Calcium Signals

Events in Time — and today, we build the detector live

Session 2 of 4 · L. Fernando Santana & Manuel F. Navedo

UC Davis SOM policy: Acceptable Use of Generative AI

HOW TODAY WORKS

Fifteen minutes of background — then we build, together, live

~15 min	Background: what's new when a signal lives in time — the indicator's real Kd, and sampling fast enough to catch a spark (Nyquist).
~30 min	The build. You watch a calcium event detector come together in stages, with Claude — sparks, then transients — and every fundamental you know becomes a line of a prompt.
~10 min	Waves and discovery. The stretch: detect a propagating wave, measure something new, and turn it into a hypothesis.

LEARNING OBJECTIVES

By the end of this hour, you'll be able to…

01 Describe a time-varying recording richly enough that Claude can build against it — all four dimensions, every number stated.

02 Turn each fundamental you already know — thresholding, segmentation, SNR, Nyquist, verification — into a concrete step of a real analysis.

03 Build and test an event detector with Claude, verifying it against known ground truth as you go.

04 Use a newly measurable property — a wave's velocity — to generate a hypothesis you couldn't have formed from a detection count.

THE SPINE, EVERY SESSION

Talk to the model → build the analysis → validate it

Same arc as always — only today you'll watch all three happen in one continuous build instead of across separate slides. The modality is a time series; the discipline is unchanged.

Reproducibility

today's anchor — identical parameters, verifiable results

Accountability

you own every threshold and every decision

Transparency

the overlay and the ground-truth test show the work

Verification

test against a known answer before you trust anything

BACKGROUND · DESCRIBING A RECORDING IN TIME

Three of four dimensions barely change — the new work is inside “imaging”

Sample, structure, question — nearly unchanged from a static image. What time adds lives in imaging: the sampling rate, whether you're looking at raw F or $\Delta F/F_0$, the cell's state, and the baseline window F_0 is measured against.

Sampling rate

lines/s — sets your temporal Nyquist

Signal type

raw F, or already-computed $\Delta F/F_0$?

Cell state

resting, paced, or field-stimulated

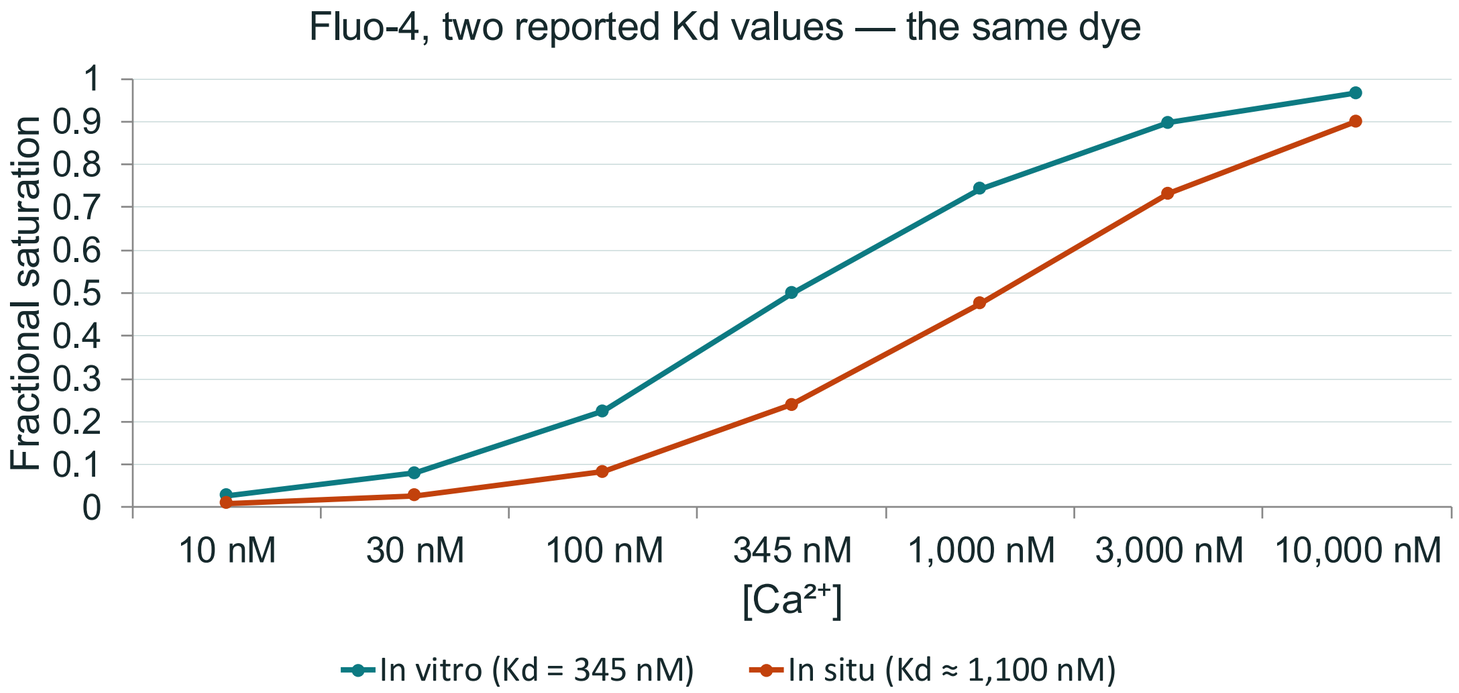
Fo window

the baseline segment, before any event

Two of these — the F_0 window and the sampling rate — become explicit lines in the very first build prompts. Hold onto them.

