Durham University

Perturbed pulses proffer predictive power!

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Outline

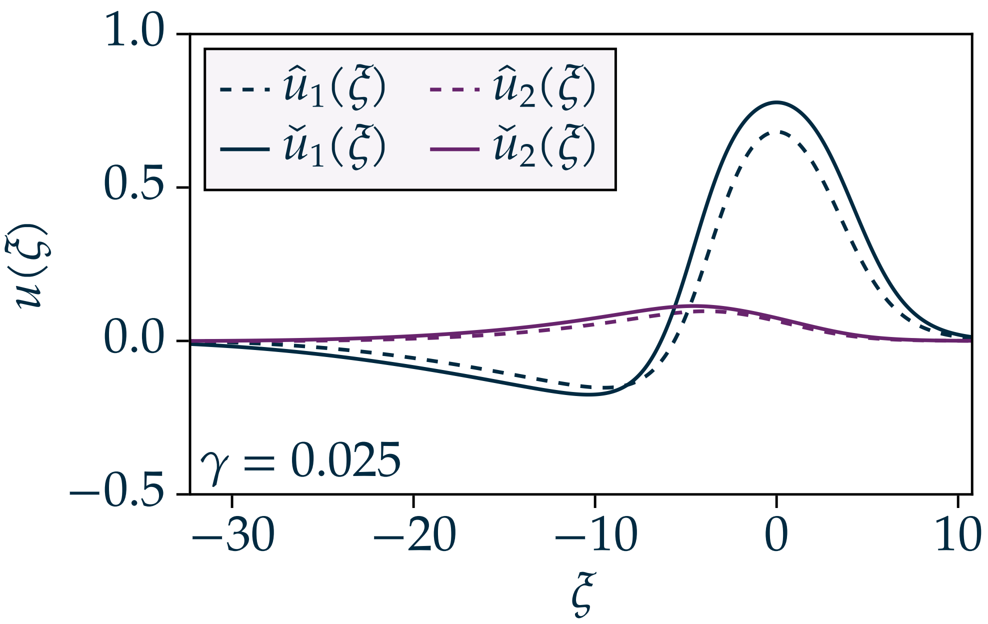

Figure 1: Fast & slow pulse solutions in FitzHugh-Nagumo for $\gamma = 0.025$.

Arrhythmias and Excitable Media

Control of Cardiac Tissue

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2. during fibrillation, the majority of the tissue is refractory or excited – *not excitable*.

> 1. Can we suppress the chaotic waves directly?
> 2. Are the perturbations for suppression predictable?
> 3. Is direct suppression more effective than generating new waves?

Dynamical Model

Consider states $u : \mathbb{R}^+ \times \mathbb{R}^d \to \mathbb{R}^k$ evolving according to the excitable model,

$$\partial_t u = D\Delta u + f(u),$$

- where $\Delta = \nabla \cdot \nabla$ is the (positive) Laplacian,
- D is a diagonal (potentially singular) matrix of diffusion coefficients, and
- $f : \mathbb{R}^k \to \mathbb{R}^k$ is a nonlinear function.

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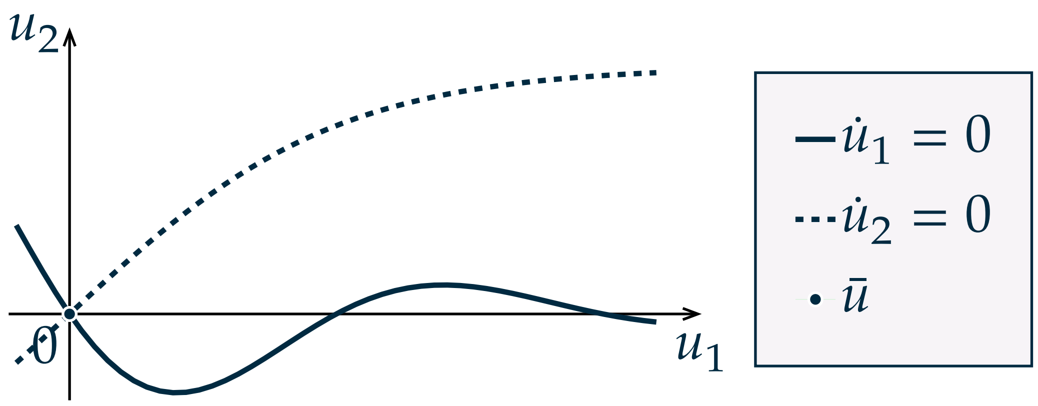
Root $\bar{u} : f(\bar{u}) = 0$ is unique, and $\bar{u}$ is (asymptotically, linearly) stable:

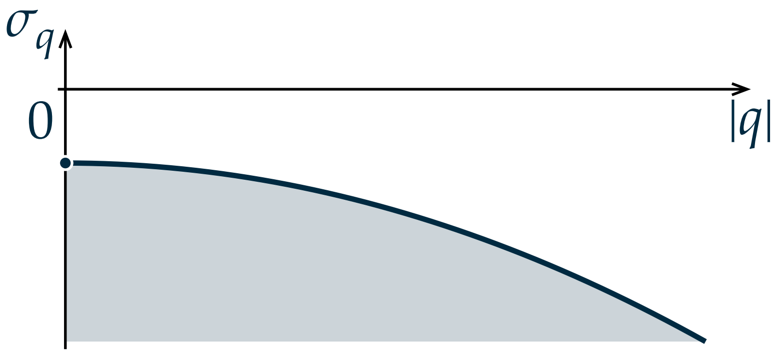
$$\operatorname{Re} \lambda(f'(\bar{u})) < 0.$$



Uniform state stability

Since $\operatorname{Re}\lambda(f'(\bar{u})) < 0$ and the spatial coupling is diffusive, the uniform rest state $\bar{u}$ is linearly stable for all wavelengths q:

$$u \to \bar{u} + U e^{iqx+\sigma_q t}$$
$$\Rightarrow \sigma_q U = \left(-Dq^2 + f'(\bar{u})\right) \cdot U$$



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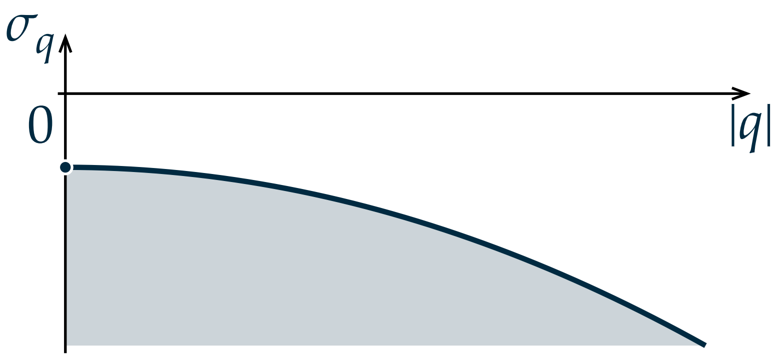

So far, this is a very boring system. We have:

1. One homogenous equilibrium state, which is
2. Linearly stable for all wavelengths q, and
3. To which almost every initial condition returns.

Pulses in Excitable media

For some parameters, the model has pulse train solutions of transient excitation, $u(\xi)$ of a comoving coordinate $\xi = x - ct$ with $u' \equiv \partial_\xi u(\xi)$, satisfying

$$Du'' + cu' + f(u) = 0, \quad u(\xi) = u(\xi + nL) \text{ with } n \in \mathbb{Z}, f \sim (1, \gamma)$$

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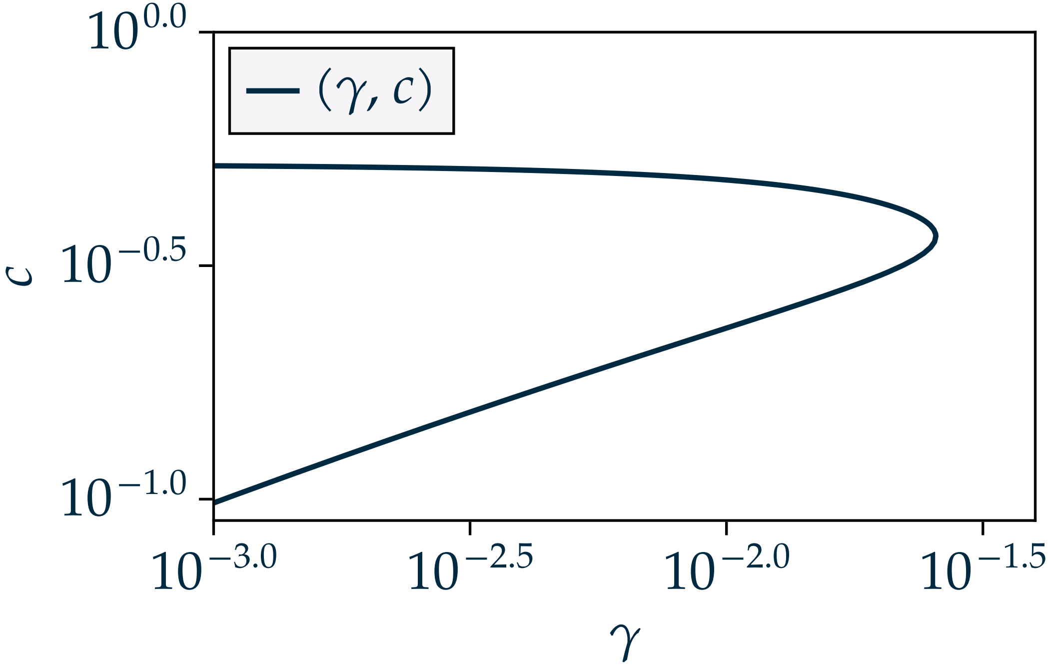
Continuing[1] one of these solutions in the speed (c) and timescale separation (γ) yields families of slow and fast pulses, which coincide for large γ.



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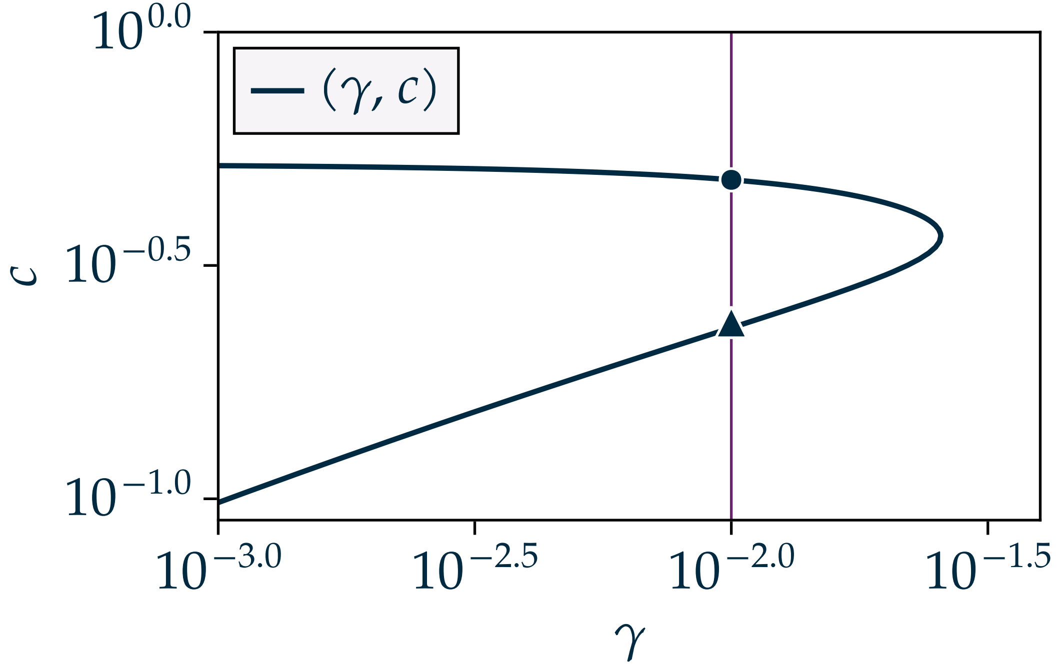
Selecting a particular value of γ yields fast and slow pulse solutions:

- an unstable, pulse $(\hat{u}, \hat{c})$ (▲)
- a stable, pulse $(\check{u}, \check{c})$ (●).



