Modeling and Simulation of Chaotic Bursting in Pacemaker Neurons

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Motivation

❶ Experimental recordings of pacemaker neurons exhibit chaotic bursting patterns.

❷ Chaotic bursting is modeled by fast and slow ionic processes represented by systems of nonlinear differential equations.

❸ Previous studies employed non-ideal explicit numerical methods to solve these stiff nonlinear equations and may result in erroneous solutions.

❹ Previous models capable of chaotic behavior were confined to a limited parameter space and did not investigate the effect of noise on chaotic dynamics.

❺ Our goal is to employ implicit numerical methods in the absence and presence of dynamic noise to determine a minimal pacemaker model capable of chaotic bursting.

Methods

❶ We simulated two minimal pacemaker models with Hodgkin-Huxley ionic dynamics (**Fig. 1a**) using both variable-time step and fixed-time step implicit solvers (**Fig. 1b**).

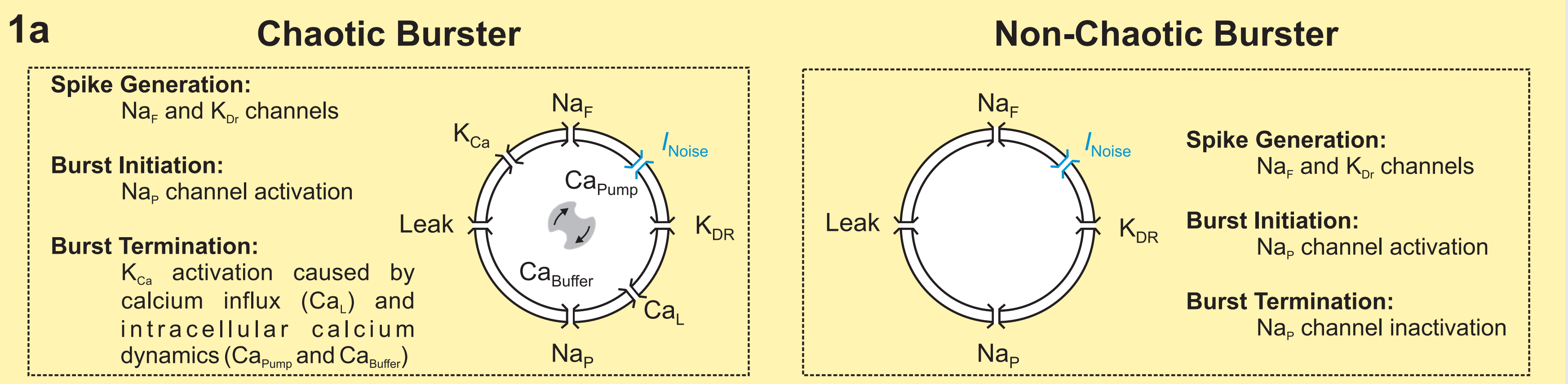
❷ We added noise to the simulations by attaching an I_{Clamp} to the soma and inducing a noise current generated by an uniform distribution (**Fig. 1a**).

❸ Burst dynamics of interest were extracted from the simulation data (**Fig. 1c**).

❹ Bursting patterns are visualized by plotting the ISI duration vs. the ISI number. Different colors represent different bursts within the same run (**Fig. 1d**).

❺ For each run, chaotic bursting dynamics were detected by employing a noise-resistant numerical chaos-titration test on the ISI time series data[1,2] (**Fig. 1e**).

1a



Chaotic Burster

Spike Generation:
Na_F and K_{Dr} channels

Burst Initiation:
Na_P channel activation

Burst Termination:
K_{Ca} activation caused by calcium influx (Ca_L) and intracellular calcium dynamics (Ca_{Pump} and Ca_{Buffer})

