SpikeSSL

A Universal Spike Inference Framework with Dynamics-Informed State-Space Layers

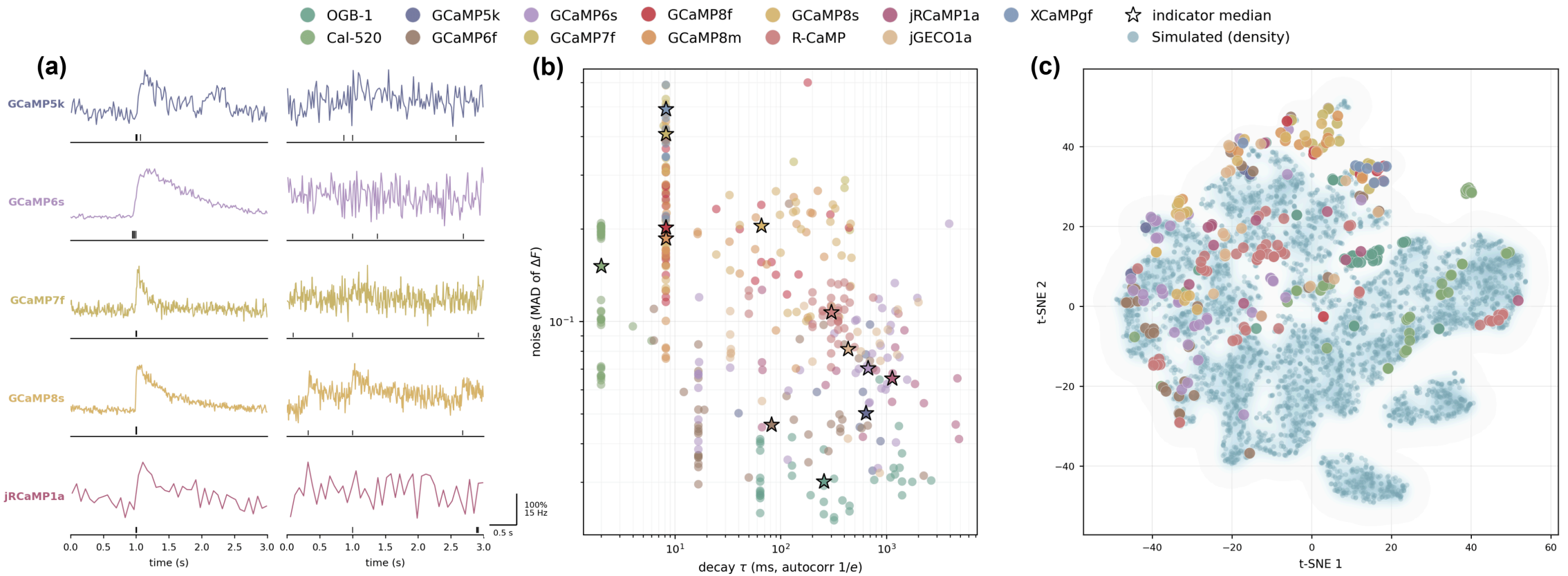
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Calcium fluorescence → neuronal spike rates

