Time-Varying Effects of Meals and Insulin on Postprandial Glucose (OhioT1DM 2018)

Causal Mediation + Representation Learning

Spencer Hilligoss

Department of Statistics, University of California, Irvine
with Dr. Annie Qu, University of California, Santa Barbara

University of California, Santa Barbara
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Introduction to Type 1 Diabetes Mellitus (T1DM)

T1DM

- T1DM is a chronic condition characterized by a patient's inability to produce insulin
- Patients' bodies are unable to break down carbohydrates on their own
- Difficult to stay within the normal blood sugar range

Treatment/Management

- Continuous Glucose Monitor (CGM)
- Basal Insulin
- Mealtime Bolus Insulin

Motivation: Background & Gap

What we know

- Carbohydrate intake and insulin dosing strongly influence glucose levels.

What's missing in prior work

- Effects are often modeled as *time-invariant* rather than time-varying post-meal.
- Limited mediation along the pathway: *meal* $\rightarrow$ *insulin* $\rightarrow$ ΔGlucose.
- Heterogeneity across individuals and *time of day* rarely quantified.

$$\text{Meal} \Rightarrow \text{Insulin} \Rightarrow \Delta\text{Glucose (0–3 hr)}$$

Study Goals & Guiding Questions (OhioT1DM 2018)

Our study

- Extract *shared dynamic patterns* across subjects (representation learning).
- Estimate *indirect* (via insulin) and *total* effects of carbs/insulin on ΔGlucose.
- Report both *average* and *individualized* time-varying effects.
- Test whether effects vary by *time of day* (morning / afternoon / evening / night).

Guiding question

How do meal and insulin effects on postprandial ΔGlucose evolve over time, through what pathways, and for whom/when are these effects strongest?

OHIO T1DM Dataset

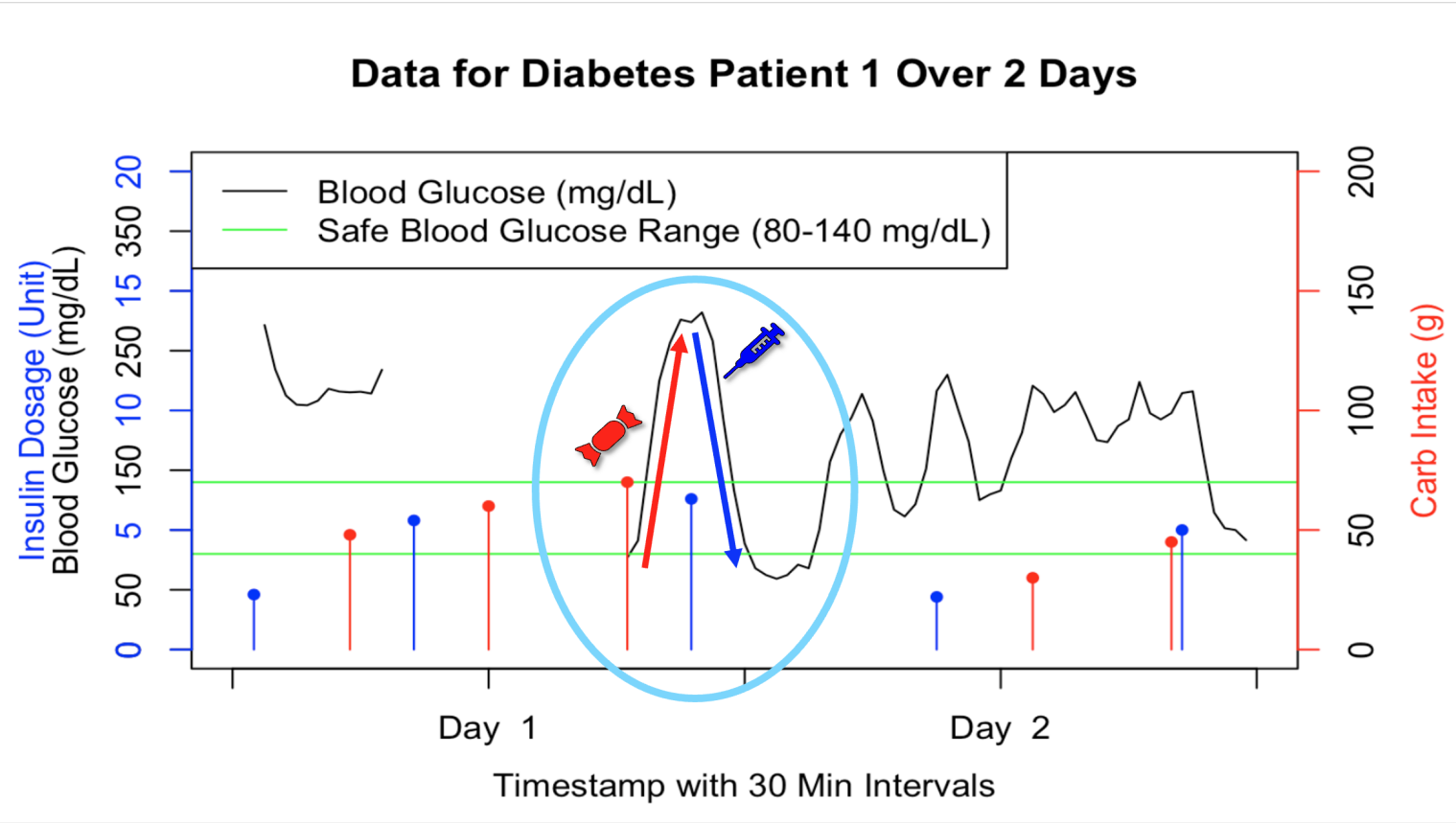
- Data from 6 patient's CGM, which records glucose levels every five minutes for around 55 days
- The data also contains each subject's carbohydrate intake (denoted **meal**) and insulin intake (denoted **bolus** and **basal**)
- Allows us to experiment with prediction without endangering patients