No indicator is linear — and Kd is the scaling factor

Fluorescence relates to calcium through a saturating binding curve — flat at low calcium, flat at saturation, steepest through the middle. The middle is Kd. The same $\Delta F/F_0$ means a different $\Delta[Ca^{2+}]$ depending where you sit.



BACKGROUND · THE TWIST

The number on the bottle isn't the number in your cell

IN VITRO — THE SPEC SHEET

Kd ≈ 345–400 nM

cuvette, defined buffer, 22 °C

IN SITU — YOUR ACTUAL CELL

Kd ≈ 1,000–1,200 nM

cytoplasm, 37 °C, protein-crowded

That 345 was measured in a cuvette. Inside a real cell — 37°C, crowded with protein — the functional Kd is roughly threefold higher. The manufacturer measured the first number; you image with the second.

THE HABIT

When a number matters, ask what condition it was measured under. Same instinct as setting a threshold from your own background, not a borrowed default.

BACKGROUND · SAMPLING FAST ENOUGH

A spark rises in ~10 ms — can you catch it?

A FLUO-4 SPARK

Rise ~10 ms. Want ≥ 5 points on the rise.

interval ≤ 10 ÷ 5 = 2 ms

→ rate ≥ 500 lines/s

Today's linescan runs at exactly 500 — the floor, not a cushion.

THE WHOLE-CELL TRANSIENT

Rise ~40 ms. Even 5 points is easy.

interval ≤ 40 ÷ 5 = 8 ms

→ rate ≥ 125 lines/s

At 500 lines/s that's ~20 points — comfortably oversampled.

Same recording, two very different margins. The spark is the binding constraint — know which event you are trusting before you report a time-to-peak. This is a rule of thumb; in the build we will measure it properly, per event, and put a number on it. And this exact rate, 500 lines/s, becomes a line in the first build prompt.

The Build

At this point in the session we left the slides and built a calcium event detector live, with Claude, in eight steps — the code getting smarter and the tool growing new panels as we went. The next slide is the map of that build.

The detector we built — and how to rebuild it yourself

Nothing on a slide could stand in for watching this get built. Each rung below was one prompt, one owned decision, one fundamental — and the homework guide walks you through rebuilding all of it, unhurried, at your own pace.

0 **Describe** the four dimensions, every number stated — no analysis instructions yet

1 **Open & display (pre-built)** choose your F_0 window (before any event), compute $\Delta F/F_0$, render the heatmap

2 **Naive detection** one global threshold, no other criteria — a few hundred “events” against 5 real. It fails on purpose

3 **Real detection** three gates you own — amplitude, duration, width: the flood → ~14 → ~9 → ~6

4 **Nyquist check** measured per event: rise → bandwidth → margin. 500 lines/s IS enough — now proven, not asserted

5 **Test** ask Claude how to verify, then implement: score against planted truth — false positives and all

6 **Metrics** amplitude, TTP, FDHM, FWHM, decay τ, signal mass, spark & transient frequency

7 **Waves** a propagating event drifts — measure its velocity. A new measurable → a hypothesis

Rebuild it yourself: *Session2_Build_Your_Own_Homework.docx* walks through the same loop with the practice linescan. The finished detector ships with your materials — but build it before you open it.

Waves & Discovery

The detector is built and verified. The velocity it just handed us is the doorway — from a number we detected to a question we couldn't have asked before.

DISCOVERY · FROM A MEASUREMENT TO A QUESTION

What would a wave's velocity tell you about the cell?

You now have a number no detection count could give you. The move that matters is what you ask next.

01 Does velocity track SR calcium load — faster waves when the store is fuller?

02 Does it report coupling between release sites — how readily one triggers the next?

03 Is there a velocity that separates a healthy propagation from a pathological one?

None of these is a measurement. Each is a hypothesis — and you couldn't have formed it before the tool handed you velocity.

WHY THIS MATTERS · THE ACTUAL HISTORY

One spark. Ten years. A theory that changed how we see the heart.

10 YEARS

1990 -> 1999 · five papers, four overlapping collaborations · one paradigm shift

Calcium-induced calcium release is regenerative — it should be all-or-none, a fuse not a dial. But whole-cell release is smoothly graded. Niggli & Lederer proposed local control in 1990; Stern modeled it in 1992; Cheng, Lederer & Cannell gave it sparks to see in 1993; Cannell, Cheng & Lederer confirmed the mechanism in 1995; Stern's group refined it in 1999.

> *The detector we built does the first step of that decade: it finds the spark. It doesn't do the other nine years — turning an observation into a theory that changed a field. That leap is what AI can help catalyze. Not faster detection — faster theory.*

HOMEWORK · BUILD YOUR OWN

You watched me build one. Tonight, build your own — unhurried.

A step-by-step prompt guide walks you through the same loop — describe, build, verify — at your own pace, with no clock and no usage-limit race.

PART A — SCAFFOLDED, EVERYONE SUCCEEDS

Rebuild the detector from the provided prompts, and verify it against ground truth you can check by hand: **the intervals are 340 ms and 420 ms.**

PART B — YOURS, FOR DISCOVERY

Same loop, your own metric — and turn in a **hypothesis it let you form.** A wave's velocity is a perfect candidate. Not a measurement — a new question.

Full guide: Session2_Build_Your_Own_Homework.docx · practice linescan + metadata + ground-truth key included.

NEXT SESSION

Colocalization & Segmentation — with Manuel Navedo

You watched the whole loop: describe a recording in time, build a detector with Claude, verify it against known ground truth, and read a new measurable as a hypothesis. Session three turns channels into objects and overlap — the same threshold-and-segment decision, applied to space.

> *Bring the tool you build tonight. Segmentation is the same decision you made today, in a new dimension — so session three won't be a cold start either.*

Thank you — see you next session.