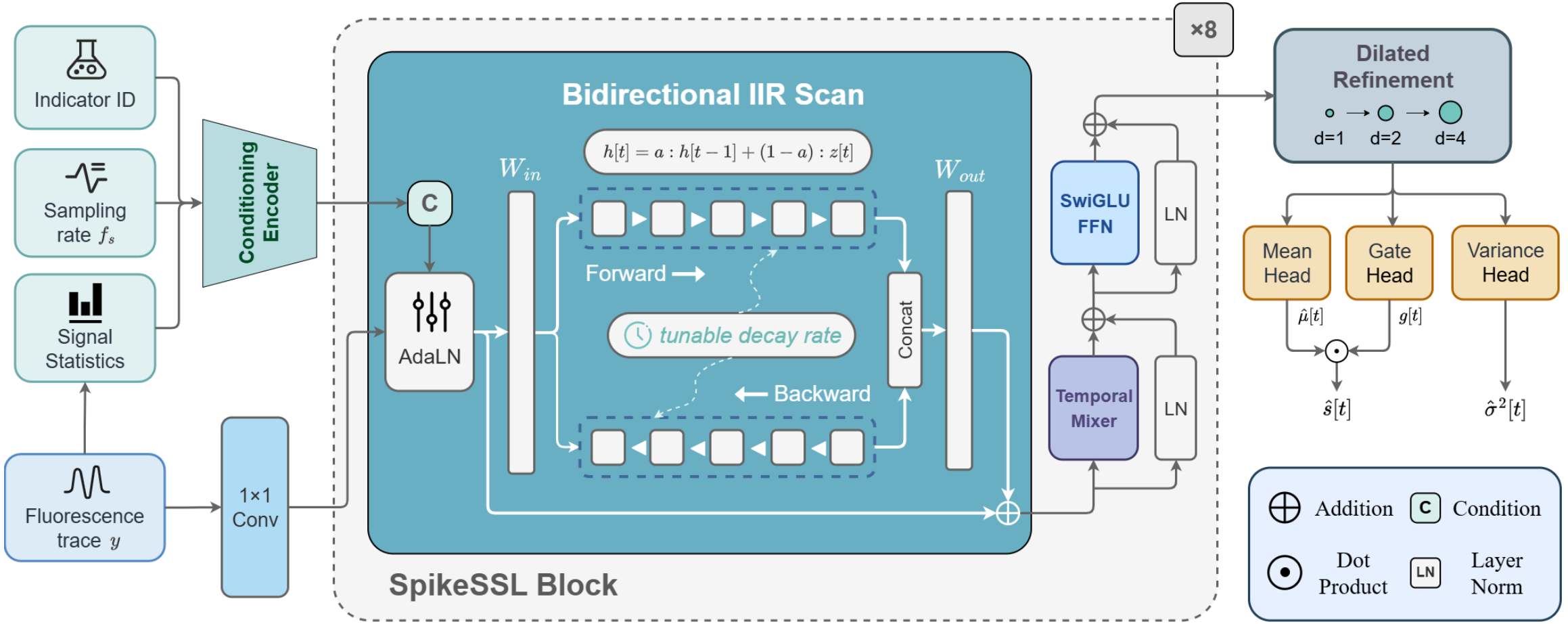
Cross-indicator spike inference

Calcium fluorescence is an indirect, noisy readout of neural activity.
We infer spike rates that generalize across indicator kinetics.



Different response shapes and shifted feature distributions create a cross-indicator domain gap.

SpikeSSL architecture



Bi-IIR backbone
Multi-scale decay dynamics

Multi-modal conditioning
ID, sampling rate, trace statistics

Rate · gate · variance
Spike estimates and uncertainty

Dynamics-informed temporal processing

Use a recurrence matched to calcium decay as a temporal inductive bias.

$$h[t] = \alpha \cdot h[t-1] + (1-\alpha) \cdot z[t]$$

Multi-scale dynamics

Forward and backward scans use both onset context and decay shape.

A learnable decay bank spans fast and slow responses.

Per-window conditioning

Indicator ID, sampling rate and seven input-window statistics condition AdaLN and effective decay rates.