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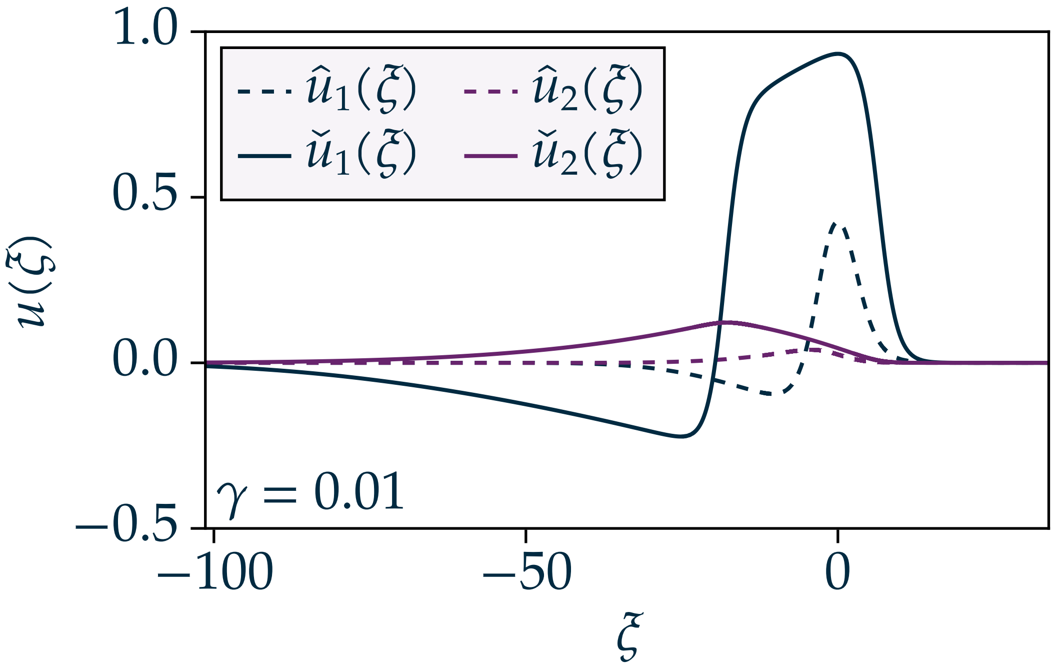
The fast wave is faster than the slow wave ($\check{c} > \hat{c}$), and importantly the fast wave is *stable*, while the slow wave is *unstable*.



Boundary Conditions: Periodic → Homoclinic

For the ODE system...

$$
\begin{aligned}
u_1' &= u_3, \\
u_2' &= -\frac{\gamma}{c} f_2(u_1, u_2), \\
u_3' &= -(c u_3 + f_1(u_1, u_2))
\end{aligned}
$$

...the Jacobian is:

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J = \begin{pmatrix} 0 & 0 & 1 \\ -\frac{\gamma}{c} f_{2,1} & -\frac{\gamma}{c} f_{2,2} & 0 \\ -f_{1,1} & -f_{1,2} & -c \end{pmatrix}
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To get an isolated pulse, we use projective boundary conditions such that $u(\xi)$

- leaves the rest state orthogonal to the stable manifold of the rest state, and
- returns to the rest state orthogonal to the unstable manifold of the rest state.

$$P_s^\top \begin{pmatrix} u(-\infty) - \bar{u} \\ u'(-\infty) \end{pmatrix} = 0, \quad P_u^\top \begin{pmatrix} u(\infty) - \bar{u} \\ u'(\infty) \end{pmatrix} = 0.$$

Where $[P_u, P_s]^\top = [E_u, E_s]^{-1}$ and $J[E_u, E_s] = [E_u, E_s][\Lambda_u, \Lambda_s]$.

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$$P_s^\top \begin{pmatrix} u(0) - \bar{u} \\ u'(0) \end{pmatrix} \approx 0, \quad P_u^\top \begin{pmatrix} u(L) - \bar{u} \\ u'(L) \end{pmatrix} \approx 0.$$

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Eigenfunctions

Given an isolated pulse (u, c) satisfying,[1]

$$0 = Du'' + cu' + f(u), \quad \mathcal{B}(u) = 0,$$

[1] The nonlinear and (right) eigenfunction problems have one left and two right boundary conditions, while the adjoint (left) eigenproblem has two left and one right boundary conditions.

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and biorthogonal (left) eigenfunctions $w_i^\dagger\sigma_i^* = \mathcal{L}^\dagger(u)w_i^\dagger$ satisfying,

$$\int_{-\infty}^{+\infty} \mathrm{d}x \, w_j(x)\mathcal{L}(u)v_i(x) = \delta_{ij}\left(\sigma_j - \sigma_i\right), \quad \mathcal{B}^\dagger(u) = 0.$$

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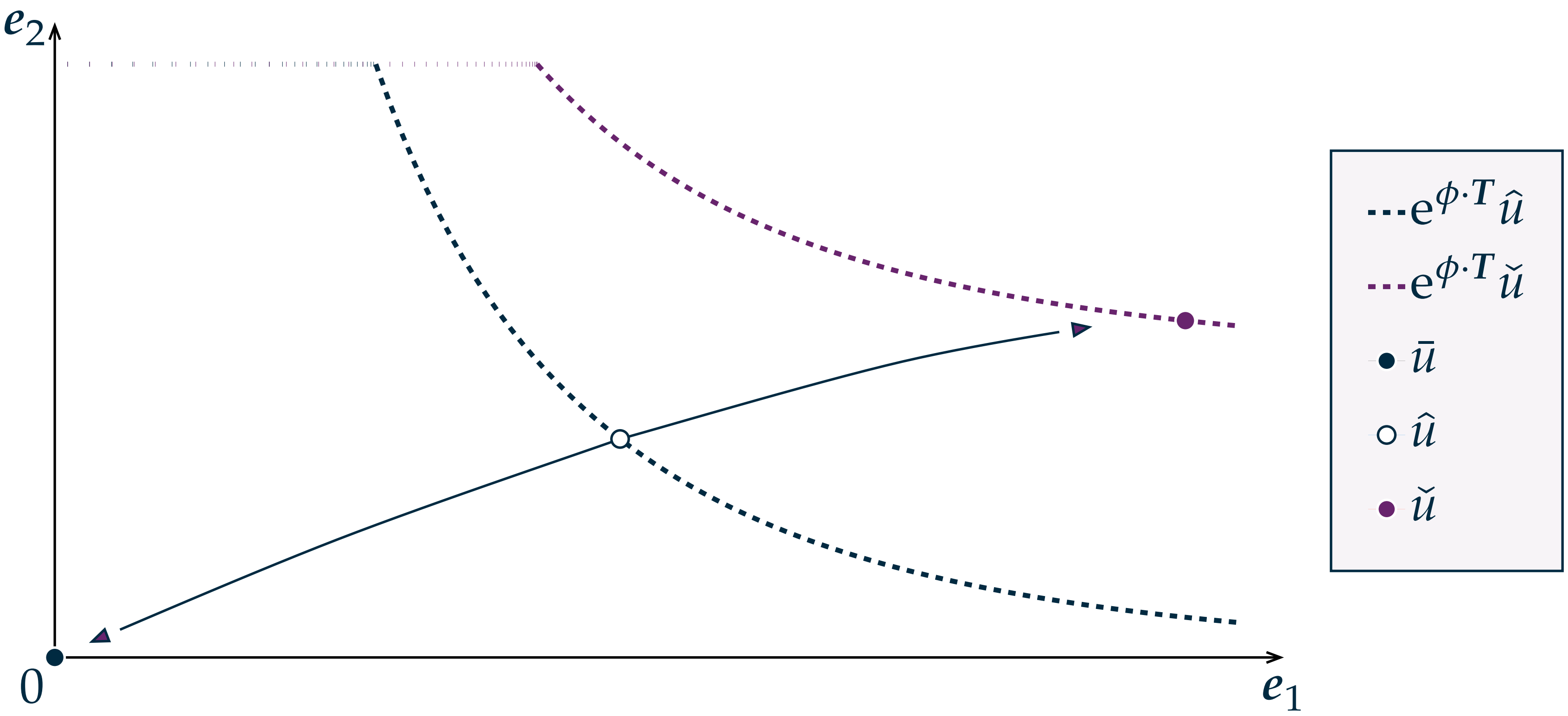
Geometrical Setting

In all the following, we think of the unstable pulse $\hat{u}$ as separating the statespace of u



Ignition

Motivation

For the ignition problem we ask[2–4]:

> Which initial conditions $u(0, x) = \bar{u} + \bar{h}(x)$ in the neighborhood of $\bar{u}$, approach the stable wave solution $\check{u}(\xi)$ as $t \to \infty$?[1]

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⇒ Use the unstable pulse solution $\hat{u}$ to investigate transition from $\bar{u} \to \check{u}$.[2]

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Linear Theory

1. Compare the initial condition to uniform solution $\bar{u}$,
2. Linearize about the (s-shifted) unstable solution $\hat{u}(\xi)$, $\xi = x - s$,
3. Project onto the leading left eigenmode, $\hat{w}_1(\xi)$.

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$$\langle \hat{w}_1(\xi) \mid \hat{h}(\xi) \rangle \stackrel{\text{def}}{=} \int_{-\infty}^{+\infty} \mathrm{d}\xi \; \hat{w}_1^\dagger(\xi) \hat{h}(\xi) = 0,$$

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$$\Rightarrow \langle \hat{w}_1(\xi) \,|\, \bar{h}(x) \rangle = \langle \hat{w}_1(\xi) \,|\, \hat{u}(\xi) - \bar{u} \rangle$$

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Three heuristics for selecting shift s:

1. minimize amplitude of $\bar{h}(x)$, or
2. minimize $\|\hat{h}(\xi)\|_2$, or
3. require $\hat{v}_2(\xi)$ is unexcited at $t = 0$.