ID	Gender	Age	Pump Model	Sensor Band	Cohort
559	female	40–60	530G	Basis	2018
563	male	40–60	530G	Basis	2018
570	male	40–60	530G	Basis	2018
575	female	40–60	530G	Basis	2018
588	female	40–60	530G	Basis	2018
591	female	40–60	530G	Basis	2018

Characteristics of the Data

What kind of complexities are present?

- Insulin is used as a treatment for carbohydrate intake, resulting in their strong correlation
- Meal time and size vary by subject



Insulin as a Mediator

Pathway of interest (post-meal, 0–3 hr):

$$\text{Meal (carbs)} \rightarrow \text{Insulin (bolus} \pm \text{basal adj.)} \rightarrow \Delta\text{Glucose}$$

Interpretation

- *Direct effect:* meal → ΔGlucose via absorption and physiology.
- *Indirect effect:* meal → insulin dosing → ΔGlucose (treatment response).

Our variables

- Exposure: meal size (carbohydrates).
- Mediator: post-meal insulin (bolus; with basal context).
- Outcome: ΔGlucose trajectory (change from pre-meal baseline) over 0–3 hr.

Goal: quantify how much of the meal's impact on ΔGlucose is explained by insulin (indirect) vs not (direct), and how this *evolves over time* and by *time of day / individual*.