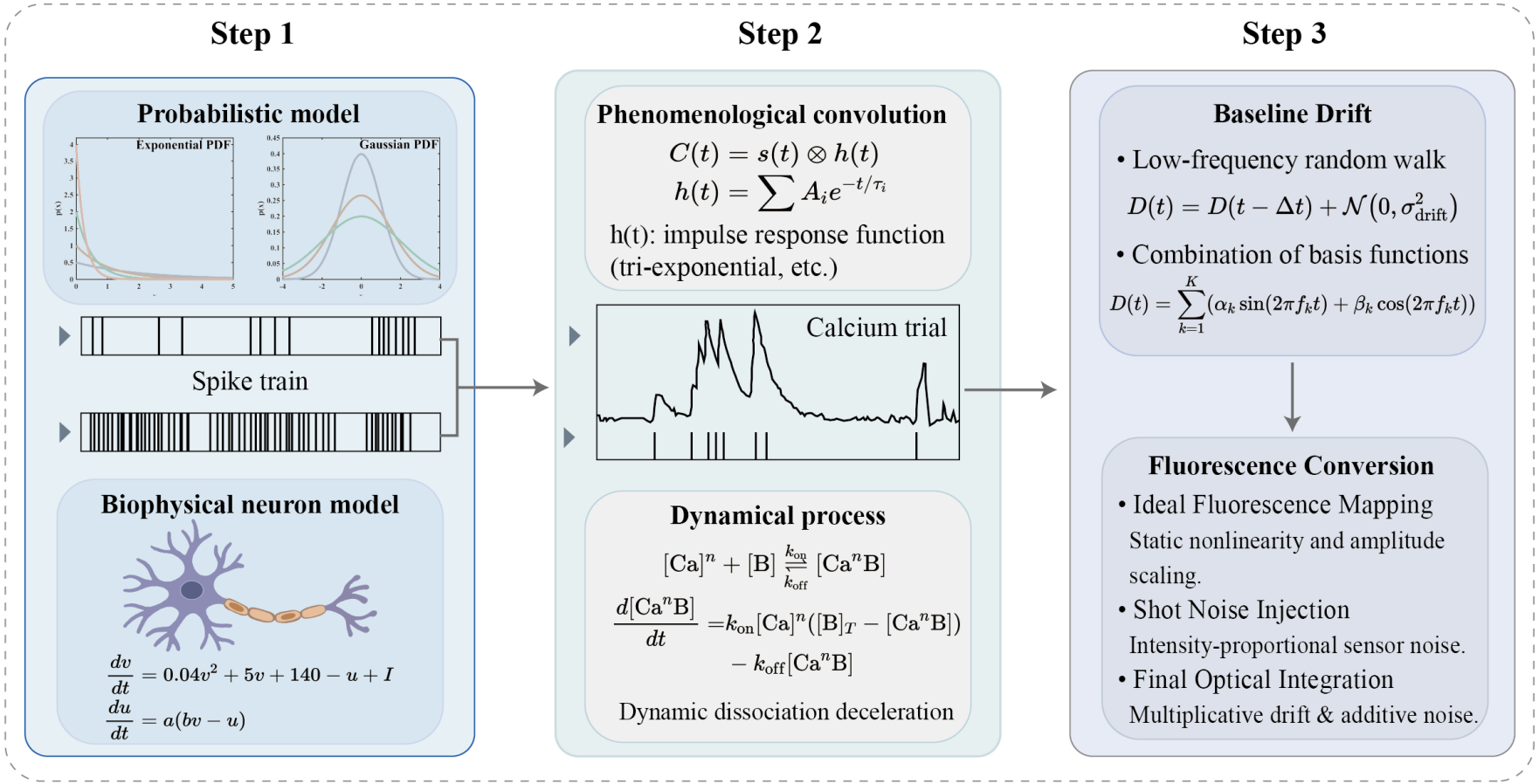
Complementary output heads

The rate head estimates spikes.

The gate suppresses false positives; the variance head estimates per-frame uncertainty.

AdaLN acts inside the IIR branch, before the residual addition.

Biophysical simulation for broader coverage



≈11,000
paired simulated traces

Vary firing, kinetics, nonlinearities, drift and noise.
Broaden coverage rather than target one indicator.

In-domain benchmark performance

33 public recording sets · 1,960 paired neuron recordings · five evaluation splits

In-domain evaluation uses per-dataset train/test separation.

