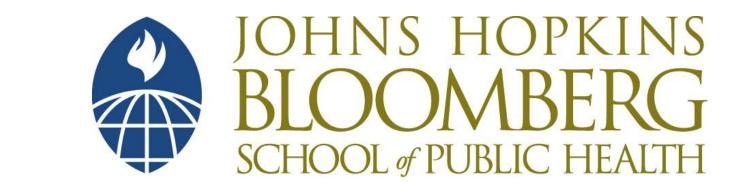


Measuring Stability Across Multiple Domains of Mood and Affect



Yao (Mike) Xiao<sup>1</sup>, Jordan Johns<sup>1,2</sup>, Lihong Cui<sup>1</sup>, Kathleen Merikangas<sup>1</sup>, Vadim Zipunnikov<sup>2</sup>

1 National Institutes of Mental Health Genetic Epidemiology Branch, 2 Johns Hopkins Bloomberg School of PublicHealth Department of Biostatistics

## Introduction

Ecological Momentary Assessment (EMA) is an efficient tool for the real time assessment of daily activities and mood states in large samples. Participants were given a preprogrammed smartphone over the course of two weeks and answered surveys four times a day on topics like mood, diet and sleep quality. Here we focus on six different EMA questionnaire items rated on 1-7 Likert scales:

sad How happy vs sad do you feel

**BP1 Subject** 

 $Z_{bp1} = 0.63$ 

BP2 Subject  $Z_{bp2} = 0.77$ 

Control Subject

Binnorm= 1.33

 $Z_{ctrl} = 0.74$ 

How relaxed vs anxious do you feel right now? anxious

active How inactive vs active do you

energetic do you feel right now? easily angered do energy

How well can you irritable concentrate or focus right now?

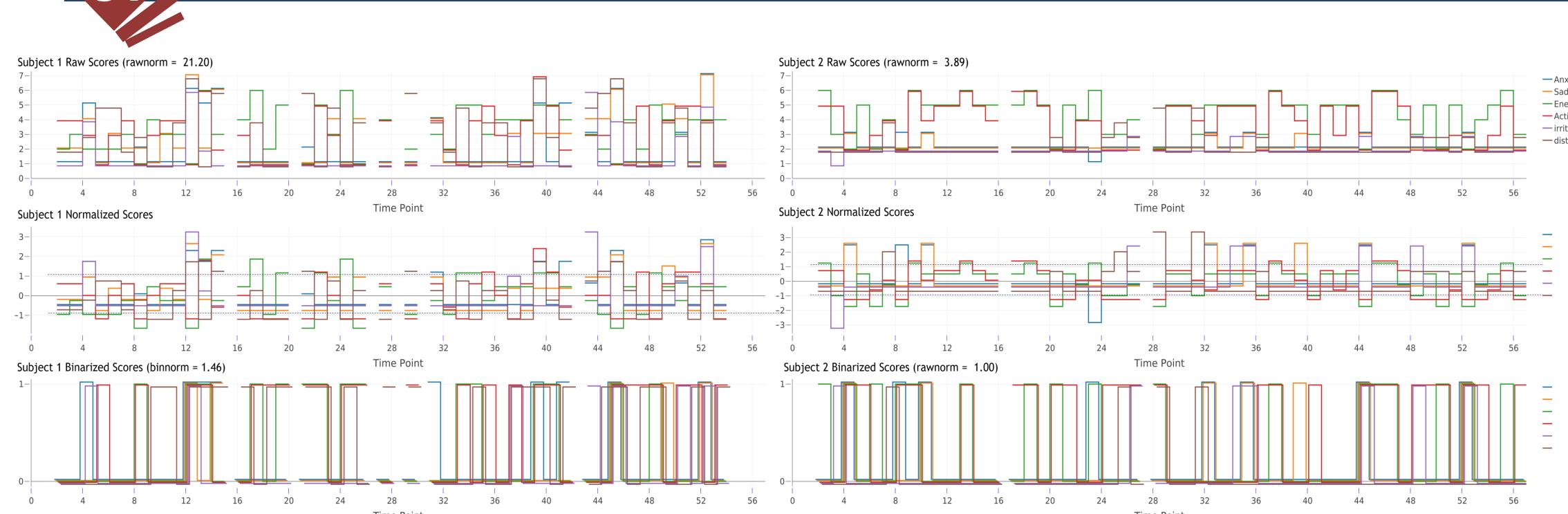
attention

We propose a novel statistical framework for capturing stability within and between domains and use this framework to develop new measures in order to investigate ways that patterns of stability are interconnected across these domains.