These all yield expressions involving $\hat{w}_{1,2}(\xi)$, $\hat{v}_{1,2}(\xi)$, $\hat{u}(\xi)$, and $\bar{u}$ and $\bar{h}(x)$:

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If we factor an amplitude from the perturbation envelope, $\bar{h}(x) = \bar{U}(s)\bar{X}(x)$, then

$$\underbrace{\langle \hat{w}_1(\xi) \mid \hat{u}(\xi) - \bar{u} \rangle = \bar{U}(s)\langle \hat{w}_1(\xi) \mid \bar{X}(x) \rangle}_{\text{Linearization}}, \quad \underbrace{N_l = \bar{U}(s)\langle K_l(\xi) \mid \bar{X}(x) \rangle}_{\text{Distance Minimization}}$$

Compatibility condition

Rewrite system in the generic form,

$$N_0 = \bar{U}(s)\langle K_0(\xi) \mid \bar{X}(x)\rangle, \quad N_l = \bar{U}(s)\langle K_l(\xi) \mid \bar{X}(x)\rangle,$$

with $\langle K_{0,l} \mid \bar{X}\rangle \neq 0$, gives a compatibility solution to determine s,

$$\Rightarrow \langle N_0 K_l - N_l K_0 \mid \bar{X}\rangle \stackrel{\text{def}}{=} \langle \bar{\Phi}_l(\xi) \mid \bar{X}\rangle = 0.$$

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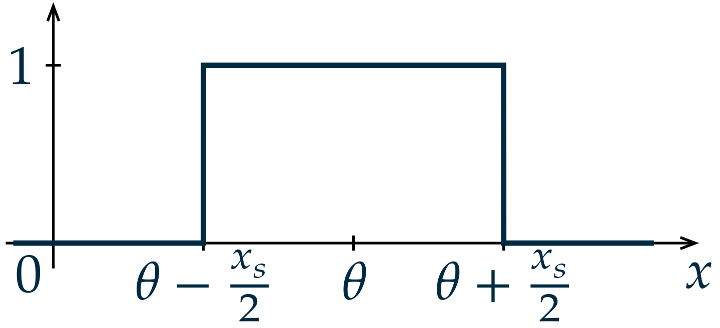
$$-\bar{X}(x; x_s) = \Theta\left(x - \frac{x_s}{2}\right)\Theta\left(x + \frac{x_s}{2}\right)$$



The root of $\langle \bar{\Phi}_l(\xi) \mid \bar{X}\rangle$ is almost unique if:

- $\bar{X}(x)$ is localized, and
- $\bar{X}(x)$ is positive semi-definite, or $\int \mathrm{d}x' \bar{X}(x')$ is càdlàg.

Quenching

Motivation

For quenching, consider perturbations to *non-uniform* states:

$$u(0,x) = \check{u}(x) + \check{h}(x-\theta),$$

and we ask a similar, almost time-reversed, question:

> Which initial conditions $u(0,x) = \check{u}(x) + \check{h}(x-\theta)$ approach $\bar{u}$ as $t \to \infty$?

Skipping the argument, we arrive at a similar result for the quenching amplitude:

$$\check{U}(s) = \frac{\langle \hat{w}_1(\xi) \mid \hat{u}(\xi) - \check{u}(x) \rangle}{\langle \hat{w}_1(\xi) \mid \check{X}(x-\theta; x_s) \rangle}$$

Reassessing Shift Heuristics

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3. require $\hat{v}_2(\xi)$ is unexcited at $t = 0$.

These yield conditions of form:

$$\langle \check{\Phi}_l(\xi; s) \mid \check{X}(x - \theta; x_s) \rangle = 0,$$

where $\check{\Phi}_l(\xi; s)$ is ~~gross~~ a sum of s-dependent weights of ξ-dependent functions,

$$\check{\Phi}_l(\xi; s) = \phi_{l,1}(s)\boldsymbol{a}_{l,1}(\xi) + \phi_{l,2}(s)\boldsymbol{a}_{l,2}(\xi).$$

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$\Rightarrow$ roots of $\check{\mu}_l(s; \theta, x_s) \stackrel{\text{def}}{=} \langle \check{\Phi}_l(\xi; s) \mid \check{X}(x - \theta; x_s) \rangle$ are *not* unique or guaranteed to exist.

Asymptotic Quenching Sketch

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- Sufficiently far perturbations will fail to quench,

$$\lim_{|\theta|\to\infty} \mathbb{P}(\text{quench} \mid x_s \text{ finite}) \to 0.$$

- Sufficiently wide perturbations have constant critical quenching amplitudes,

$$\lim_{x_s\to\infty} \partial_{x_s}|\check{U}| \to 0^-.$$

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$$\lim_{|\theta| \to \infty} \mathbb{P}(\text{quench} \mid x_s \text{ finite}) \to 0.$$

- Sufficiently wide perturbations have constant critical quenching amplitudes,

$$\lim_{x_s \to \infty} \partial_{x_s} |\check{U}| \to 0^-.$$

Guaranteed at least one successful quench for x_s large, $|\theta|$ small, and $|\check{U}|$ ‘small’.
⇒ *Continue asymptotic quenching solution!*

Uniqueness through continuation

Continuation plan:

1. compute shift s for very wide perturbations ($x_s \gtrsim L$), and
2. continue the solution branch to small widths ($x_s \ll L$), while
3. recording the amplitude $\check{U}(s)$ as s varies with $x_s \in (0, L]$.

---

[1]The path (x_s, s) will reach a limit point where $x_s'(s) = 0$, at which point the continuation solution is not unique for fixed x_s, which is the entire point – we don't want multiple solutions.

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At some point, the solution branch will end[1], thus we get away with 'natural' continuation:

$$x_s^{n+1} = x_s^n - \delta x_s^n \Rightarrow s^{n+1} = s^n - \delta s^n,$$

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In contrast to ignition, for some (x_s, θ) there are *no* finite quenching amplitudes.

[1]The path (x_s, s) will reach a limit point where $x_s'(s) = 0$, at which point the continuation solution is not unique for fixed x_s, which is the entire point – we don't want multiple solutions.

Numerics

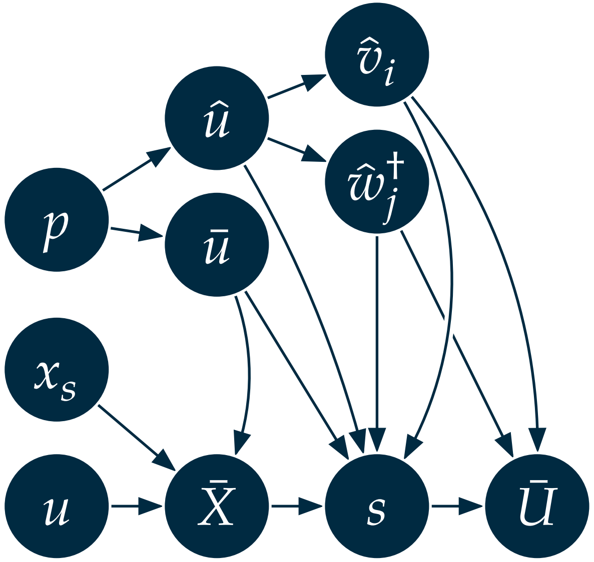
Linear Theory Prediction

To evaluate the ignition linear theory for (u, p), compute:

1. the stable rest state $\bar{u}$,
2. the unstable pulse $\hat{u}$,
3. the leading eigenmodes $\hat{v}_{1,2}$ & $\hat{w}^{\dagger}_{1,2}$.

And then:

1. determine the shift s, and
2. finally predict $\bar{U}(s)$.



Only then have we made a prediction – verification comes later…

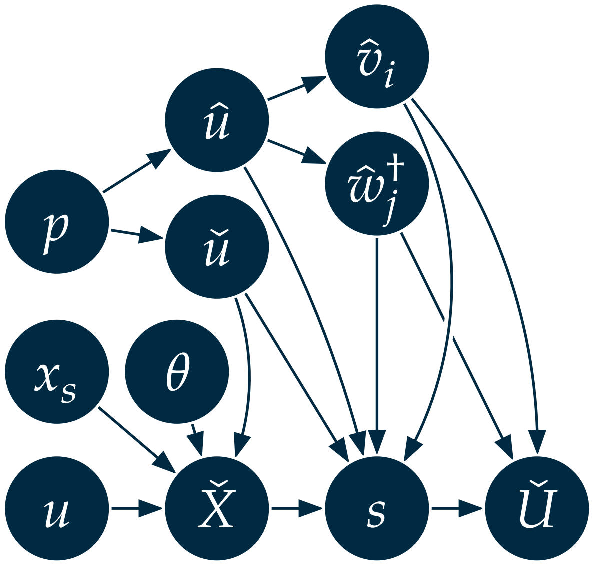
Linear Theory Prediction

To evaluate the quenching linear theory for (u, p), compute:

1. the stable rest state $\bar{u}$,
2. the unstable pulse $\hat{u}$,
3. the leading eigenmodes $\hat{v}_{1,2}$ & $\hat{w}^{\dagger}_{1,2}$.

And then:

1. select or determine θ,
2. determine the shift s, and
3. finally predict $\check{U}(s)$.



Only then have we made a prediction – verification comes later...

Linear Theory Prediction

1. Compute standard inner products over N-discretized space, $O(N)$

$$\langle f(\xi) \mid g(\xi) \rangle = f(\xi)^\top g(\xi)$$

2. Compute the convolutional inner products with Fourier Transform, $O(N \log N)$

$$\langle f(\xi) \mid g(\xi + s) \rangle = \mathcal{F}_s^{-1}\left\{ \mathcal{F}_q(f) \odot \mathcal{F}_q(g) \right\}$$

3. Compute the root(s) of the phase selector(s), $O(N)$

$$\hat{s}_l^* : \langle \bar{\Phi}_l(x - s) \mid X(x) \rangle = 0, \quad \check{s}_l^* : \langle \check{\Phi}_l(x - s; s) \mid \check{X}(x - \theta; x_s) \rangle = 0,$$

4. Interpolate over s to find quenching amplitude, $O(1)$

$$\bar{U}(s) = \frac{\langle \hat{w}_1(\xi) \mid \hat{u}(\xi) - \bar{u} \rangle}{\langle \hat{w}_1(\xi) \mid \bar{X}(x) \rangle}, \quad \check{U}(s) = \frac{\langle \hat{w}_1(\xi) \mid \hat{u}(\xi) - \check{u}(x) \rangle}{\langle \hat{w}_1(\xi) \mid \check{X}(x - \theta; x_s) \rangle}$$

Only then have we made a prediction – verification comes later...

Direct Numerical Simulation

Verification of predictions with DNS:

Perturb exact state $u_0 \in \{\bar{u}, \check{u}\}$ with a perturbation $X_0 \in \{\bar{X}, \check{X}\}$,

$$u(0,x) = u_0 + AX_0(x)$$

evolve the system and compare a solution norm

$$\psi(t) \stackrel{\text{def}}{=} \Psi(u(t,x) - \bar{u})$$

to that of the unstable pulse $\hat{u}$, $\hat{\psi} \stackrel{\text{def}}{=} \Psi(\hat{u}(x) - \bar{u})$

$$\lim_{t\to\infty} \psi(t) \gtrless \hat{\psi}.$$

to bisect on the value of A, comparing to the predicted critical amplitude $\bar{U}$ or $\check{U}$...

Direct Numerical Simulation

Verification of predictions with DNS:

For pulses, we are interested in the deviation of the state from the rest state in the fast variable(s),

$$\psi(t) \stackrel{\text{def}}{=} \Psi(u(t,x) - \bar{u}) \equiv \int_0^L \mathrm{d}x \ |u_1(t,x) - \bar{u}_1|.$$

Nicely maps onto the intuition for 'large, fast' or 'small, slow' pulses, but *not* unique.

We require that $\check{\psi} \gg \hat{\psi} \gg \bar{\psi} \equiv 0$.

If $\hat{\psi}$ is too small $\Rightarrow$ difficult to distinguish from the rest state.
If $\hat{\psi}$ is too large $\Rightarrow$ difficult to distinguish from the stable pulse.

Direct Numerical Simulation

Verification of predictions with DNS:

We approach the DNS in two ways:

- finite-difference approximation with fully-implicit time-adaptive solvers, and
- spectral discretization with manually tuned IMEX time-steppers.

Finite-Difference

- Sparse $O(h_x^{12})$ central differences
- Solver `CVODE_BDF(GMRES)`[5]
- Spacestep h_x is fixed, *a priori*
- Approximate norm with spline

→ fast, reliable, low(er)-accuracy

Spectral

- Chebyshev-τ / Fourier basis[6],
- Step with `RK443`[7]
- Tuned timestep $h_t = 2^{\lceil \log_2(\frac{t}{T}) \rceil} h_T$
- *Exact* integral with interpolant

→ slow, semi-reliable, very accurate

→ Compare outcomes to ensure consistency.