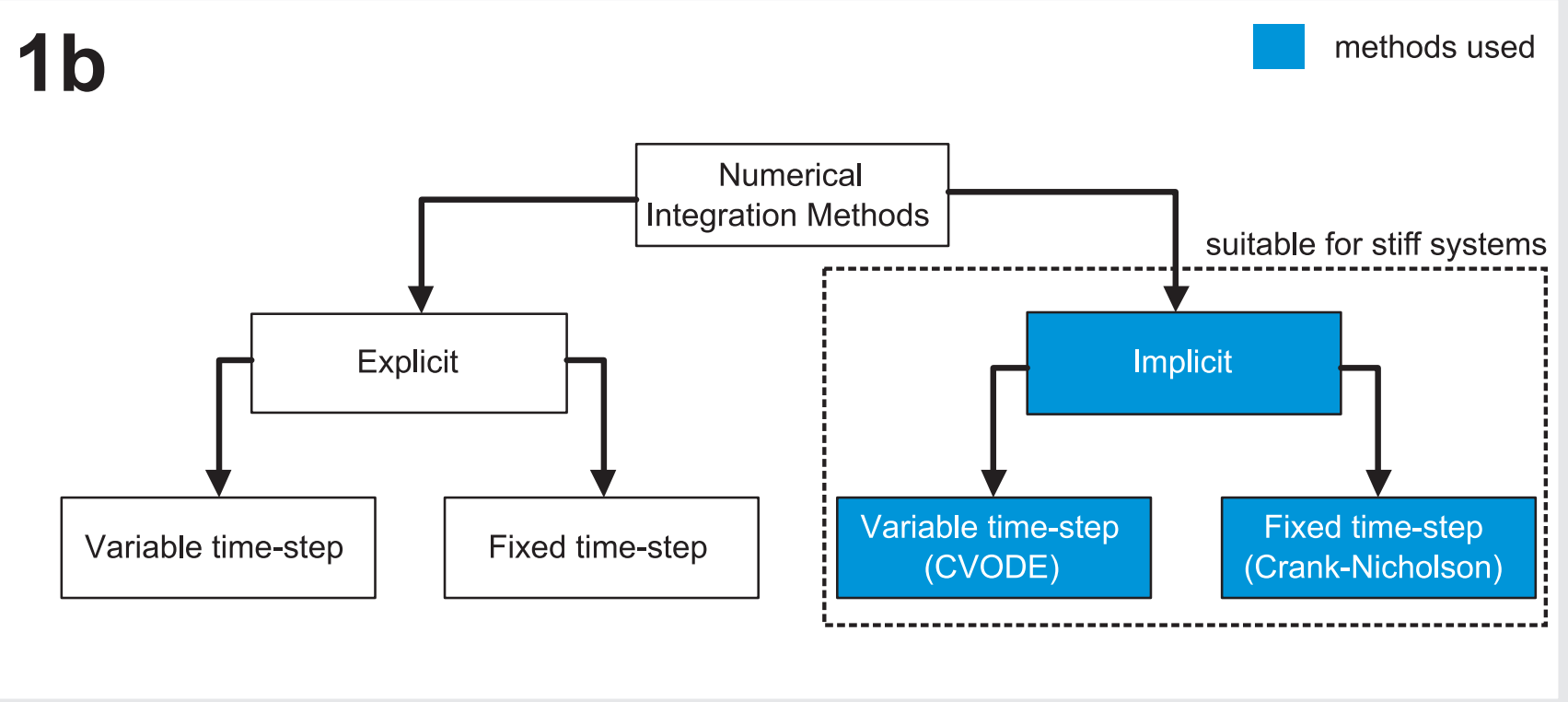
Non-Chaotic Burster

Spike Generation:
Na_F and K_{Dr} channels

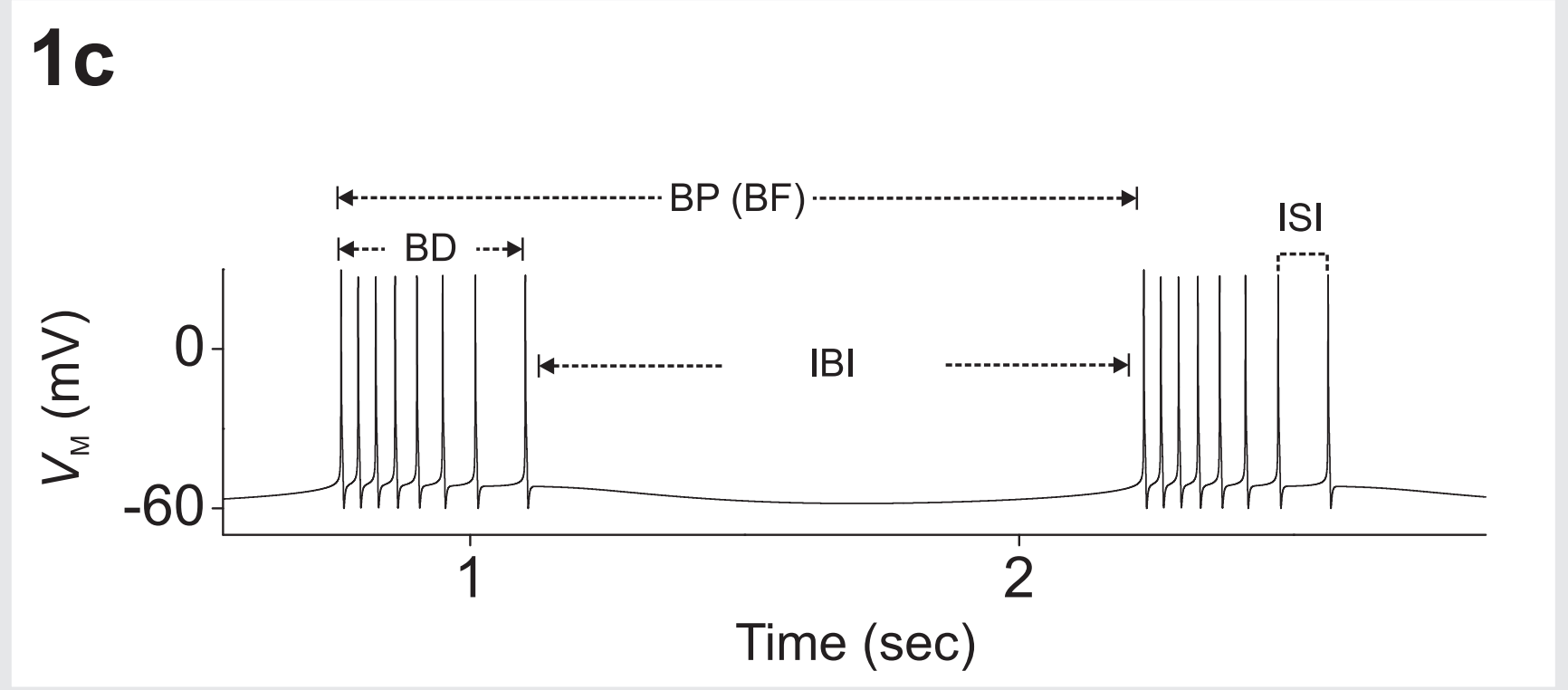
Burst Initiation:
Na_P channel activation

