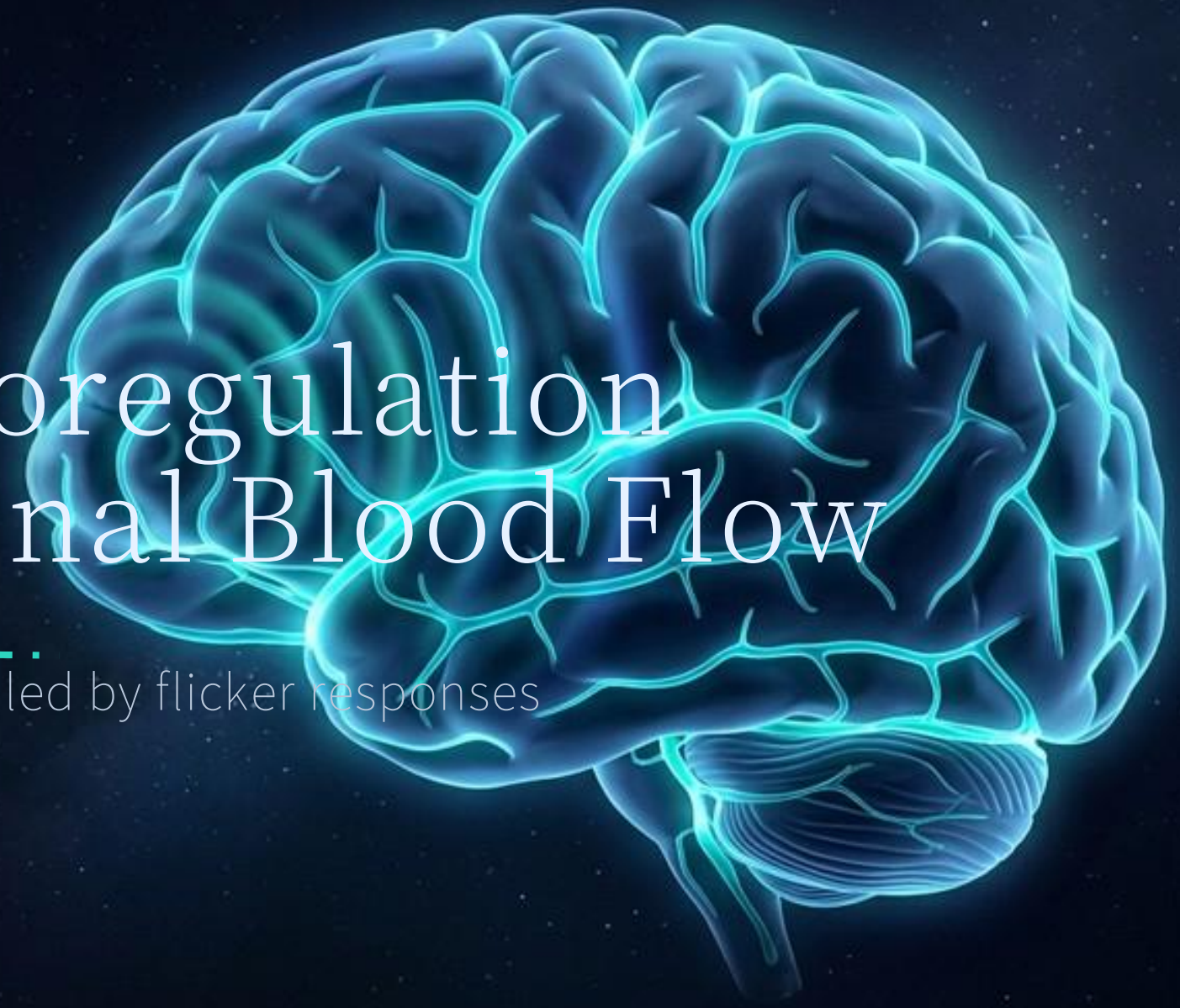
# Reading Autoregulation through Retinal Blood Flow

Phenotypes of dysfunction revealed by flicker responses



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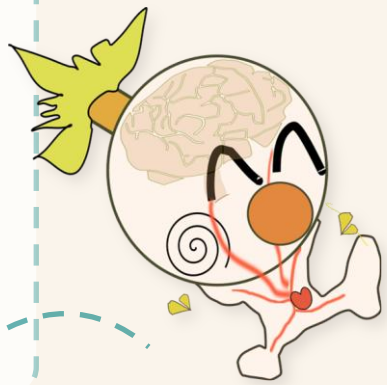
# Why now? Quantifying “state changes” in ophthalmology

## An “invisible mismatch” in clinic

“Eye strain,” “deep ocular pain,” “heavy head”—even with normal findings,
autonomic tone and perfusion may still fluctuate.



