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The role of synchronous spiking in the encoding of vibrotactile stimuli by low-threshold mechanoreceptors

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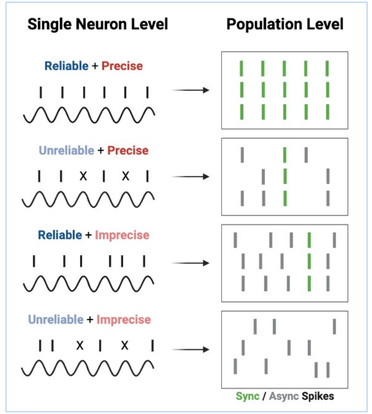
Background

- Spike synchrony is vital for spike propagation, but the role of synchrony for signal propagation between low threshold mechanoreceptors (LTMRs) and their post-synaptic targets remains unclear.
- The influence of stimulus features (e.g frequency) on this synchrony is unclear.
- **Synchronous spiking** in response to periodic stimuli like vibration relies on:
  - a. **Reliability** → the probability of a spike occurring on every cycle
  - b. **Precision** → spike timing relative to the phase of the cycle
- Changes in reliability & precision at the single neuron level impacts synchrony at the population level.
- In rodents, the reliability and precision of LTMRs in response to vibration have yet to be well characterized.

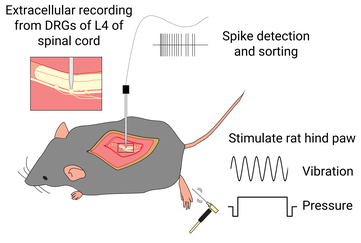


Project Goals

1. **Characterize reliability and precision of LTMR responses to vibration.**
2. **Investigate the impact of changes in reliability and precision on synchrony and the encoding of vibrotactile stimuli by LTMRs.**
3. **Model LTMRs to explore the mechanisms supporting (1) & (2).**

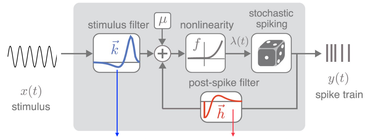
Methods

In vivo recording of LTMRs



Generalized Linear Model (GLM)

GLMs are statistical encoding models that we fit to experimental data and used to simulate LTMR spike trains.



Modified from Pillow & Weber (2017)

Analysis of response per trial

A. Reliability

Measured as % Entrainment (100% = 1 spk/cycle):

$$\%\,Ent = \frac{\#\ of\ spk/sec}{\#\ of\ stimulus\ cycles/sec}$$

Higher % Entrainment = Higher Reliability

B. Precision

Measured as Temporal Dispersion (TD):

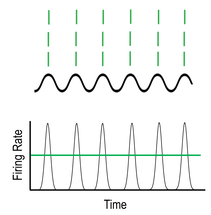
$$TD = \frac{\sqrt{2(1-r)}}{2\pi f}$$

r = vector strength
f = frequency

Lower TD = Higher Precision

Analysis of population synchrony

Synchrony was assessed using raster plots (top) and firing rate histograms (FRH, bottom):

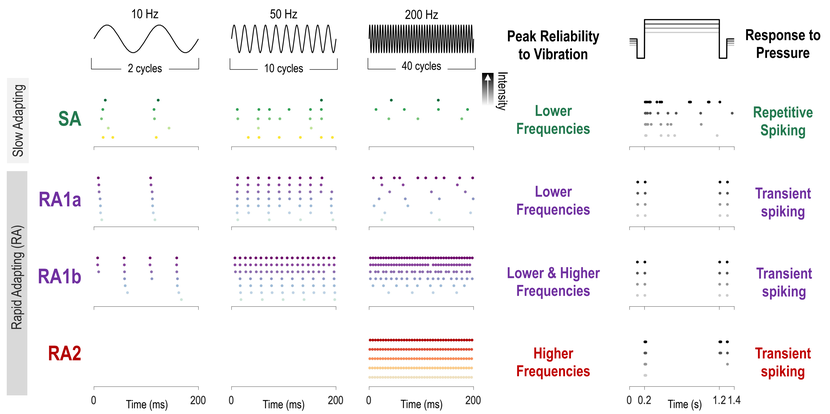


Spikes were labelled **sync** if they fell within the same 0.5 ms window

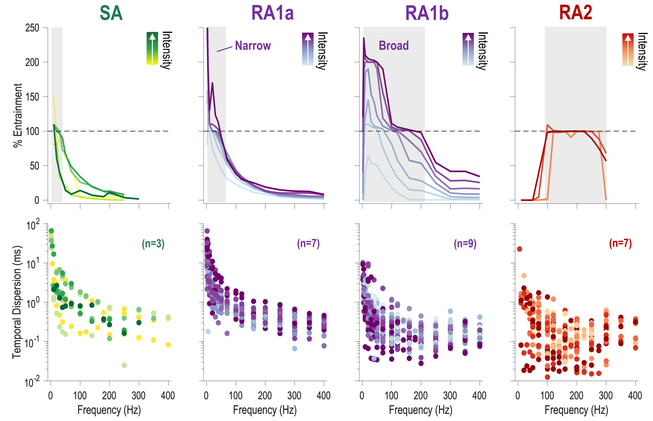
Population synchrony was achieved if the FRH passed **synchrony threshold** using a narrow Gaussian kernel (σ = 0.5 ms)

Results

Result 1: Rodent LTMRs can be classified into four subtypes based on their differential responses to vibration and sustained pressure



Result 2: As stimulus frequency increases, changes in reliability differ per LTMR subtype but precision increases for all LTMRs.



