the subject sample.

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Computational programs at NIMH

Theoretical and Computational Neuroscience Program
Division of Neuroscience and Basic Behavioral Science, NIMH

This Program supports empirical and theoretical studies of self-organizing behavior in neuronal systems, mathematical approaches to modeling non-stationary neuronal processes, functional imaging of dynamical systems, and the modeling of all levels of neuronal processing, from single cell activity to complex behaviors. Projects typically combine mathematical and computational tools with neurophysiological, neuroanatomical, or neurochemical techniques in order to decipher the mechanisms underlying specific neuronal and behavioral systems.

Computational Psychiatry Program
Division of Translational Research, NIMH

This program fosters biologically-based computational frameworks to identify and validate biomarkers and novel treatment targets relevant to the prevention, treatment, and recovery of psychiatric disorders. The program supports translational research using analytical approaches for the prediction of risk and treatment response and the understanding of the pathophysiology underlying mental disorders.