Sympathetic

Parasympathetic

## Autoregulation = “reserve” of flow homeostasis

The ability to maintain flow despite changes in perfusion pressure.
Because it is coupled to autonomic responses, it may provide an entry point to quantify “state” in ophthalmology.

# Gap: No repeatable “state” biomarker

## Challenges to date

- Invasive tests cannot be repeated frequently
- “Fatigue” and “stress” rely on self-report (low objectivity)
- Static, single-point measures miss dynamic regulatory capacity (reserve)

## Our proposal

- Continuous, noninvasive LSFG measurement
  Light only; repeatable.
- Feature extraction from time series (LF)
  Infer autonomic state from blood-flow fluctuations.

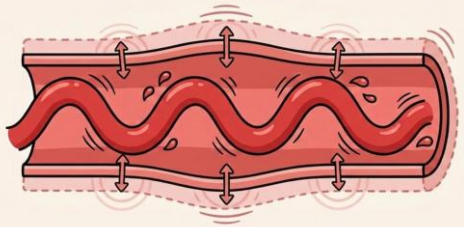
# Core idea: Use LF to read “autoregulatory reserve”

Even with the same flicker stimulus, responses may differ depending on the pre-stimulus LF state (blood-flow variability).

Flicker stimulus

## High LF (high variability)

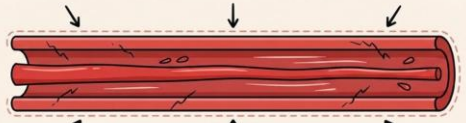
Parasympathetic dominance
Larger fluctuations → more flexibility



Stable, mild response

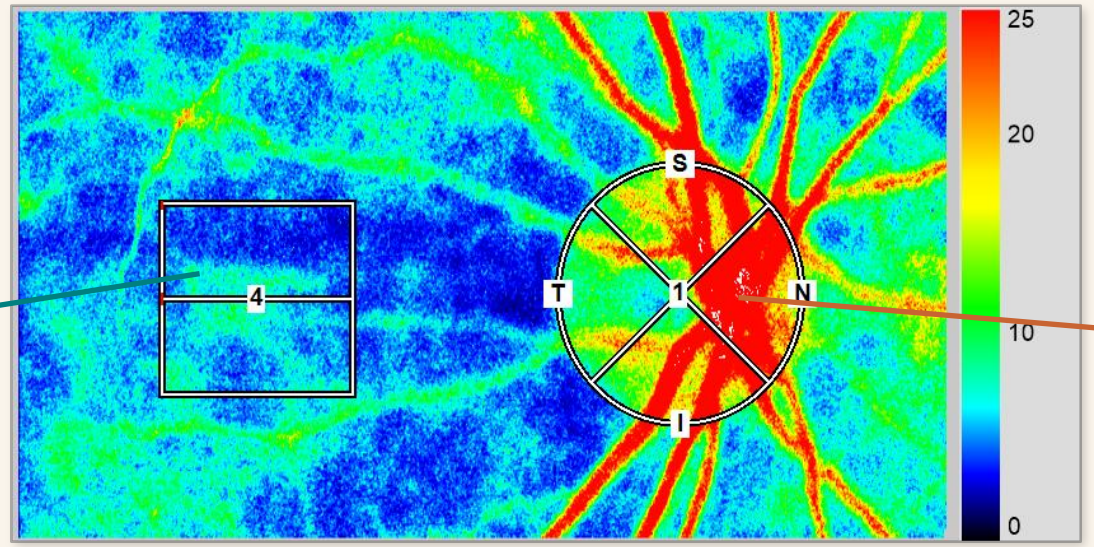
## Low LF (low variability)

Sympathetic activation / fatigue
Smaller fluctuations → limited reserve



Exaggerated, or absent?

# The fundus as a window into circulation (ONH × choroid)




## Choroid (CHD)

- Representative of peripheral circulation
- Rich autonomic innervation
- Vascular tone is observable

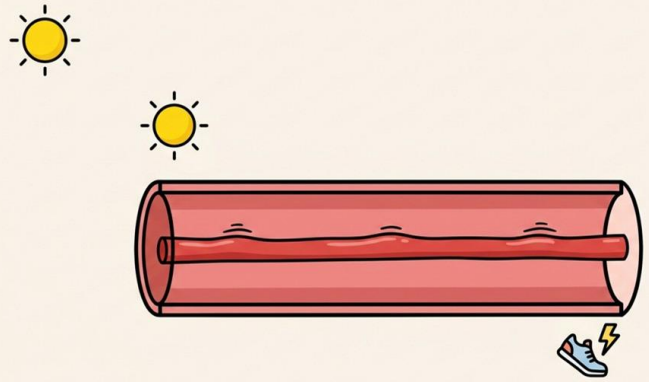
## Retinal arteries (ONH)