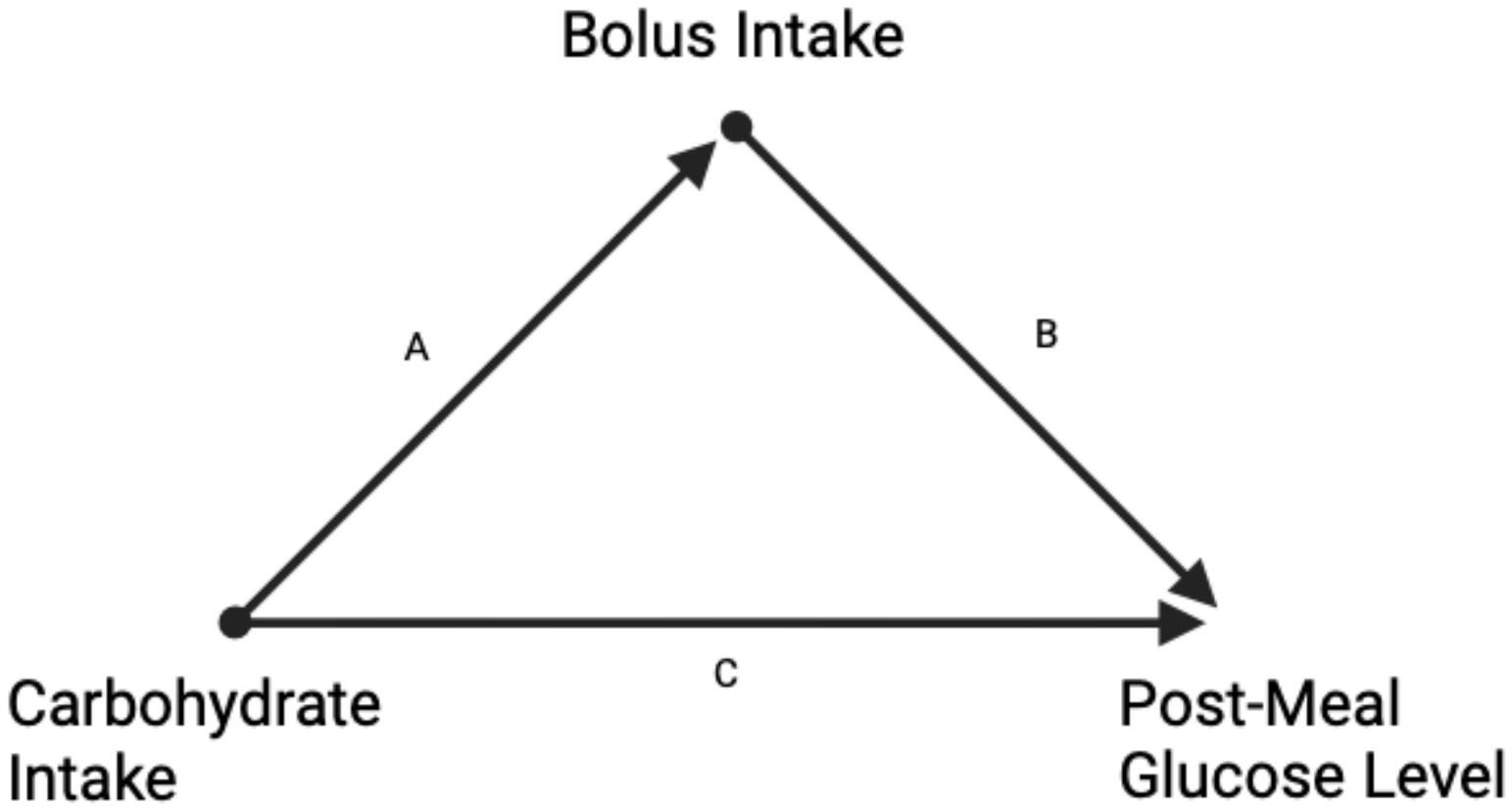
CMA: Decomposing Meal Effects

Goal: Split the meal (carbs) effect on postprandial ΔGlucose into pathways.

- **ATE** (Total Effect): overall change in ΔGlucose from higher vs. lower carbs.
- **ACME** (Indirect): portion *through insulin* (meal → insulin → ΔGlucose).
- **ADE** (Direct): portion *not through insulin* (meal → ΔGlucose holding insulin fixed).

Time-varying: estimate ACME_t, ADE_t, and ATE_t over 0–3 hr post-meal.