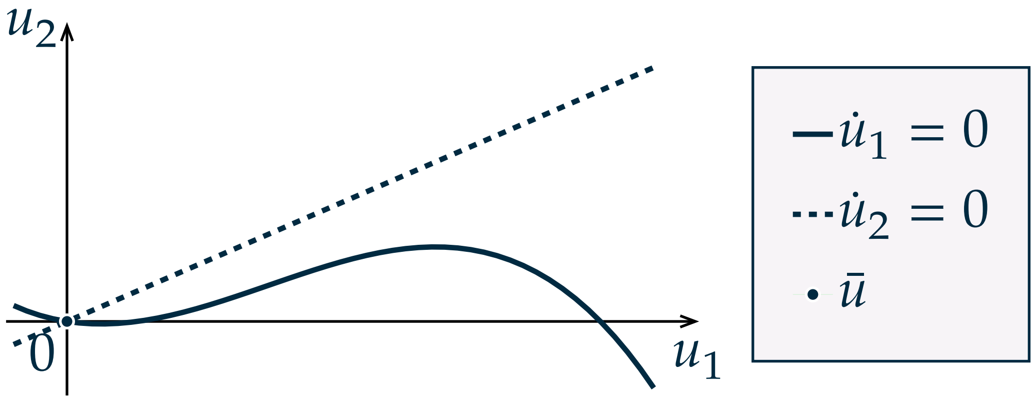
Results

Ignition – FitzHugh Nagumo

FitzHugh-Nagumo model[8,9]

$$\partial_t u_1 - \Delta u_1 = u_1(1-u_1)(u_1-\beta) - u_2, \quad \partial_t u_2 = \gamma(\alpha u_1 - u_2),$$

With $\alpha = 0.37$, $\beta = 0.131$, and $\gamma \in [10^{-10}, 10^{-1})$ varied.



Ignition – FitzHugh Nagumo

Compute linear theory ingredients and for each x_s:

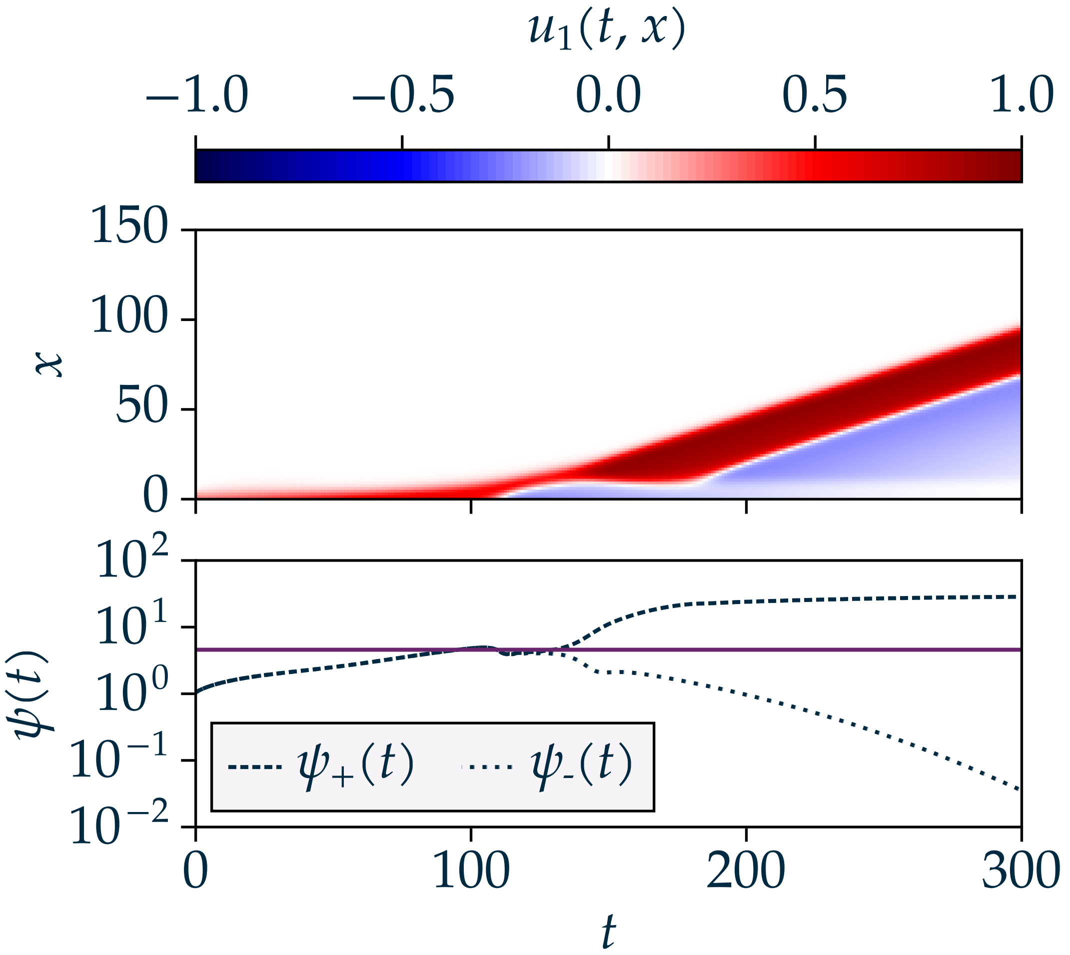
Linear Theory

- compute reference shifts s_l, and
- predict ignition amplitudes $\bar{U}(s_l)$

DNS

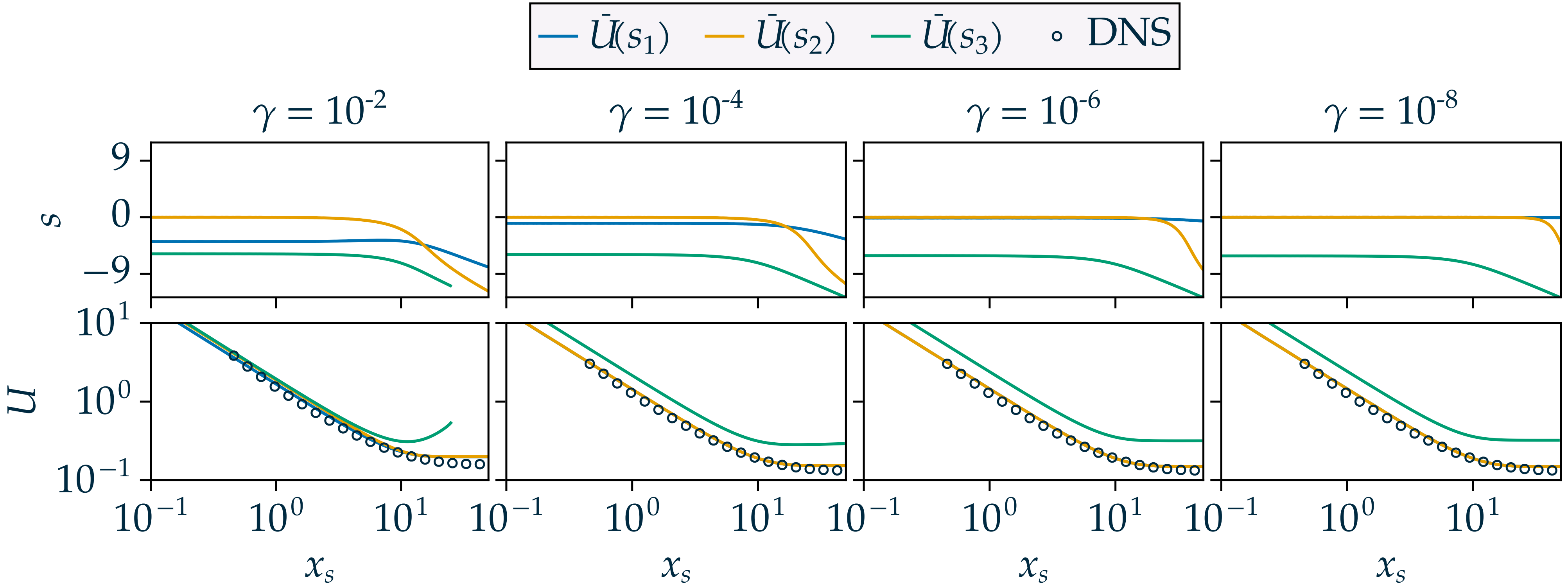
- solve bisection problem:

$$f(A) = \lim_{t\to\infty} \psi_A(t) - \hat{\psi},\ A \in [10^3, 0).$$



Ignition – FitzHugh Nagumo

Predict critical ignition amplitudes across several decades in x_s, and many more in γ, with some predictions managing exceptional accuracy.



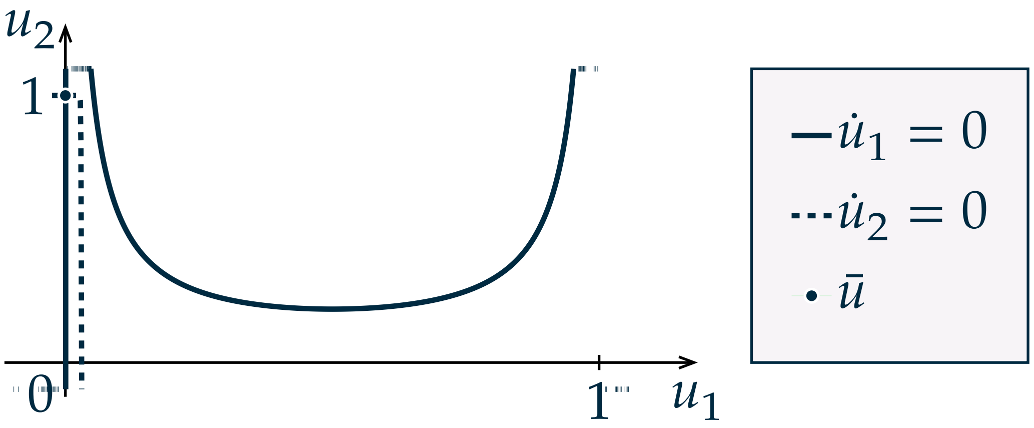
Ignition – Mitchell-Schaeffer

Mitchell-Schaeffer is a model derived via an asymptotic reduction of the Fenton-Karma model, and still incorporates multiple decay timescales for the system.[10,11]

$$\partial_t u_1 - \Delta u_1 = u_1^2(1-u_1)u_2 - u_1\frac{\tau_i}{\tau_u},$$

$$\partial_t u_2 = \gamma\left((1-\vartheta_1)(1-u_2)\left(\frac{\tau_c}{\tau_o}\right) - \vartheta_1 u_2\right), \quad \vartheta_1 = \Theta\left(u_1 - u_g\right)$$