- Closer to central circulation (heart/brain)
- Strong autoregulation
- Influenced by blood pressure

One exam captures both “central-like” and “peripheral-like” circulation

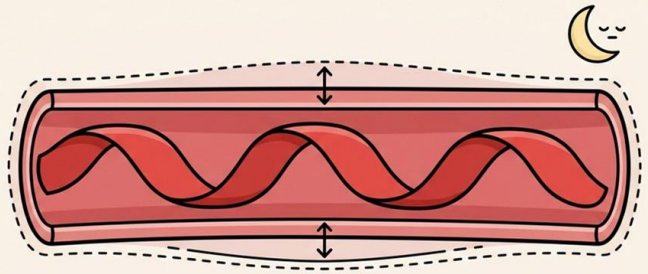
# LF as State: LF captures the current state

## Morning: active mode



Sympathetic dominance
Lower LF (tighter control)

## Evening / fatigued

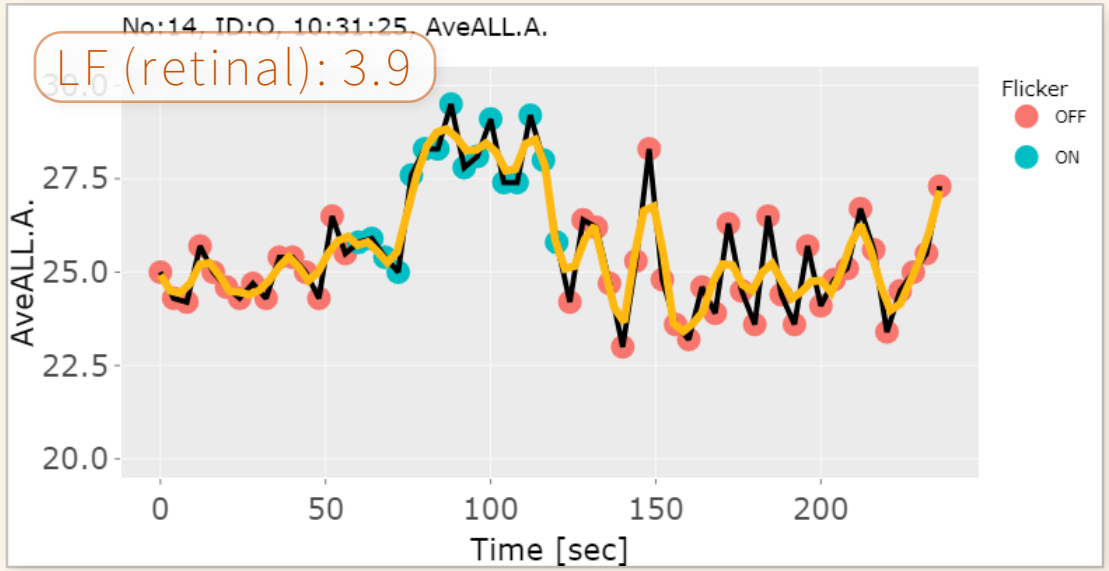


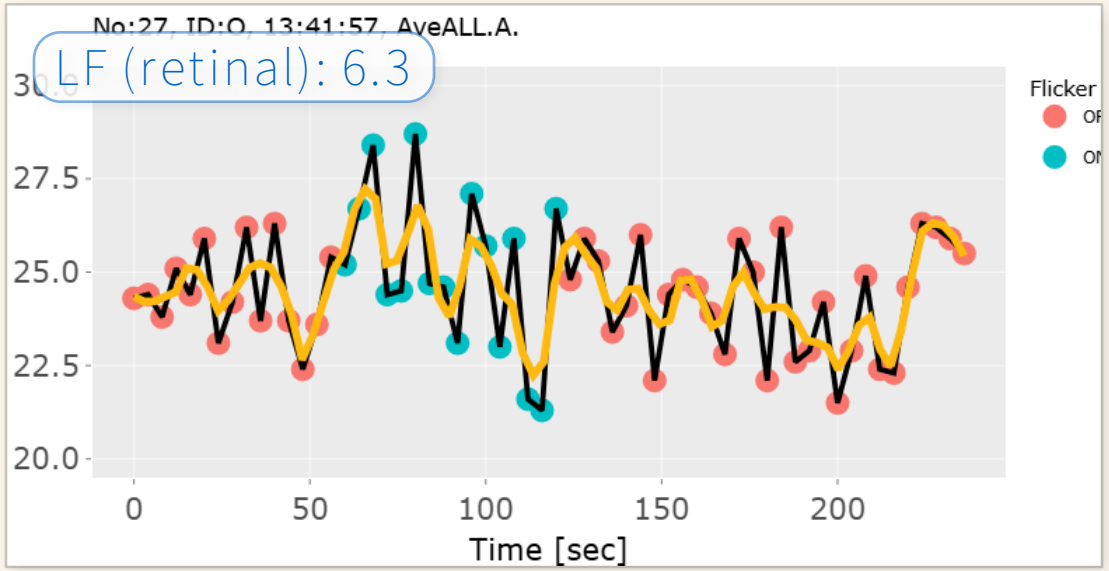
Parasympathetic dominance
Higher LF (looser fluctuations)