Sample tuning curves illustrate the influence of stimulus intensity & frequency on % Entrainment for different LTMR subtypes.

Frequency preference, where reliability is ≥100% (grey), differs per LTMR subtype. RA1b's have broader preference than RA1a's.

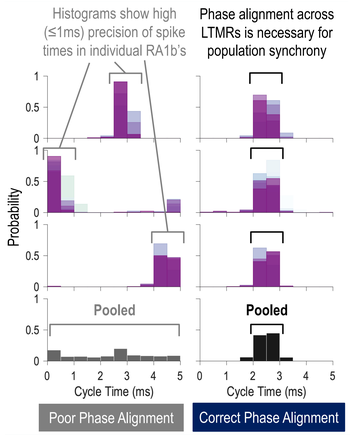
Temporal dispersion of the first spike in each stimulus cycle decreases as frequency increases.

This result is independent of LTMR subtype or stimulus intensity.

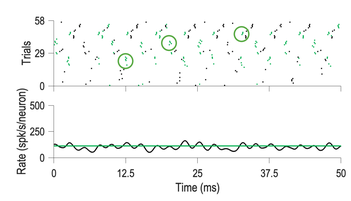
Data for precision are pooled across all LTMRs of each subtype.

Result 3: RA1b LTMRs have high precision at high frequencies, but require phase alignment to achieve population synchrony.

Response of RA1b LTMRs to 200 Hz Vibration



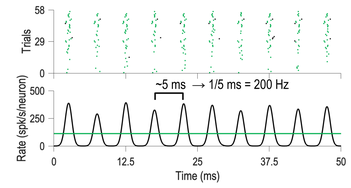
Poor Phase Alignment Across LTMRs → Low Population Synchrony



Synchronous spikes only occur across trials in the same LTMRs

The FRH rarely passes synchrony threshold

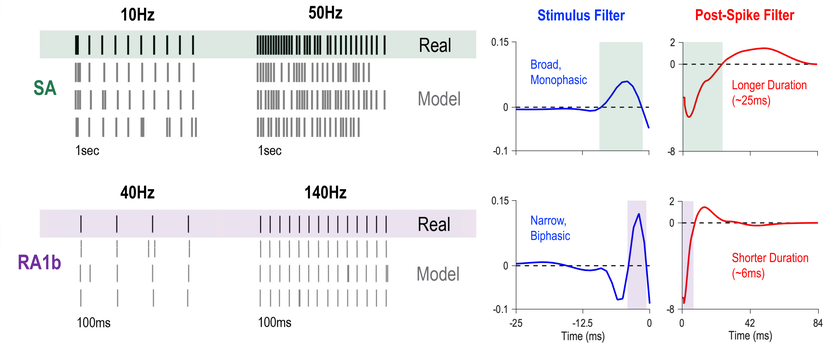
Correct Phase Alignment Across LTMRs → High Population Synchrony



More spikes across the RA1b population are deemed synchronous

The FRH passes threshold in a pattern that supports encoding of stimulus frequency

Result 4: The GLM reproduces LTMR responses to vibration and highlights key mechanistic differences between RA1b and SA LTMRs



- The GLM was fit to experimental data from SA (n=1) and RA1b (n=1) LTMRs.
- These models (grey) reliably reproduced the spike trains of both LTMR subtypes (black) to various stimulus frequencies.
- **RA1b LTMRs have a narrower stimulus filter and shorter post-spike filter (i.e. refractory period) than SAs. These unique filter properties allow RA1b LTMRs to have high reliability and precision at high frequencies.**

Conclusions

1. Rodent LTMRs can be classified as SA, RA1a, RA1b, or RA2 based on their differential responses to sustained pressure and vibration.
2. The influence of frequency on reliability varies per LTMR subtype, but increasing frequency universally increases precision.
3. Population synchrony is achieved through high reliability and precision in individual neurons, as well as phase alignment across LTMRs.
4. Our models reproduce the firing patterns and tuning properties of SA and RA1b LTMRs and further predicts that a shorter refractory period in RA1b's allows them to respond to and synchronize at higher frequencies than SAs.

Future Research: A cluster analysis will be done to confirm our LTMR classification. Further analysis of precision, phase alignment, and synchrony will be assessed at low–high frequencies across all LTMR subtypes. The GLM will be fit to RA1a and RA2 LTMRs.

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