Burst Termination:
Na_P channel inactivation

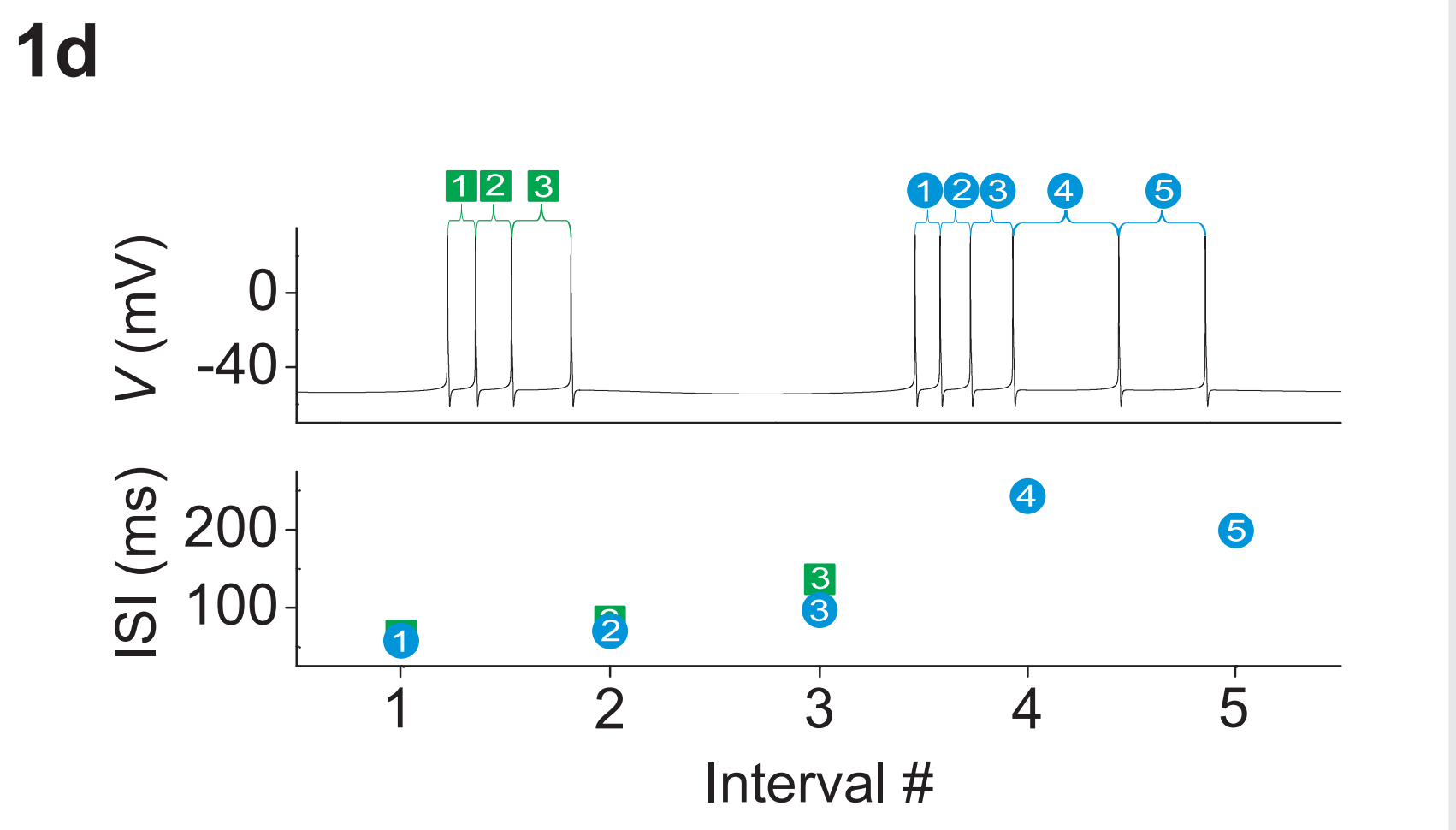
1b



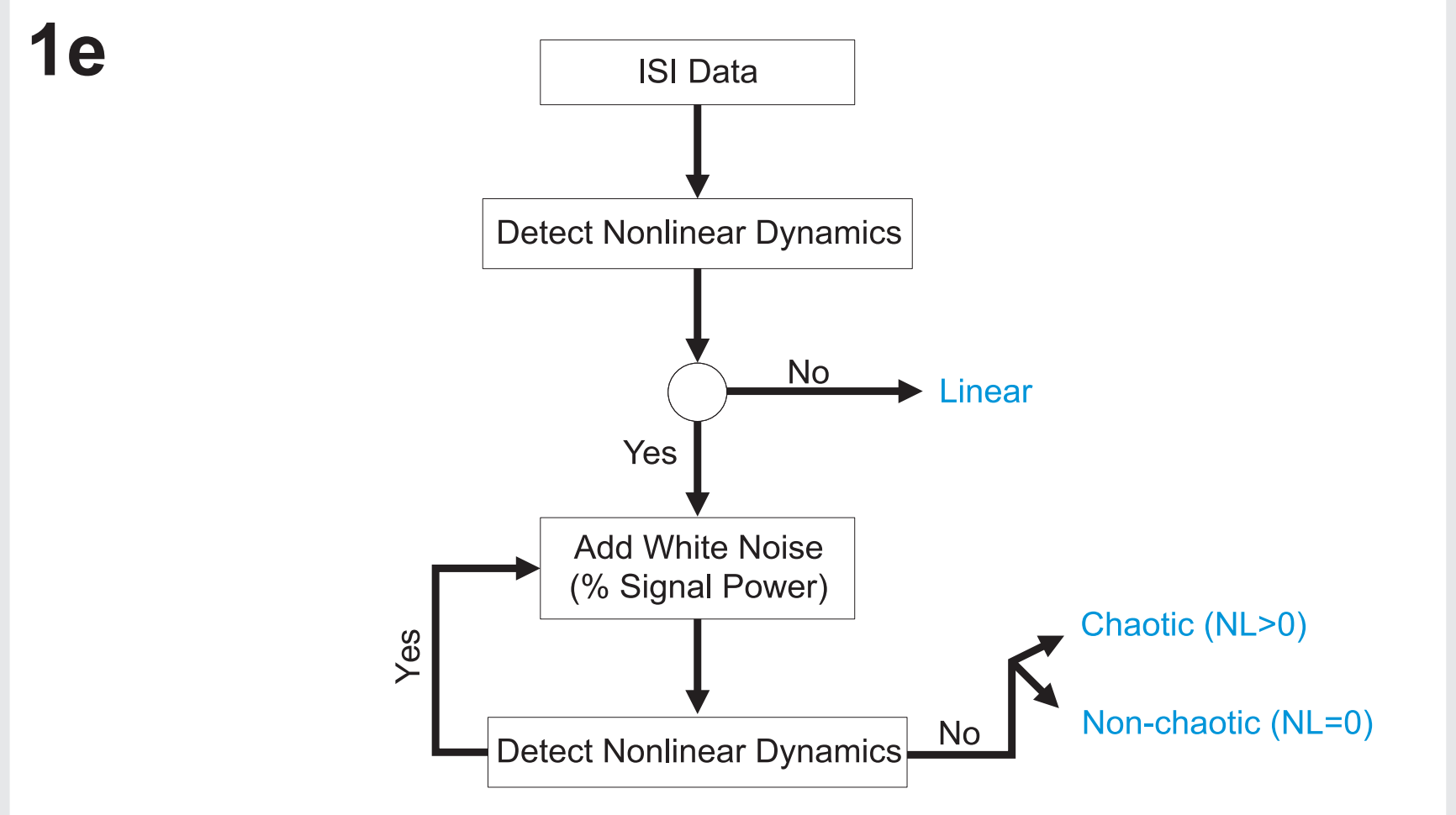
1c



1d

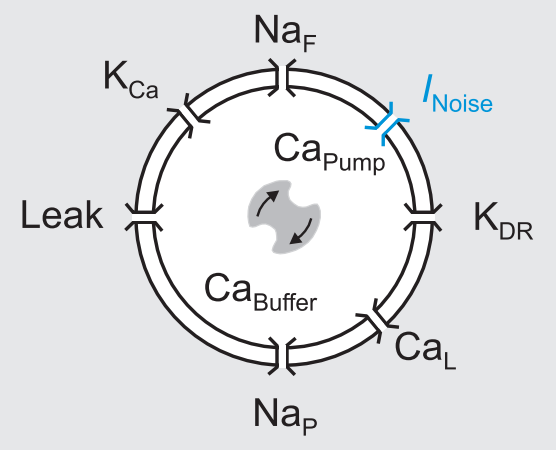


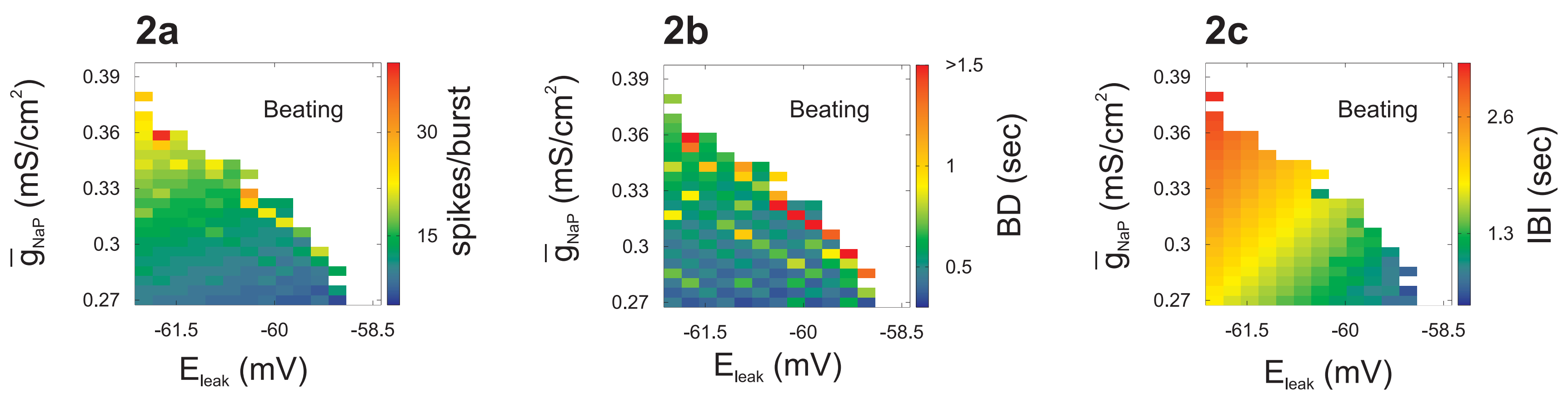
1e



Results

Chaotic burster



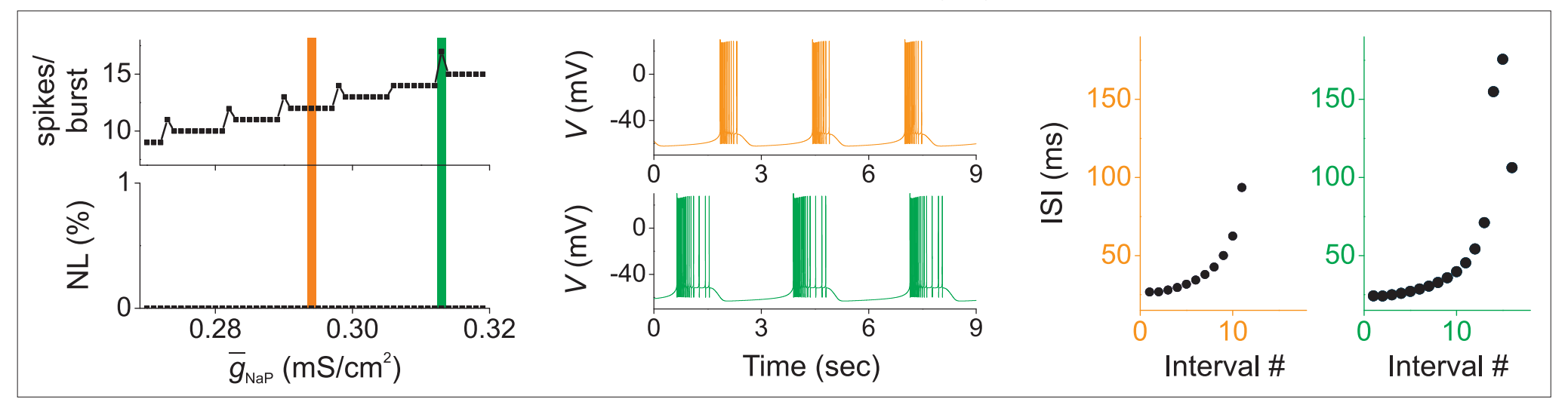