Method	V1-OGB			V1-GCaMP6s			V1-GCaMP8			Other-RCaMP			SC-GCaMP6s			Mean	Params
	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	
OASIS	0.298	1.157	−0.481	0.332	0.973	−0.883	0.493	0.878	−0.659	0.504	1.054	−0.508	0.365	0.975	−0.964	0.398	—
MLSpike	0.363	4.379	3.244	0.224	1.017	−0.928	0.558	0.935	−0.887	0.354	1.369	−0.761	0.307	1.005	−0.919	0.361	—
CASCADE [16]	0.613	1.117	−0.250	0.361	1.718	**0.520**	0.825	3.246	3.108	0.675	1.060	−0.388	0.149	1.005	−0.639	0.524	34K
ENS^2 [28]	0.641	1.032	−0.368	0.358	2.265	1.354	0.775	1.827	1.596	0.695	**0.884**	−0.509	0.256	1.116	**−0.154**	0.545	145K
SpikeSSL	**0.743**	**0.810**	**−0.067**	**0.579**	**0.945**	−0.741	**0.915**	**0.565**	**0.017**	**0.731**	1.269	**0.234**	**0.736**	**0.764**	−0.704	**0.741**	3.9M

Higher Corr and lower error / absolute bias are better. Bold / underline mark the best / second-best.

0.741

Mean correlation

Highest correlation on all five evaluation splits.
ENS^2 reaches 0.545 mean correlation.

Zero-shot cross-indicator generalization

LOIO holds out each split in turn, with no target-domain training data or fine-tuning.

LOIO · real-data training

Method	V1-OGB			V1-GCaMP6s			V1-GCaMP8			Other-RCaMP			SC-GCaMP6s			Mean
	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑
OASIS	0.298	1.157	−0.481	0.332	0.973	−0.883	0.493	0.878	−0.659	0.504	1.054	−0.508	0.365	0.975	−0.964	0.398
MLSpike	0.363	4.379	3.244	0.224	1.017	−0.928	0.558	0.935	−0.887	0.354	1.369	−0.761	0.307	1.005	−0.919	0.361
CASCADE	0.560	1.208	**−0.144**	0.304	2.571	1.614	0.757	3.723	3.602	0.551	1.086	−0.300	0.126	1.083	−0.442	0.460
ENS^2	0.574	**1.005**	−0.366	0.310	3.401	2.654	0.716	2.038	1.715	0.635	0.966	−0.454	0.178	1.092	**−0.391**	0.483
SpikeSSL	**0.650**	1.979	0.675	**0.509**	**0.944**	**−0.677**	**0.853**	**0.513**	**−0.091**	**0.717**	1.172	0.606	**0.542**	**0.911**	−0.892	**0.654**