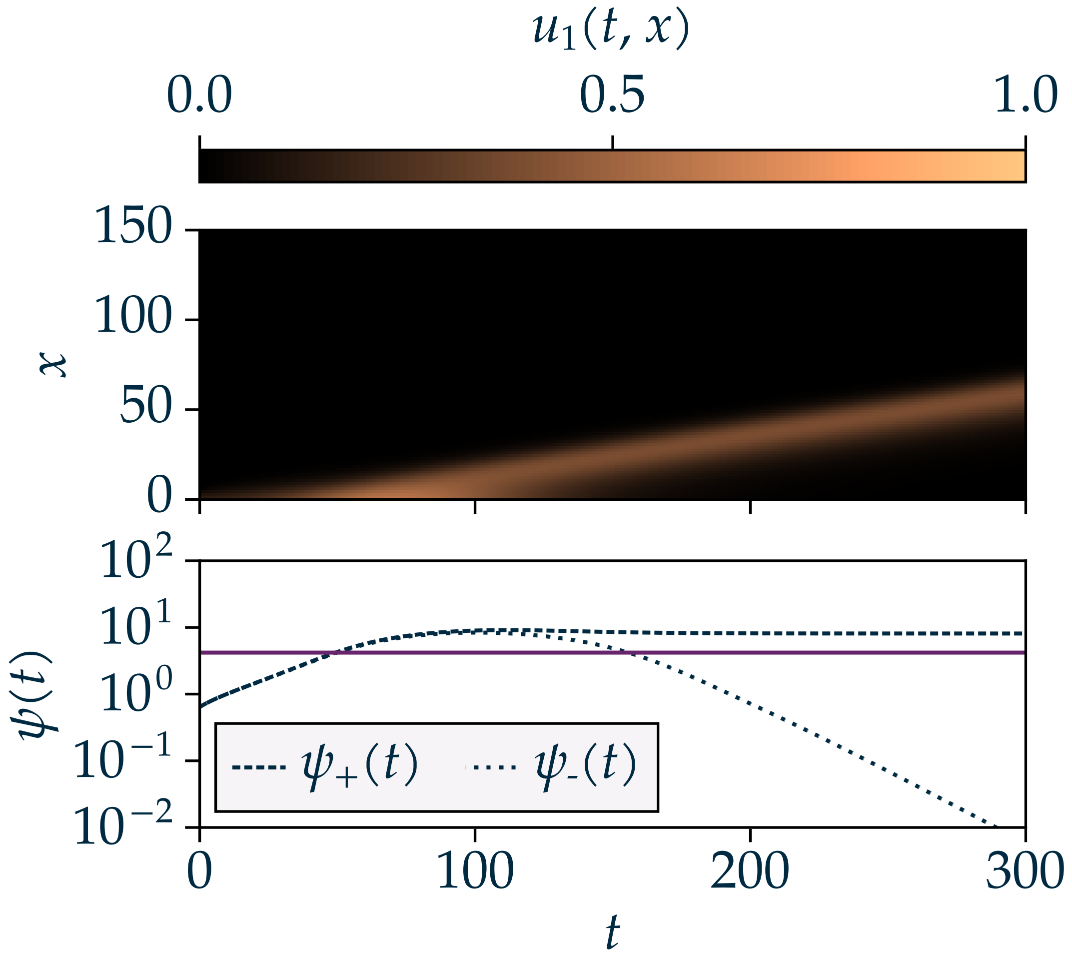
With $\tau_i = 0.3$ ms, $\tau_u = 6$ ms,
$\tau_c = 150$ ms, $\tau_o = 120$ ms,
$u_g = 0.03$, and $\gamma \in [10^{-10}, 10^{-1})$ varied.



Ignition – Mitchell-Schaeffer

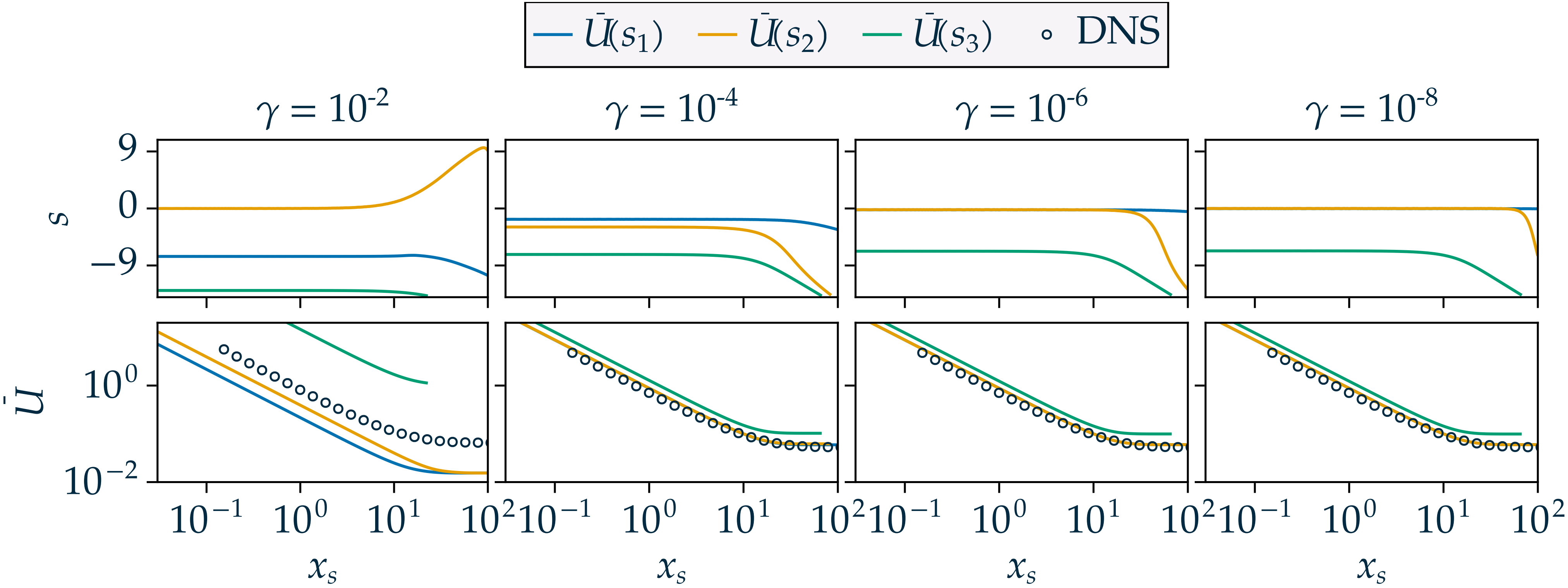
Mitchell-Schaeffer is a tad more compelling than FitzHugh-Nagumo if we are interested in *cardiac control*.

Since the model has multiple time-scales, we get a better sense for where the linear theory struggles with physiological excitations.



Ignition – Mitchell-Schaeffer

Somewhat less successful for large γ than FitzHugh-Nagumo – due to slow convergence of $\hat{u}$ to $\bar{u}$ for large γ.



Predicting Ignition

1. We can reliably predict the threshold for ignition of stable pulses in slow-fast[1] models of excitable media,
    - for varying time-scale separations and
    - for a large range in perturbation amplitude.

   Limited by the deviation of the critical pulse solution from the rest state.

2. The linear theory is parsimonious and efficient compared to
    - optimal perturbation construction, or
    - nonlinear energy optimization methods, and

   Thus presents opportunities for optimization and multi-fidelity approaches.

[1]Note that some difficulty arises when the time-scale separation vanishes; since the models are not self-adjoint, one can get arbitrarily slow convergence of the eigenfunctions.

Quenching – Additional Equivariance

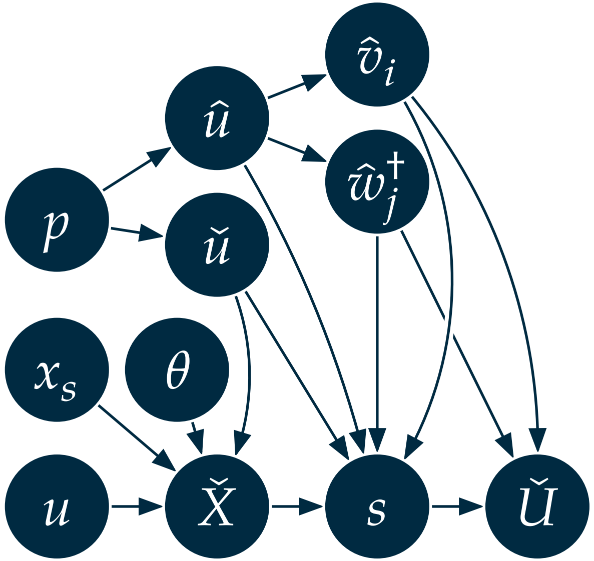
Quenching perturbations need to account for the position along $\breve{u}$, θ.

Quenching – Additional Equivariance

Quenching perturbations need to account for the position along $\check{u}$, θ.

- For each θ,
  - iterate over (or continue in) x_s,
    - predict the quenching amplitude $\check{U}$, *or*
    - solve the bisection problem for $\check{U}$.

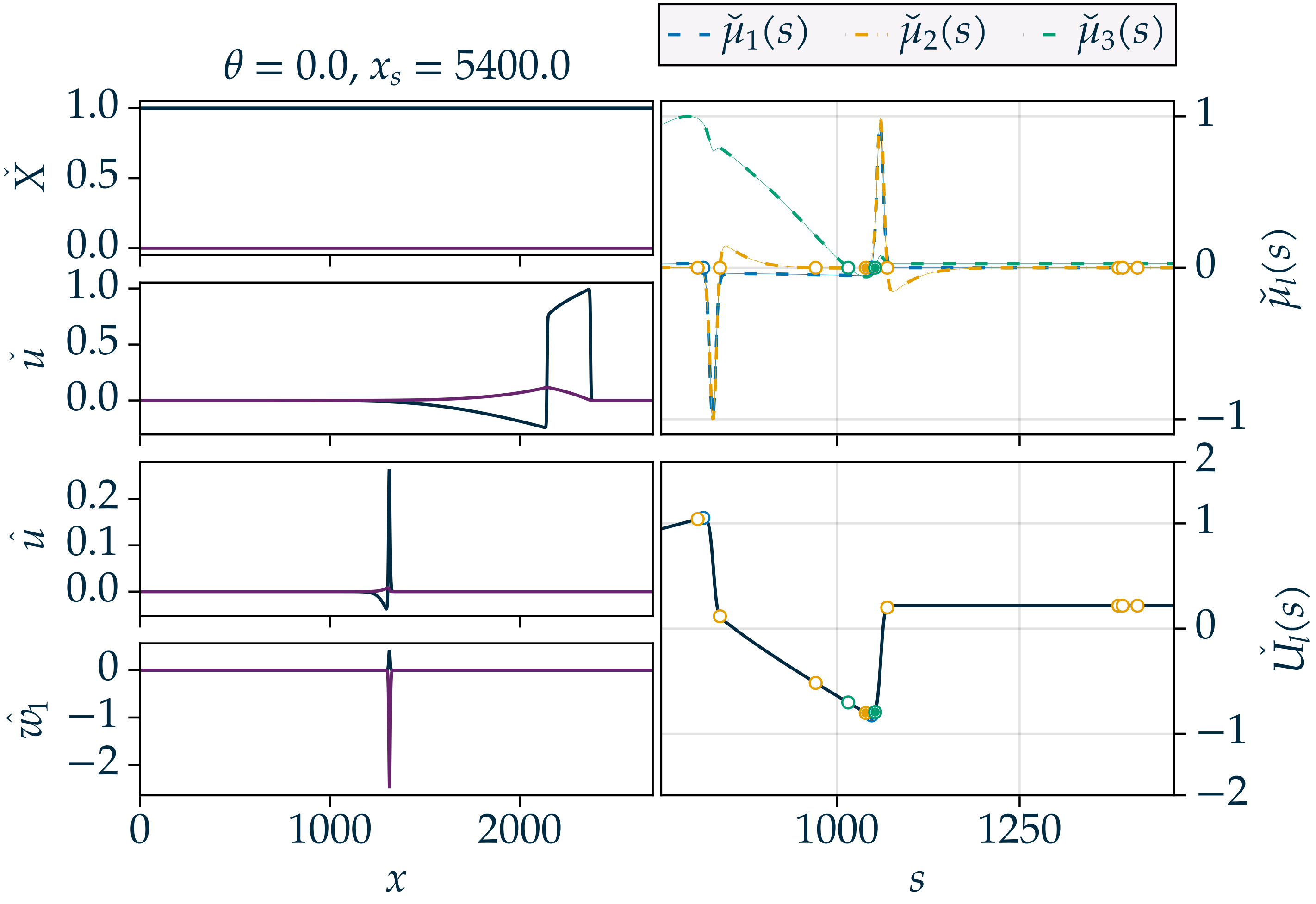
Sampling the 3-dimensional parameter space (x_s, θ, A) to resolve the embedded 2-dimensional manifold, $\check{U}(x_s, \theta)$.