❶ For a given E_{leak}, the number of spikes/burst (**Fig. 2a**) and burst duration (**Fig. 2b**) was determined by $\bar{g}_{NaP}$.

❷ The interburst interval was dependent on both $\bar{g}_{NaP}$ and E_{leak} (**Fig. 2c**).

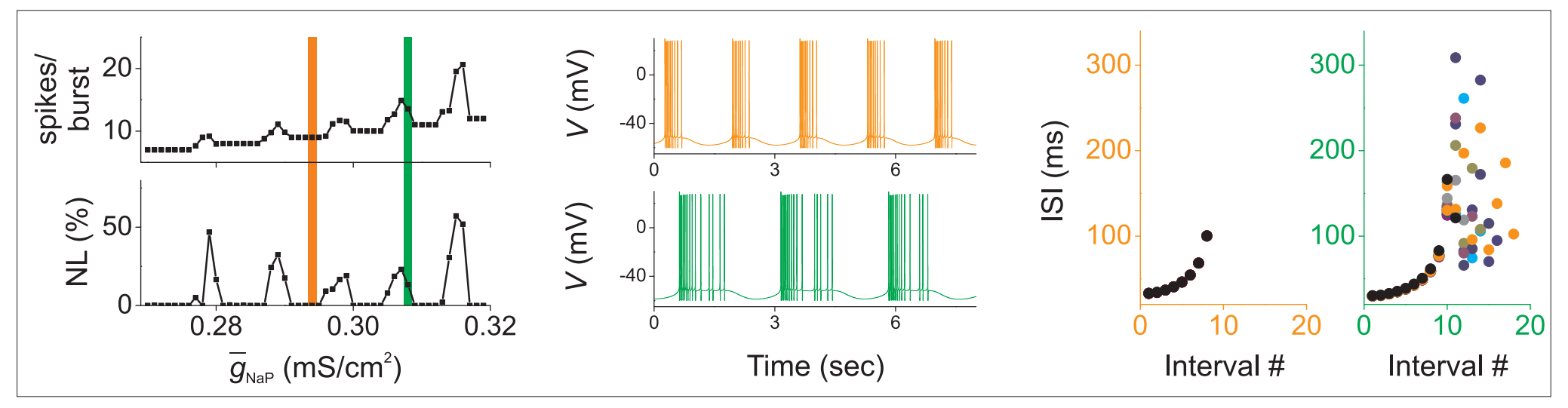
❶ For E_{leak}=-62mV a gradual increase in number of