CMA Diagram: Meal → Insulin → ΔGlucose



Schematic of pathways used to decompose ATE into ACME (indirect via insulin) and ADE (direct, not via insulin).

Mediator & Outcome Modeling (for CMA)

Why we model both:

- **Mediator model (insulin):** how meals influence insulin dosing.
- **Outcome model (ΔGlucose$_t$):** how meals and insulin jointly affect glucose over time.
- Together, these identify and estimate **ACME**, **ADE**, and **ATE** (time-varying over 0–3 hr).

Pre-treatment covariates:

- Include relevant pre-meal info (e.g., prior glucose, time of day, subject factors) to meet identification assumptions.

Why an Autoencoder for Pre-Treatment?

Goal: capture rich *pre-meal state* to reduce confounding and improve CMA models.

What the AE learns (from pre-treatment windows):

- Recent glucose dynamics: level, slope, curvature, volatility.
- Temporal context: time of day / circadian patterns.
- Subject-specific state: habitual control patterns, responsiveness.
- Recent history: prior insulin/meal context without hand-engineering.

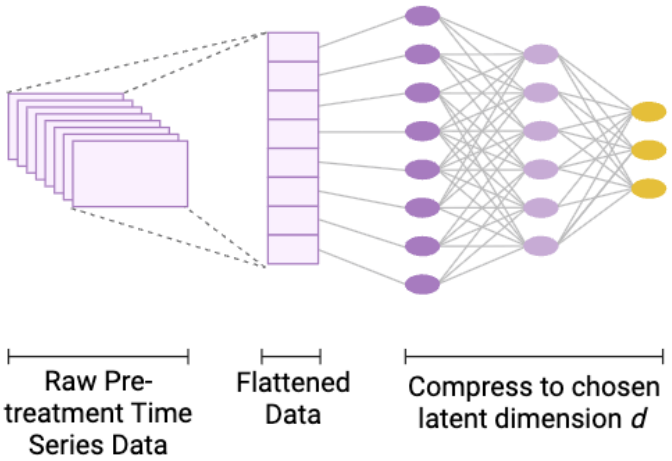
Why it helps:

- Provides low-dimensional embeddings that summarize key dynamics.
- Improves adjustment $\Rightarrow$ closer to ignorability.

How We Use the AE in CMA

Workflow

- Train AE on *pre-meal* windows to learn latent embedding z.
- Use z as a covariate in:
  - **Mediator model:** meal → insulin (better prediction of dosing response).
  - **Outcome model:** meal & insulin → $\Delta\text{Glucose}_t$ (smoother, individualized dynamics).
- Result: more accurate models ⇒ sharper estimates of **ACME**, **ADE**, **ATE** over time.



AE extracts z from pre-treatment; z enters mediator & outcome models.

Models Used for CMA

Mediator model (linear):

$$M_{ij} = \alpha_0 + \alpha_x X_{ij} + \boldsymbol{\alpha}_z^\top \mathbf{Z}_{ij} + \varepsilon_{M,ij}$$