The transition from *ignition* to *quenching* involves the solution of higher codimension bisection problems.

Quenching – Linear Theory Continuation

For $x_s \to \infty$, two solutions... matching $\check{u}$ and $\hat{u}$ on the wavefronts or on the wavebacks.

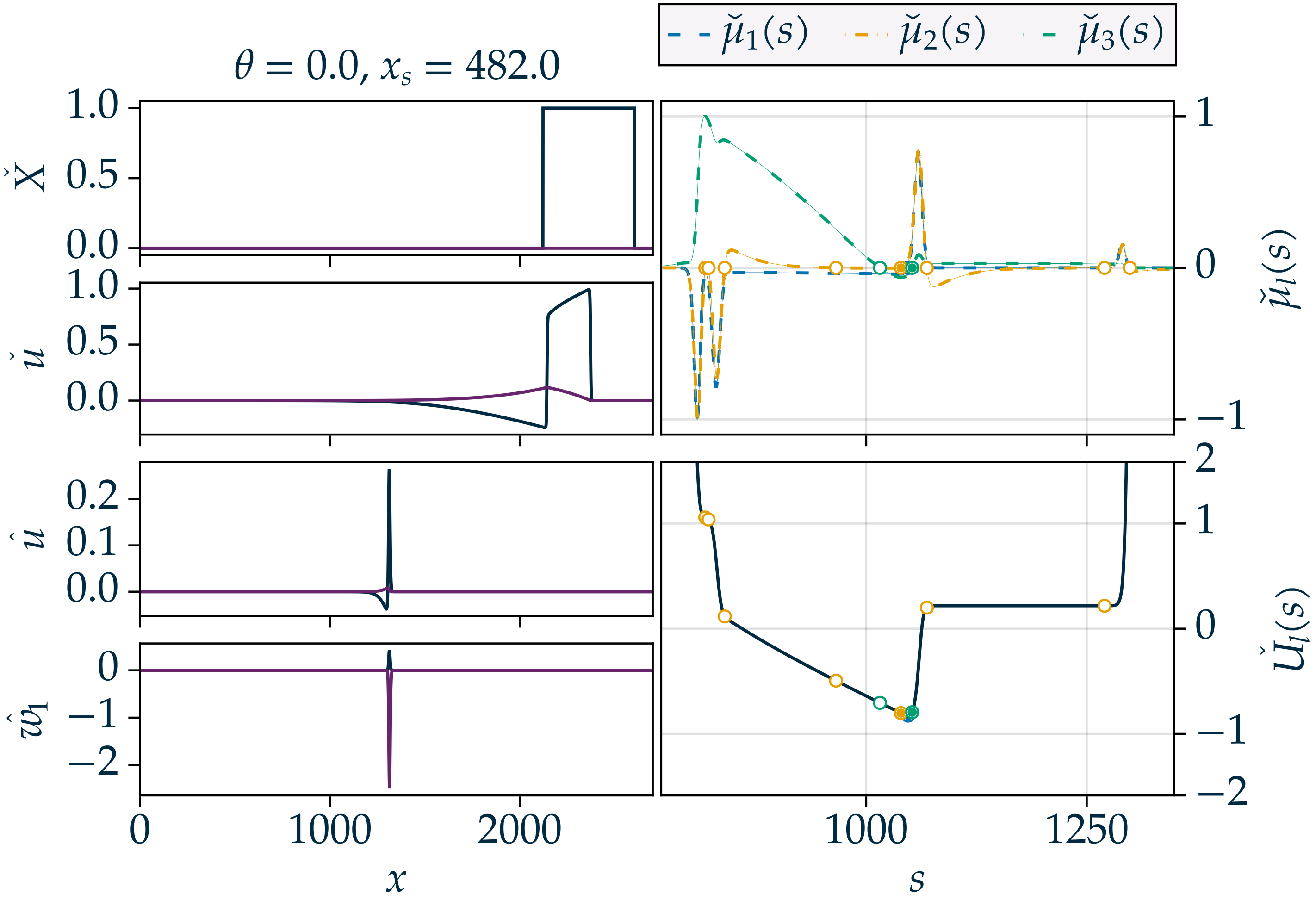


Quenching – Linear Theory Continuation

For intermediate x_s

$$x_s \sim \int_0^L \mathrm{d}x\ \Theta(\check{u}(x)),$$

then $\check{\mu}_l(s)$ deforms significantly, except near the solution, as when $x_s \to \infty$.