spikes/burst could be observed in response to an increase in $\bar{g}_{NaP}$ (**Fig. 3a**).

3a E_{leak} = - 62 mV; $I_{Noise}/I_{NaP(Rest)}$ = ± 0 %



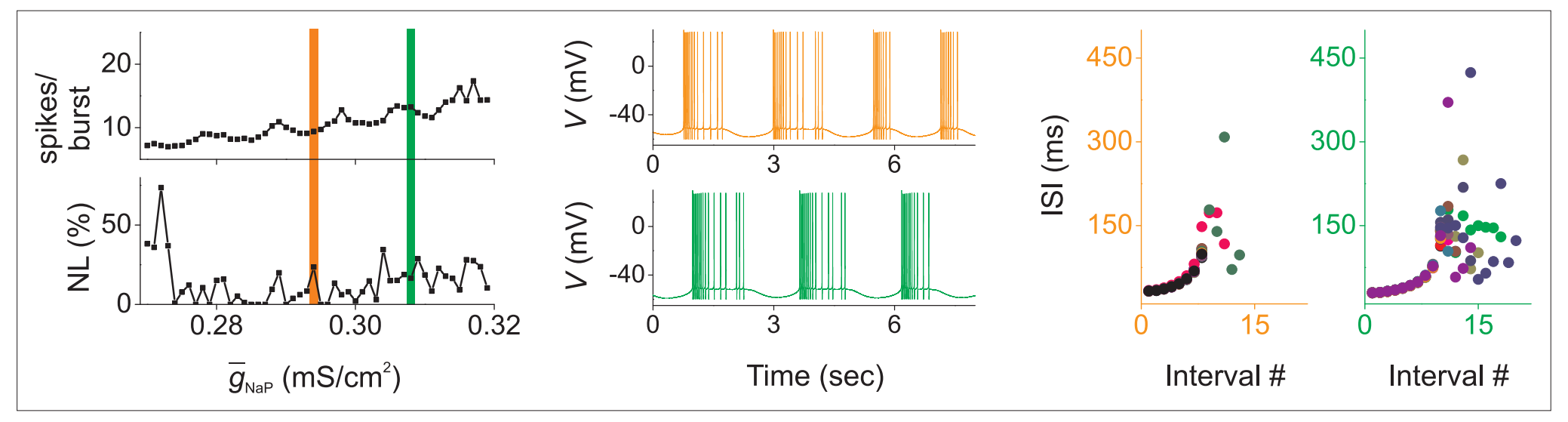
❷ Higher excitability evoked chaotic behavior at the transitions between two number of spikes per burst levels (**Fig. 3b**).