#### Questions

- How can we characterize stability in each domain taking into account the subjectivity of the Likert scale responses?
- What are some different ways to aggregate data from all six domains and what are the pros and cons of each approach?
- Which domains tend to affect each other the most with regards to stability, and are these relationships different across diagnostic subgroups (bipolar I, bipolar II, major depression)?

### Methods



bipolar I

bipolar II

control

Binarization (above): Raw scores from each domain are normalized within subject by calculating z-scores with respect to the subject specific mean and standard deviation. This normalized data is then binarized into two states, the O state, defined as the score inside 1 SD of the subject mean, and the 1 state, the score outside 1 SD of the subject mean. Subject 1 uses a large portion of the 1-7 scale for every domain, resulting in a large norm of the Type 2 MMSSD matrix calculated on raw scores. Subject 2 uses a much smaller portion of the scale in all domains except Energy and Activity and as a result has a much smaller raw norm.

However, after the data is binarized and the Type 2 MMSSD matrix norm calculated, the ratio between the scores are much closer, which more accurately reflect the degree to which the patterns in fluctuation in the two subjects are similar.

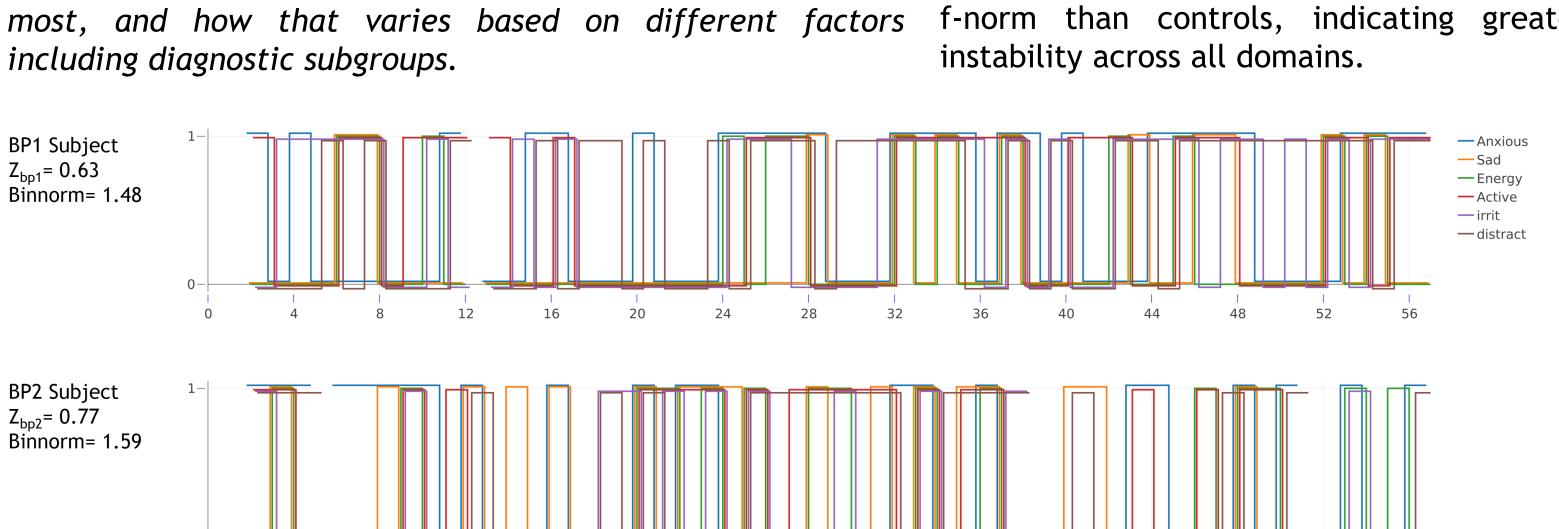
Multivariate MSSD (below): Mean of squared sequential differences, or MSSD, is a traditional measure of variance and stability in EMA data, accounting for shifts in the subject mean over time. When applied to binarized data representing two states, the result can be expressed as a function of joint and marginal probabilities. Using the definitions in the pink box, MSSD for a single domain is exactly equal to the marginal probability that the domain will fluctuate at any given timepoint. We then define several multivariate measures that capture the tendency for a pair of domains to fluctuate together. Type 2 MMSSD for two domains gives exactly the joint probability that domain 1 and 2 will fluctuate together. Type 1 MMSSD is equal to the total probability the two domains fluctuate together in the same direction minus the total probability the two domains fluctuate together in the opposite direction. Additional measures can be derived which capture other probabilities of interest.