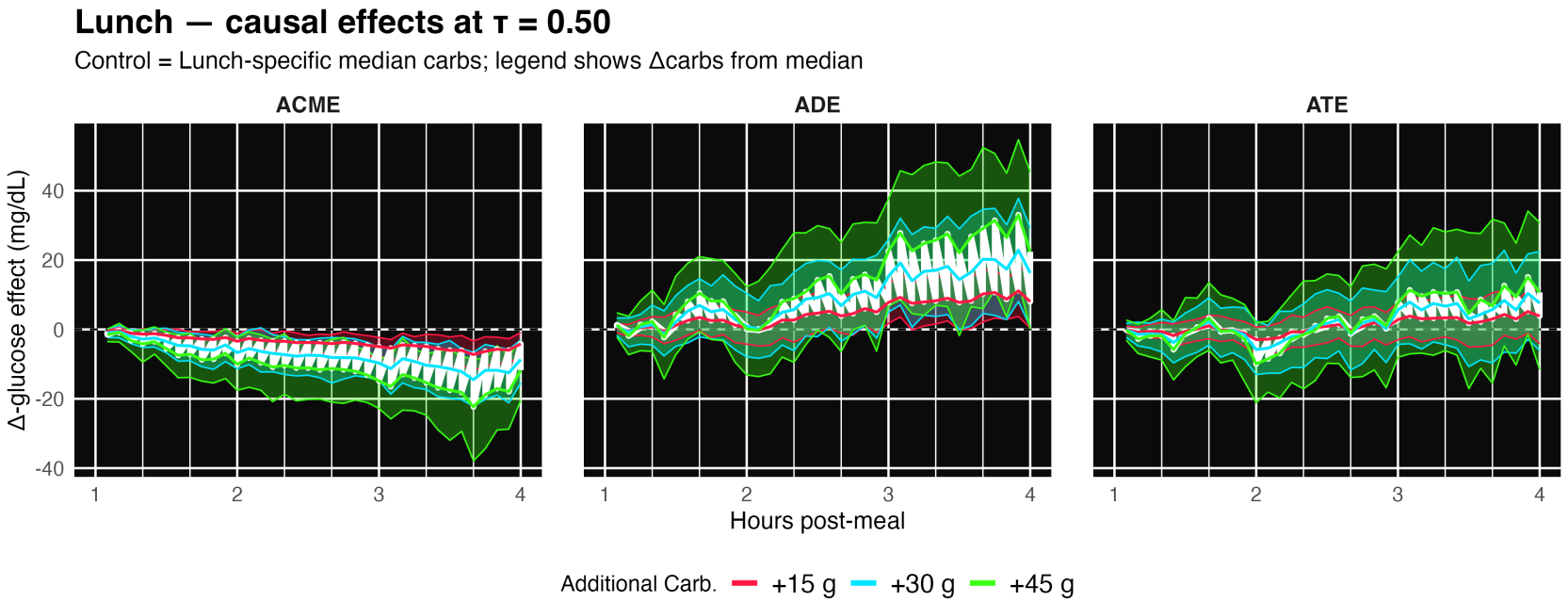
M_{ij}: post-meal insulin (bolus) for subject i, meal window j; X_{ij}: meal carbs; $\mathbf{Z}_{ij}$: pre-treatment covariates; $\varepsilon_{M,ij}$: noise.

Outcome model (quantile regression at level τ):

$$Q_{Y_{ijt}}\left(\tau \mid X_{ij}, M_{ij}, \mathbf{Z}_{ij}\right) = \beta_0(\tau, t) + \beta_x(\tau, t) X_{ij} + \beta_m(\tau, t) M_{ij} + \boldsymbol{\beta}_z^\top(\tau, t) \mathbf{Z}_{ij}$$