3b E_{leak} = - 60 mV; $I_{Noise}/I_{NaP(Rest)}$ = ± 0 %



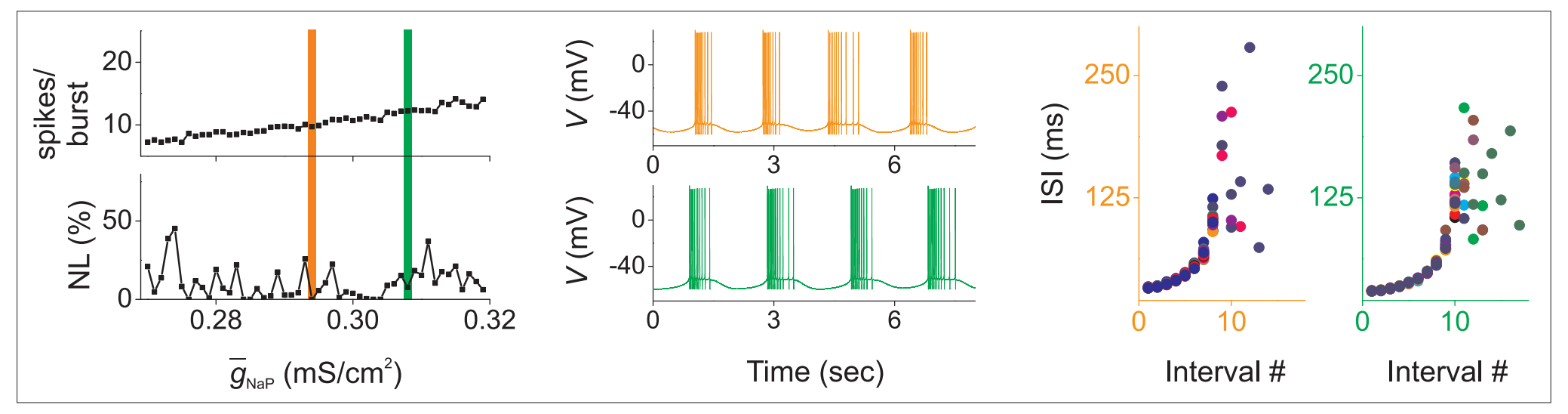
❸ The addition of small amount of noise caused a higher prevalence of chaos in the parameter space (**Fig. 3c**).

3c E_{leak} = - 60 mV; $I_{Noise}/I_{NaP(Rest)}$ = ± 1.3 %



❹ Further noise increase caused an oscillation between chaotic and non-chaotic behavior over the entire tested parameter space (**Fig. 3d**).