Single Domain MSSD  $MSSD(k) = \frac{1}{S'} \sum_{s'} (b_{s+1}^k - b_s^k)^2$ 

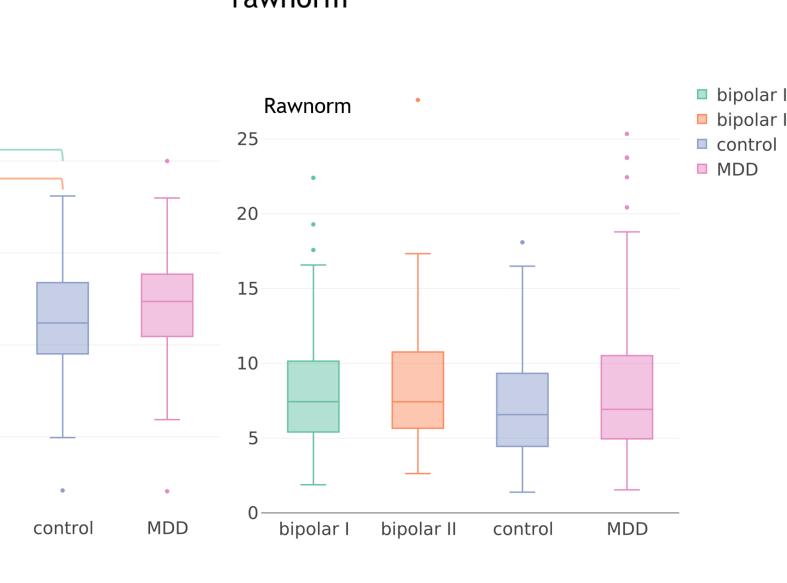
# Examples of Application

domain trajectories of three subjects over the course of 2 the relationship between the f-norm of the Type 2 weeks, recorded at 56 timepoints roughly 4 hours apart MMSSD matrix calculated on raw versus binary throughout each day. The subjects are equally representative scores. The lack of correlation shows that of the subgroup they belong to (bipolar I, bipolar II, control) binarization of the data provides new signals about and were selected based on the Z score of the Type 2 MMSSD patterns of stability that does not overlap with f-norm within their group, which is an aggregate index we variation in the raw data. The boxplots (bottom proposed to measure overall tendency for a subject to right) further show some advantages of the fluctuate within and across the six domains. At every binarization process. (1) The binarized data is more timepoint, you can observe whether each domain is in the 0 resistant to outliers and (2) binarized data may be or 1 state and whether it will fluctuate or stay the same into more sensitive patterns of fluctuation in the data the next timepoint, by itself or simultaneously with other domains. At the population level, it would be interesting to range of the Likert scale response across subjects. parse out the type of signal demonstrated in the plots and We found that BPI (p<0.01) and BP2 (p<0.01) subjects understand which domains tend to affect each other the have significantly higher means of the Type 2 MMSSD most, and how that varies based on different factors including diagnostic subgroups.