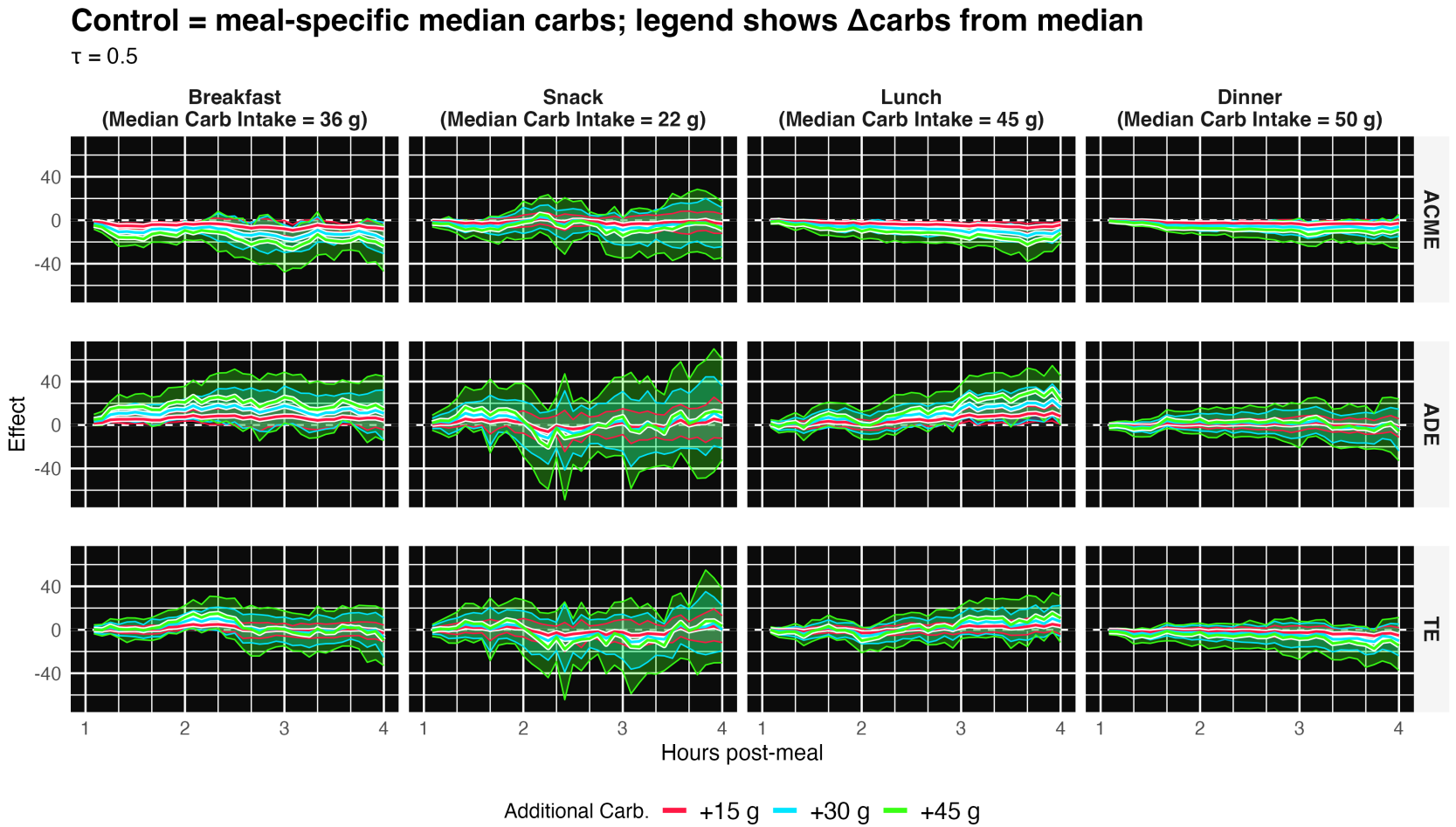
Y_{ijt}: ΔGlucose at time $t \in [0, 180]$ min post-meal; results focus on $\tau = 0.50$ (median).

CMA Results: Lunch (Median, $\tau = 0.50$)



Indirect (ACME), Direct (ADE), and Total (ATE) effects over 0–3 hr post-meal for lunch windows.

CMA Results by Meal Type (Median, $\tau = 0.50$)



Time-varying ACME, ADE, and ATE stratified by meal type.

Takeaways & Next Steps

What we achieved

- Meal-centered windows; modeled postprandial ΔGlucose (0–3 hr).
- Insulin as mediator; CMA to estimate **ATE**, **ACME**, **ADE** (time-varying).
- Mediator (LM) and outcome (QR, τ=0.50) models with strong pre-treatment control via AE embeddings.

Next steps

- Learn *explicit time-varying shared* dynamics across subjects.
- Inject these dynamics into mediator & outcome models for sharper ACME_t, ADE_t, ATE_t.
- Broaden to multiple quantiles and add robustness/sensitivity checks.

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