Time

Treat LF not as a fixed trait but as a momentary “ state”
— then its fluctuations become interpretable

# Hypotheses: Does baseline LF shape flicker responses?



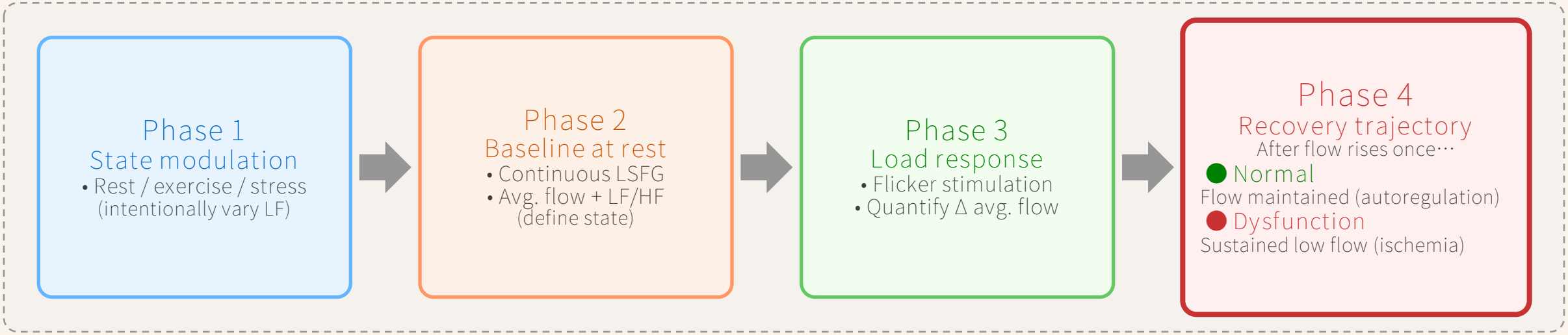

## Hypothesis 1: Low LF (tight)

- Flow increase after flicker ON is easier to detect
- "State" differences affect response visibility
- Reflect autonomic / vascular tone?

## Hypothesis 2: High LF (variable)

- Response is mild / buried and harder to detect
- Parasympathetic "reserve"?
- Test reproducibility (within-subject variability)

# Proposed study design: Toward visualizing autoregulation




[Key point: Visualizing ischemia during recovery]
Normal physiology maintains flow via autoregulation; otherwise there may be no response, or flow may drop after the load and stay low (ischemia).
Breakdown in the recovery phase (Phase 4) is the key strength bridging ophthalmology and neuroscience.

## Other validation points

1) Within-subject reproducibility: LF–response correlation across diurnal/day-to-day variation
2) Regional differences: divergence between ONH (central-like) and choroid (peripheral-like)
3) Optimize LF region: which region best reflects “state” sensitively

# Metrics: Pairing state and function

## State

- LF or HF
  Estimate autonomic balance
- LF ratio
  LF proportion in total variability
- Regional difference
  Synchrony: ONH vs choroid

## Function

- ΔMBR (magnitude)
  Percent increase with flicker
- Time-to-peak
  Rise speed
- Recovery half-life
  Return speed after stimulus

# Expected outcomes and impact

LF × flicker
Standard protocol

Quantitative
phenotyping

Ophthalmology-derived
“state” biomarker

## Potential applications beyond ophthalmology

- Neurology: autonomic dysregulation in functional disorders (e.g., migraine, depression)
- Neuroscience: reduced vascular reactivity as a predisposition to CSD (cortical spreading depression)
- Systemic medicine: quantitative tool for mind–body interactions via the autonomic nervous system

Use fundus blood-flow LF as a
“state marker”,
and flicker responses as a
“functional marker”.

Shall we take the next step together toward visualizing autoregulation failure?

Thank you for your attention.