3d E_{leak} = - 60 mV; $I_{Noise}/I_{NaP(Rest)}$ = ± 2.6 %



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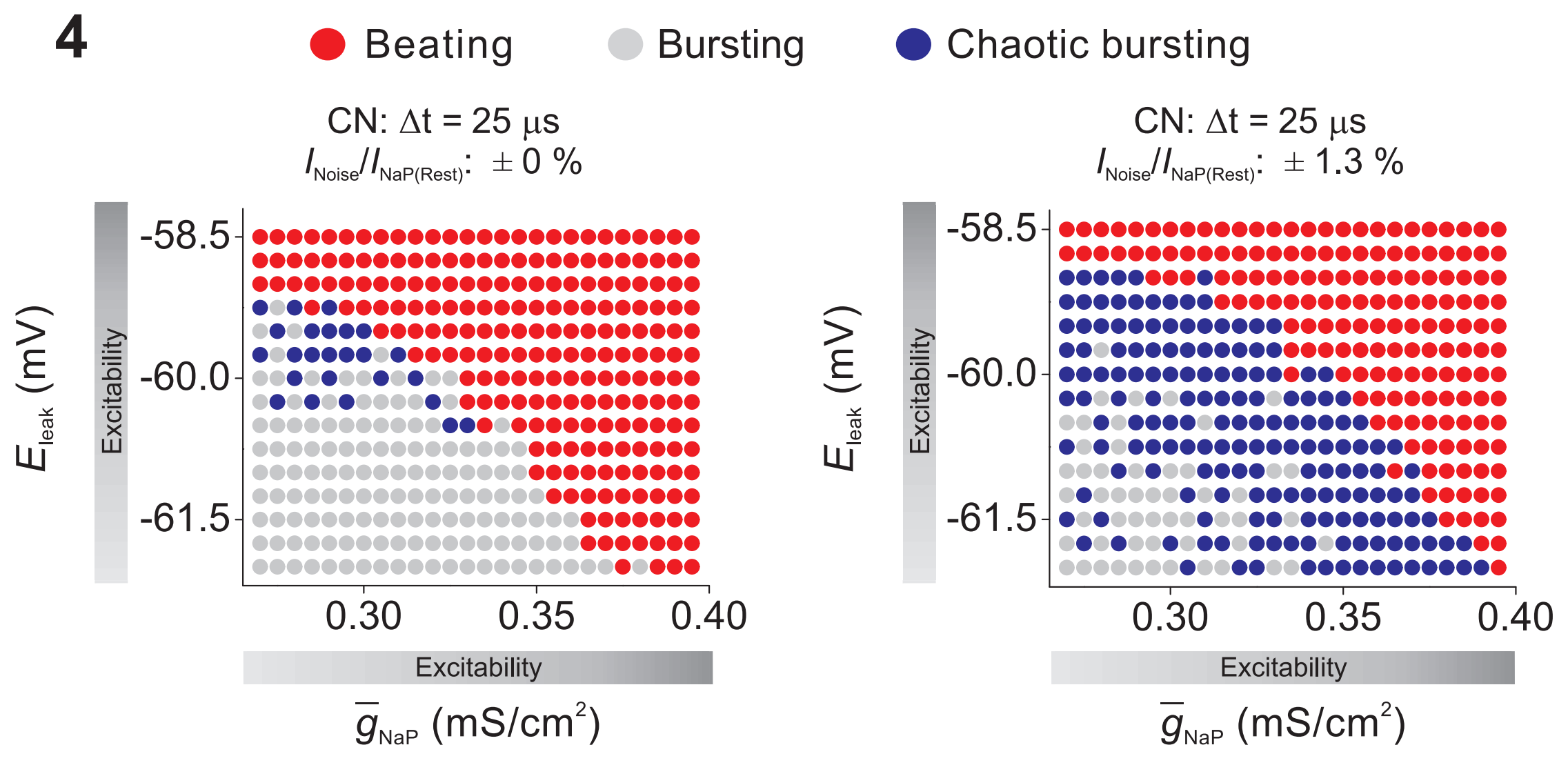
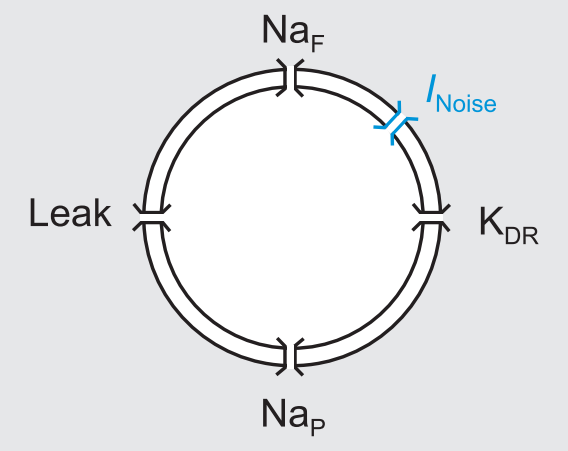


❶ The parameter space displayed chaotic dynamics near the transition from bursting to beating in the absence of noise (**Fig. 4, left**).

❷ In the presence of noise almost the entire bursting parameter space exhibited chaos (**Fig. 4, right**).