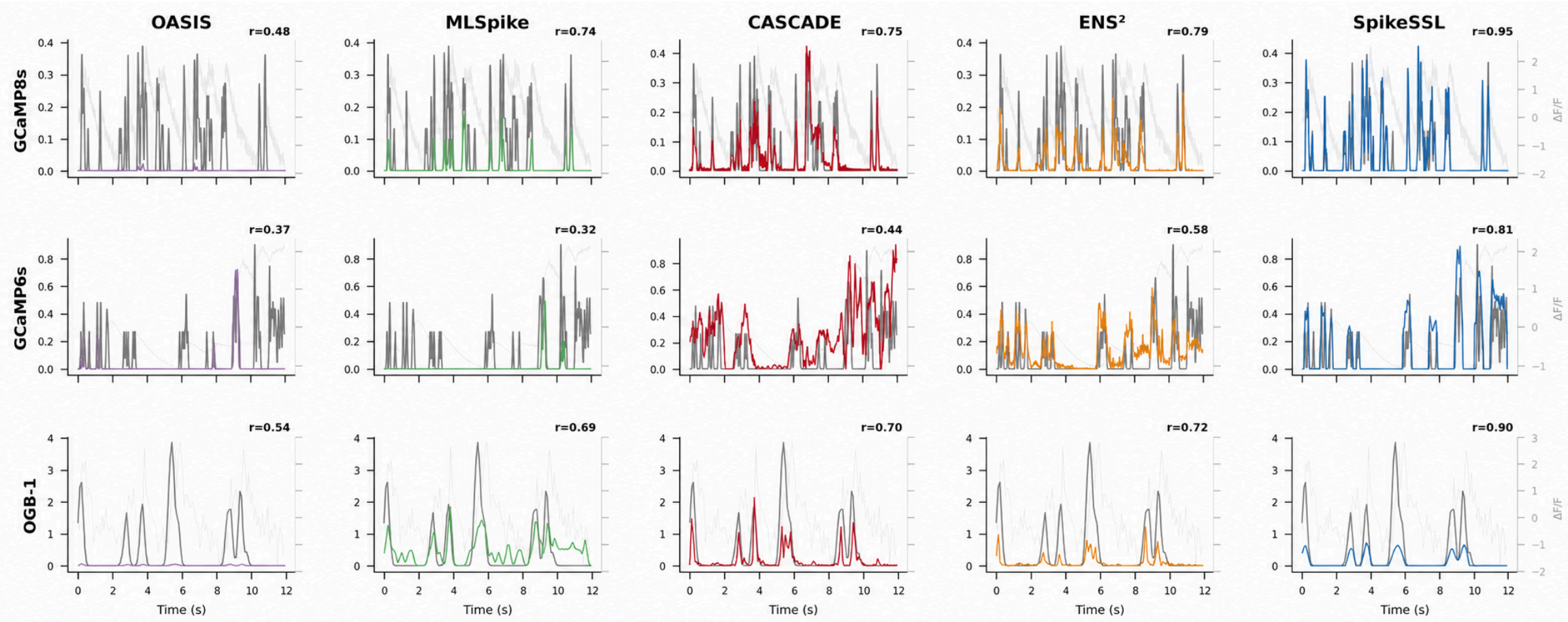
LOIO · simulation-augmented training

Method	V1-OGB			V1-GCaMP6s			V1-GCaMP8			Other-RCaMP			SC-GCaMP6s			Mean
	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑	Err ↓	Bias ↓	Corr ↑
CASCADE + Sim.	0.552	2.418	1.423	0.439	1.522	**0.691**	0.716	1.408	1.018	0.642	1.421	0.614	0.405	3.206	2.084	0.551
ENS^2 + Sim.	0.486	1.634	0.592	0.447	2.146	1.418	0.796	1.882	1.487	0.588	1.764	0.756	0.461	2.291	1.054	0.556
SpikeSSL + Sim.	**0.697**	**1.441**	**0.419**	**0.533**	**0.931**	−0.697	**0.902**	**0.523**	**0.175**	**0.708**	**0.849**	**−0.505**	**0.678**	**0.771**	**−0.653**	**0.704**

Mean correlation rises from 0.654 to 0.704 (+0.050), with the highest correlation on every split.