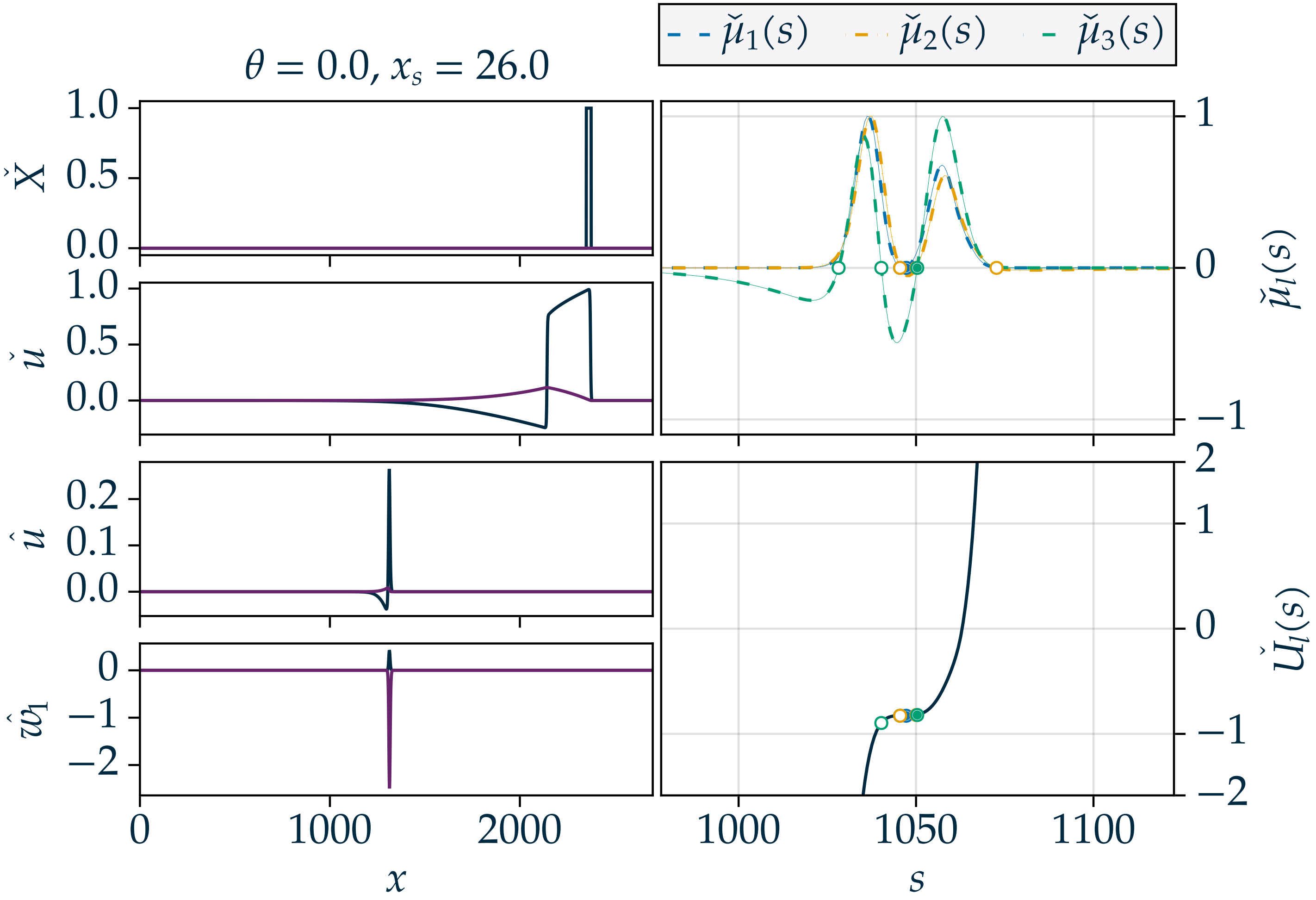


Quenching – Linear Theory Continuation

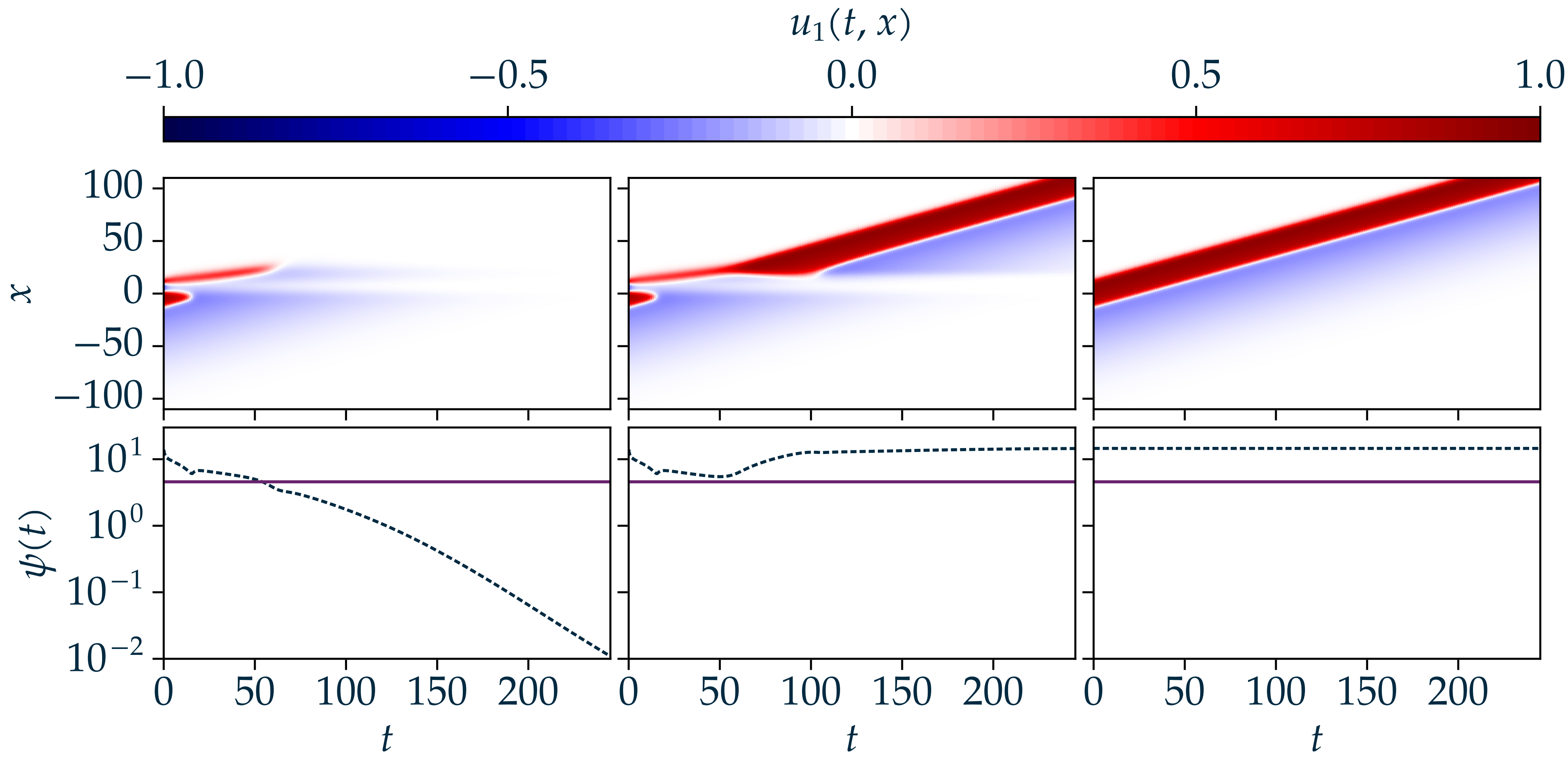
For small widths,

$$x_s < \int_0^L \mathrm{d}x\, \Theta(\check{u}(x)),$$

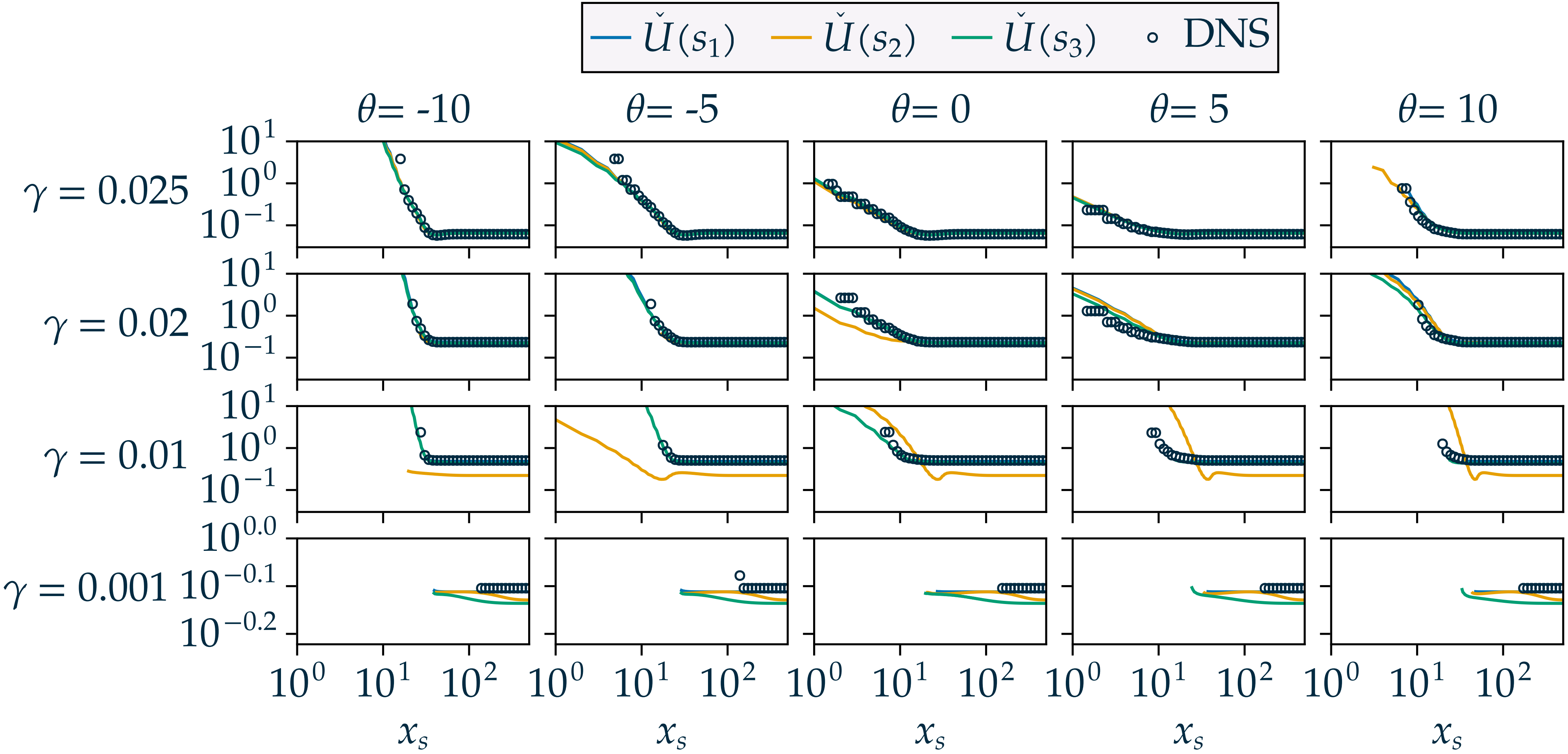
then we are in danger of losing the root in $\check{\mu}_l(s)$, ending the branch of solutions.



Quenching – FitzHugh Nagumo

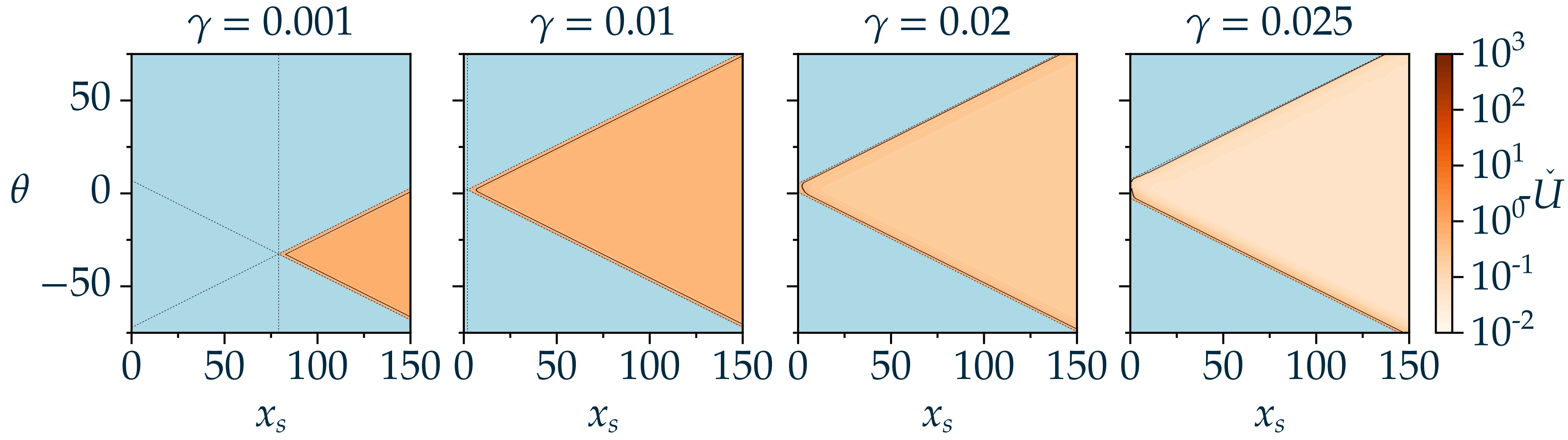


Quenching – FitzHugh Nagumo



Quenching – FitzHugh Nagumo

Stepping back, we can see the consequences of having no solutions for some (x_s, θ).



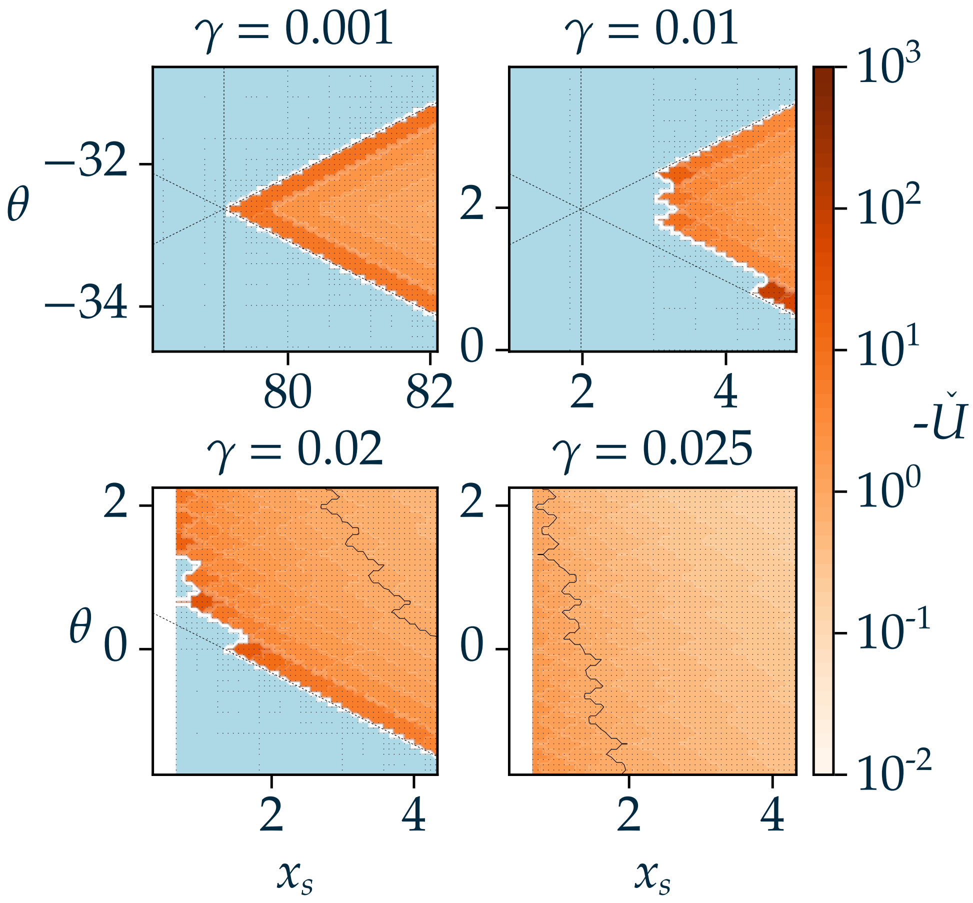
The solution regions are bounded by lines $|x_s - x_s^0| \lesssim \pm\frac{1}{2}\,|\theta - \theta^0|$, for some $\left(x_s^0, \theta^0\right)$.

Quenching – FitzHugh Nagumo

Zooming in, we can see the culprit:

For some (x_s, θ) there is *no critical quenching ampltitude*...
$\Rightarrow$ There is a width below which the wave can not be quenched.

The bisection is conservative – no solution $\Rightarrow \check{U} \leq -10^4$, while $A \in [-10^4, 0)$, and $\check{U} \gtrsim -1.4 \times 10^2$.