Subject profiles (bottom left): These plots show the binary Raw vs. Binarized (top right): This scatterplot shows that may have been masked by the variability in the f-norm than controls, indicating greater overall



1.5

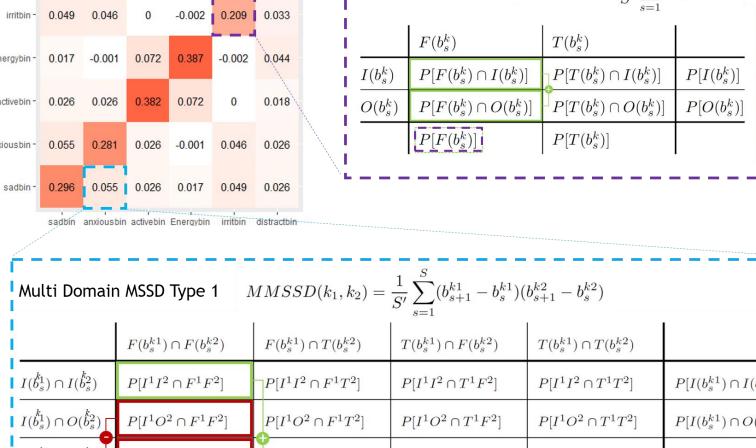


 $O(b_s^k)$  is the event that  $b_s^k = 1$  $F(b_s^k)$  is the event that  $b_s^k$  changes value at the next time point s+1, so when  $b_{s+1}^k - b_s^k \neq 0$ . This represents fluctuation in state.  $T(b_s^k)$  is the event that  $b_s^k$  has the same value at the next time point s+1, so when  $b_{s+1}^k - b_s^k = 0$ . This represents staying in the same state.  $MSSD(k) = \frac{1}{S'} \sum_{s=1}^{\infty} (b_{s+1}^k - b_s^k)^2$ Where S' is the total number of time points s for which  $b_{s+1}$  is known. For a MSSD for Single Domain +1 +1 +1 +1 Type 1 MMSSD for Domain Pair

For domain k and time point s:

 $I(b_s^k)$  is the event that  $b_s^k = 0$ 

 $b_s^k$  is the value of domain k at time point s.  $b_s^k \in \{1,0\}$ 



Multi Domain MSSD Type 1  $MMSSD(k_1,k_2)=rac{1}{S'}\sum_{s=0}^\infty (b_{s+1}^{k1}-b_s^{k1})(b_{s+1}^{k2}-b_s^{k2})$  $F(b_{\circ}^{k1}) \cap F(b_{\circ}^{k2})$   $F(b_{\circ}^{k1}) \cap T(b_{\circ}^{k2})$   $T(b_{\circ}^{k1}) \cap F(b_{\circ}^{k2})$   $T(b_{\circ}^{k1}) \cap T(b_{\circ}^{k2})$  $P[I^1O^2 \cap T^1T^2]$  $P[I(b_s^{k1}) \cap O(b_s^{k2})]$  $O(b_s^{k_1}) \cap I(b_s^{k_2})$   $P[O^1I^2 \cap F^1F^2]$  $O(\hat{b}_s^1) \cap O(\hat{b}_s^2)$   $P[O^1O^2 \cap F^1F^2]$   $P[O^1O^2 \cap F^1T^2]$   $P[O^1O^2 \cap T^1F^2]$ Multi Domain MSSD Type 2  $T2MMSSD(k_1,k_2) = \frac{1}{S'}\sum_{s=1}^{S'}|b_{s+1}^{k1}-b_s^{k1}||b_{s+1}^{k2}-b_s^{k2}|$ 

Multivariate MSSD (continued): For each subject, we can calculate a 6x6 matrix for a MMSSD measure, where the diagonals are equal to the single domain MSSDs and the triangles represent the 15 MMSSD values for each unique pair of the 6 domains. We aggregate the Type 2 MMSSD matrix by taking its f-norm and use it as an overall index of stability across the 6 domains. In the yellow box to the right, the plot shows how MSSD and Type 1 MMSSD process each type of event. For example, at s=31 on the bottom plot, Anxious fluctuates from 0 to 1 and Sad fluctuates from 1 to 0 at the transition to the next timepoint. Since the two domains are fluctuating simultaneously in opposite directions, a value of -1 is recorded. The scores are then summed and divided by the total number of eligible time points to arrive at the value for Type 1 MMSSD.

### Future Goals

- Permutation testing to investigate if domains pairs are fluctuating at a higher/lower rate than if they are behaving independently
- Explore measures that take into account conditional probability
- Explore how best to incorporate domain specific patterns into measures of stability
- Explore machine learning techniques to leverage the information from hundreds of other EMA survey items