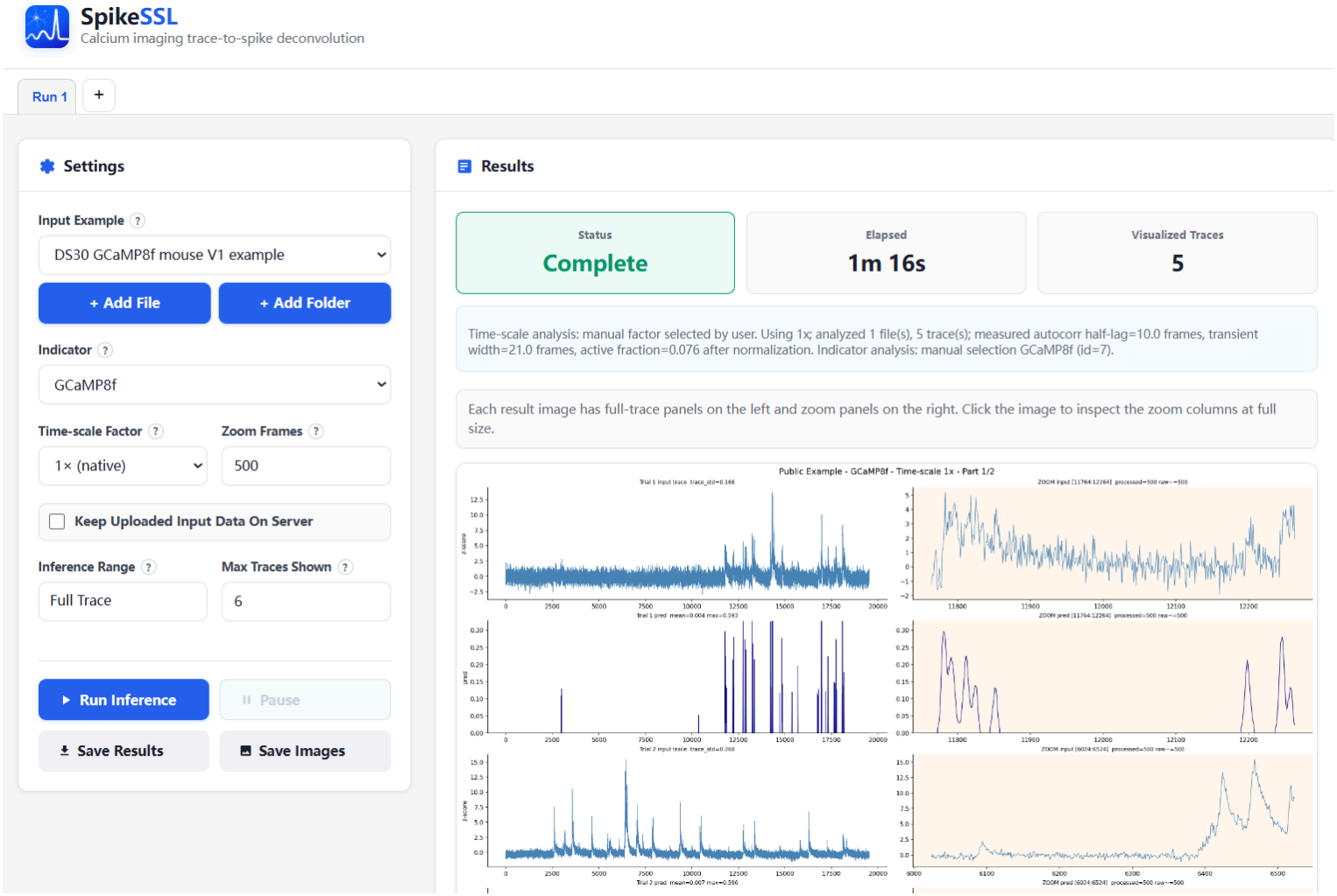
Qualitative spike-inference comparison

Representative held-out GCaMP8s, GCaMP6s and OGB-1 neurons.



Grey curves denote ground-truth spike rates; SpikeSSL preserves sharper event structure.

A practical interface for spike inference



Upload · infer · inspect

Load fluorescence traces, choose an indicator and time scale, then inspect full-trace and zoomed predictions.

Unseen indicators

Select Unknown Indicator (ID=0). Sampling rate and current-window statistics provide additional conditioning, without target labels or fine-tuning.

github.com/detimage123/SpikeSSL

Conclusions

0.741
In-domain correlation

0.654
Zero-shot LOIO correlation

0.704
LOIO + simulation correlation

01 Dynamics-informed modelling

Bi-IIR processing and conditioning provide a structured temporal bias.

02 Broader zero-shot transfer

Simulation expands training coverage across diverse kinetic regimes.

03 Practical availability

Open code, a released checkpoint and a browser-based interface.

Paper

Repo

Learn dynamics. Generalize better.