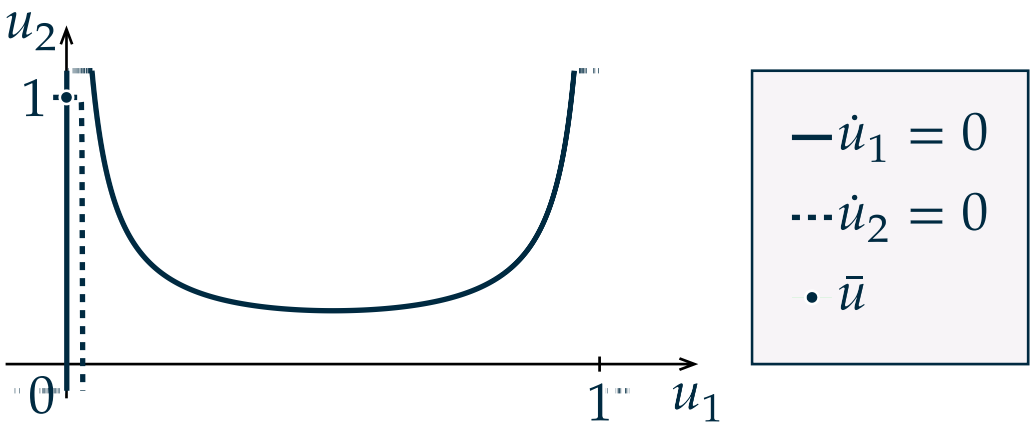


Quenching – Mitchell-Schaeffer

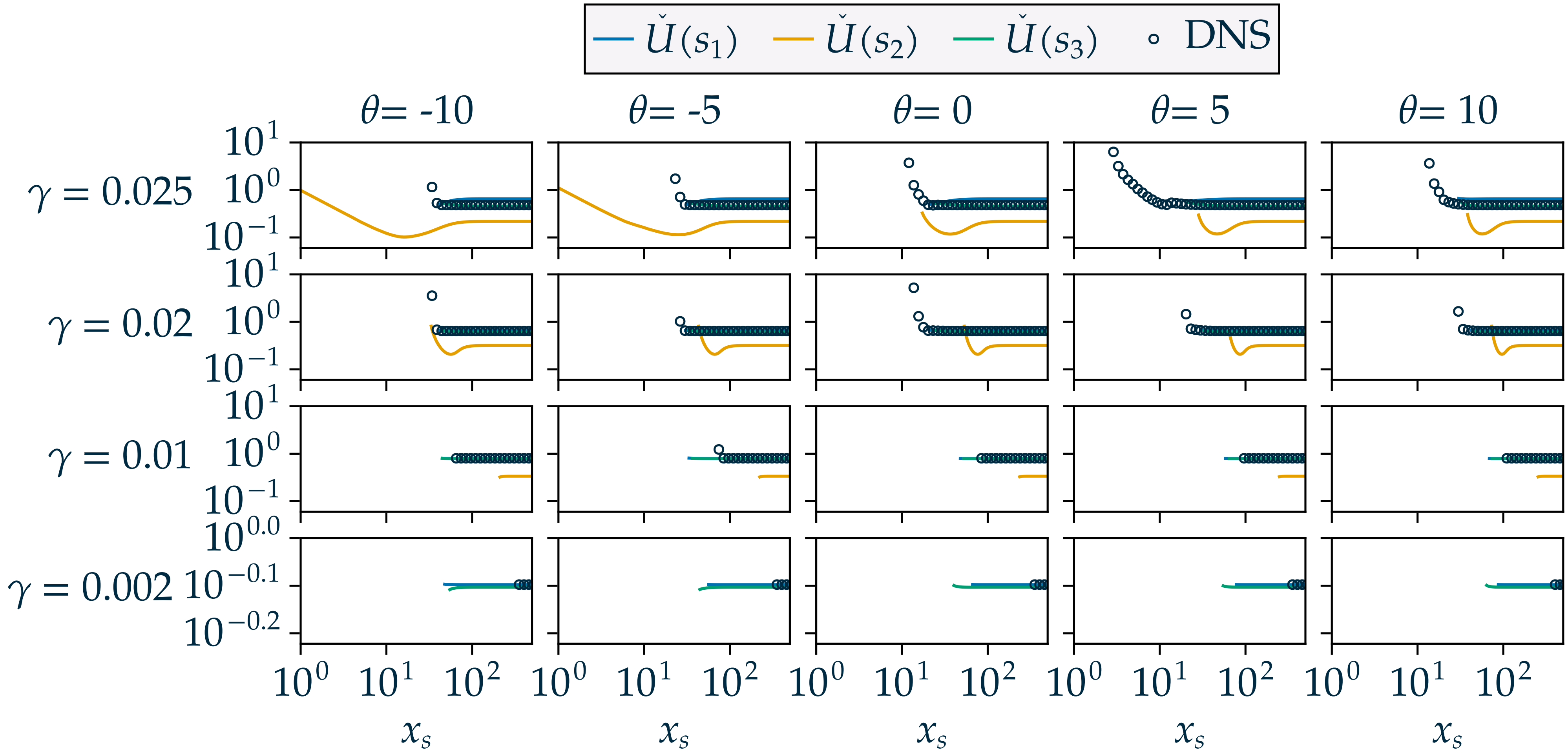
$$\partial_t u_1 - \Delta u_1 = u_1^2(1-u_1)u_2 - u_1\frac{\tau_i}{\tau_u},$$

$$\partial_t u_2 = \gamma\left((1-\vartheta_1)(1-u_2)\left(\frac{\tau_c}{\tau_o}\right) - \vartheta_1 u_2\right), \quad \vartheta_1 = \Theta\left(u_1 - u_g\right)$$

Mitchell-Schaeffer presents some difficulty for quenching – it is more stiff than FitzHugh-Nagumo, and exhibits less variation in the critical amplitude.

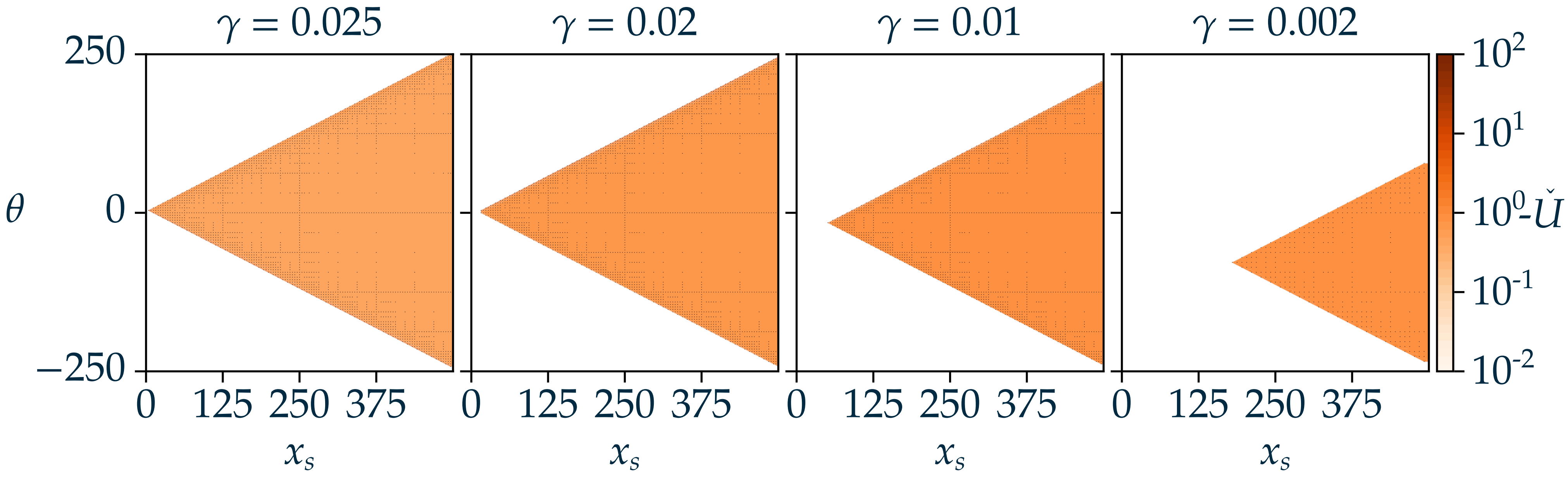


Quenching – Mitchell-Schaeffer



Quenching – Mitchell-Schaeffer

Mitchell-Schaeffer shows the same transition to nonlinear effects near the boundary of the quenchable region as FitzHugh-Nagumo, but we are less able to expand the linear theory predictions into that regime.



Predicting Quenching

Successes

- We can reliably predict the threshold for quenching of stable pulses in some models of excitable media, for varying time-scale separations and a large range in amplitude.
- For models and parameters with bounded quenchable regions (x_s, θ), we are able to approximate the boundary of this region via the linear theory.

Open Questions

- Unclear *why* the linear theory is able to capture this super-exponential growth in $|\check{U}|$ near the boundary of the solution region.
- Extending theory to non-Tikhonov systems (typical for cardiac models)
- Explanation for why $\check{\mu}_2$ produces inaccurate shifts is incomplete

Future Work & References

Future Work

Physical

- Transient amplification for stochastically parameterized excitable media
- Comparing nonlinear energy optimization & optimal perturbation methods
- Bidomain and Ephaptic coupling influences on stable transitions

Mathematical

- Fractional diffusion ($\Delta^{2s}, 0 < s < 1$) effects on the unstable pulse, eigenfunctions
- Perturbation theory for front quenching – boundary terms no longer vanish
- Flexibility of the method for higher-dimensional problems, e.g. target waves

Computational

- Actor model of concurrency for accelerating large multi-dimensional bisection
- h^p-adaptivity for quenching problems in cardiac models with sharp features
- Adjoint differentiation through ODE solvers for the DNS critical amplitude

References

Predicting critical ignition in slow-fast excitable models[12]

Predicting effective quenching of stable pulses in slow-fast excitable media[13]

1. Doedel, E. J. *et al.* AUTO-07P: Continuation and bifurcation software for ordinary differential equations. (2007).
2. Idris, I. & Biktashev, V. N. Critical Fronts in Initiation of Excitation Waves. *Physical Review E - Statistical, Nonlinear, and Soft Matter Physics* **76,** 1–6 (2007).
3. Idris, I. & Biktashev, V. N. Analytical Approach to Initiation of Propagating Fronts. *Physical Review Letters* **101,** 244101 (2008).
4. Bezekci, B. & Biktashev, V. N. Fast-Slow Asymptotic for Semi-Analytical Ignition Criteria in FitzHugh-Nagumo System. *Chaos: An Interdisciplinary Journal of Nonlinear Science* **27,** 93916 (2017).
5. Gardner, D. J., Reynolds, D. R., Woodward, C. S. & Balos, C. J. Enabling New Flexibility in the SUNDIALS Suite of Nonlinear and Differential/Algebraic Equation Solvers. *ACM Transactions on Mathematical Software* **48,** 1–24 (2022).
6. Burns, K. J., Vasil, G. M., Oishi, J. S., Lecoanet, D. & Brown, B. P. Dedalus: A flexible framework for numerical simulations with spectral methods. *Physical Review Research* **2,** 23068 (2020).
7. Ascher, U. M., Ruuth, S. J. & Spiteri, R. J. Implicit-explicit Runge-Kutta methods for time-dependent partial differential equations. *Applied Numerical Mathematics* **25,** 151–167 (1997).
8. FitzHugh, R. Impulses and physiological states in theoretical models of nerve membrane. *Biophysical journal* **1,** 445–466 (1961).
9. Nagumo, J., Arimoto, S. & Yoshizawa, S. An active pulse transmission line simulating nerve axon. *Proceedings of the IRE* **50,** 2061–2070 (1962).
10. Mitchell, C. C. & Schaeffer, D. G. A two-current model for the dynamics of cardiac membrane. *Bulletin of mathematical biology* **65,** 767–793 (2003).
11. Fenton, F. & Karma, A. Vortex dynamics in three-dimensional continuous myocardium with fiber rotation: Filament instability and fibrillation. *Chaos: An Interdisciplinary Journal of Nonlinear Science* **8,** 20–47 (1998).
12. Marcotte, C. D. & Biktashev, V. N. Predicting critical ignition in slow-fast excitable models. *Physical Review E* **101,** 42201 (2020).
13. Marcotte, C. D. Predicting effective quenching of stable pulses in slow-fast excitable media. *Physical Review E* **110,** 64210 (2024).