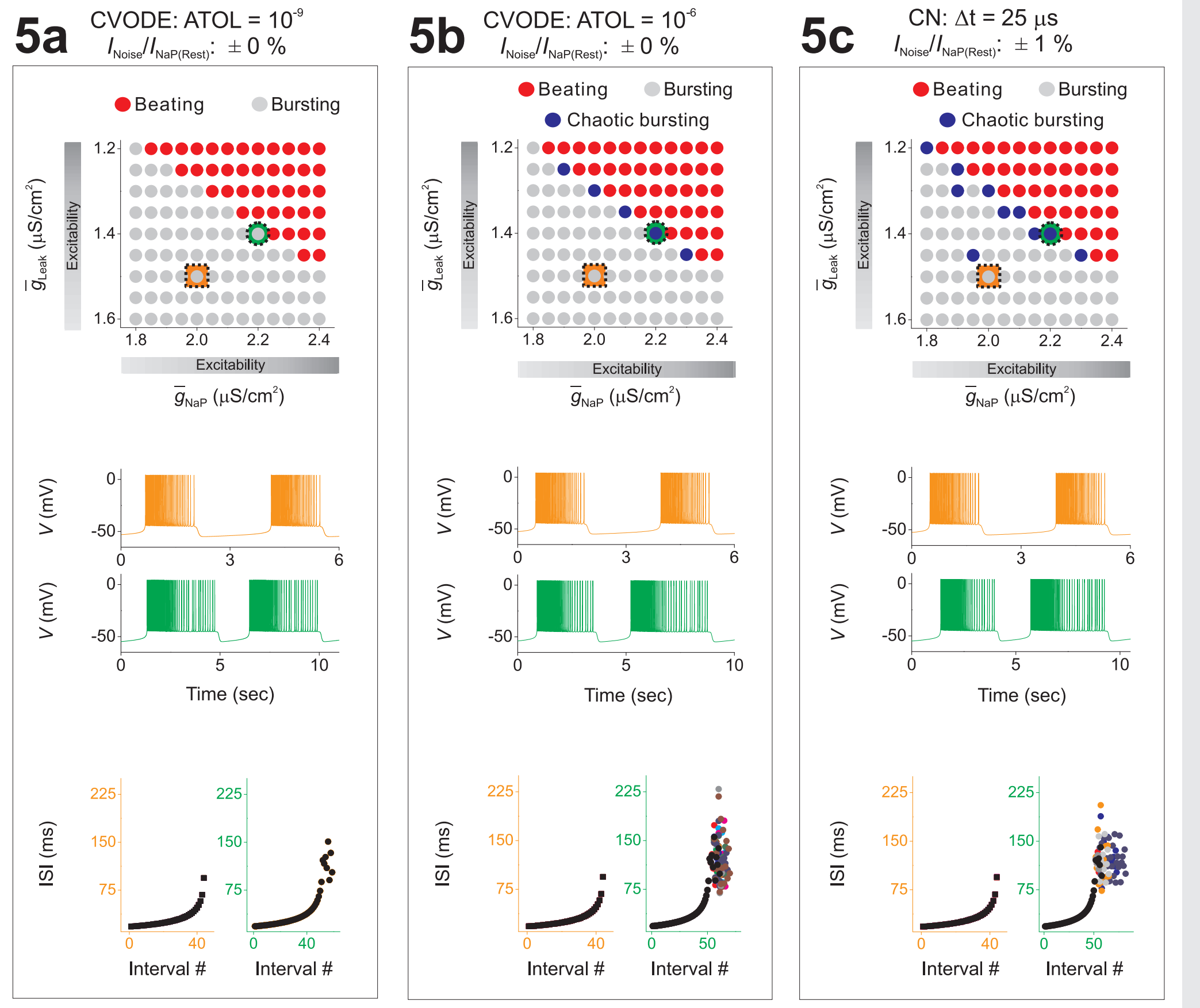
Non-Chaotic Burster



❶ High accuracy simulation of a simple pacemaker model displays no chaotic dynamics near transition from bursting to beating (**Fig. 5a**).

❷ Low accuracy simulation of the same parameter space results in chaotic dynamics near transition from bursting to beating (**Fig. 5b**).

❸ Highly accurate fixed-time-step simulation can evoke chaotic dynamics near transition from bursting to beating with the addition of dynamic noise (**Fig. 5c**).



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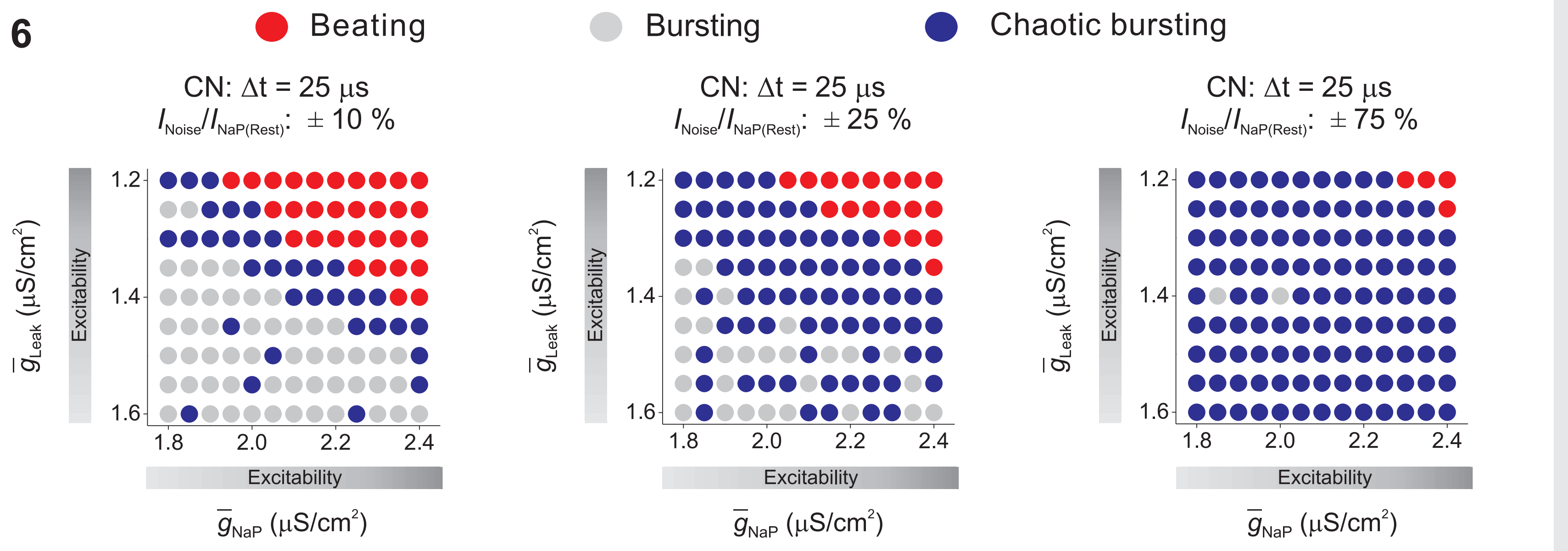

❶ Adding large amplitude dynamic noise causes almost entire parameter space to display chaotic dynamics (**Fig. 6**).

Conclusion

❶ Computational models of pacemaker neurons are sensitive to errors caused by particular numerical integration methods.

❷ A minimal chaotic pacemaker model requires calcium dynamics, and displays chaos only at the transition between bursting to beating, and at parameters that change the number of spikes/burst.

❸ Dynamic membrane noise may play a significant role in shaping bursting patterns of pacemaker neurons.

References

① Barahona, M. & Poon, C.-S. Detection of nonlinear dynamics in short, noisy time series. Nature 381, 215 - 217 (2002).
② Poon, C.-S. & Barahona, M. Titration of chaos with added noise. Proc Natl Acad Sci U S A 98, 7107--7112 (2001).

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