Geometric Singular Perturbation Theory (GSPT)

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Overview

1. Scaling, perturbation methods, and singular limits
2. Examples
3. Fast-slow systems
4. Geometric singular perturbation theory
5. A glimpse of applications
6. Glycolytic oscillator
7. Mitotic oscillator
8. Extensions, outlook, plan?
1. Scaling, perturbation methods, and singular limits
Scaling and perturbation arguments are crucial in applied mathematics

class: ODE or PDE models

- processes on very different scales are approximately decoupled
- neglecting couplings gives simpler models
- simple theories are limits of more general theories
- simple models must be coupled to approximate full problem
Rescaling makes hidden details visible

“macro” - state: $U(X,T)$

“micro” - state: $u(x,t)$

$\epsilon \to 0, \ \delta \to 0$
Rescaling makes hidden details visible

“macro” - state: $U(X, T)$

scalings for $u$?

$$u = \varepsilon^\alpha \delta^\beta U$$

matching
This can lead to regular perturbation problems

- full problem: \( F(u, \varepsilon) = 0 \), solution \( u_\varepsilon \), \( \varepsilon \ll 1 \)
- limit problem: \( F(u, 0) = 0 \), solution \( u_0 \)
- regular perturbation:
  - 1. \( u_\varepsilon \to u_0 \) smoothly
    \[ u_\varepsilon = u_0 + \varepsilon u_1 + \varepsilon^2 u_2 + \cdots \]
  - 2. convergent expansion
  - 3. implicit function theorem
Typically this leads to singular perturbation problems

- full problem: \( F(u, \varepsilon) = 0 \), solution \( u_\varepsilon, \varepsilon \ll 1 \)

- limit problem: \( F(u, 0) = 0 \), solution \( u_0 \)

- singular perturbation:
  1. \( u_0 \) may develop singularities
  2. no smooth approximation by a single limit problem
  3. several scalings with different limit problems are needed
  4. approximation by matched asymptotic expansions
2. Examples
Example 1: singularly perturbed second order ODE

singly perturbed second order ODE
\[ \varepsilon \ddot{u} + p(t) \dot{u} + q(t)u = f(t) \]

initial - or boundary value problem
limit problem
\[ p(t) \dot{u} + q(t)u = f(t) \]

first order ODE; simpler, but cannot satisfy all initial or boundary conditions
⇒ boundary layers, internal layers
Rescaling gives another limit problem

\[ t \in [0, T], \quad p(0) = \lambda > 0 \quad \Rightarrow \quad \text{boundary layer near } t = 0, \quad \text{fast scale } \tau := \frac{t}{\varepsilon} \]

\[ u'' + p(\varepsilon\tau)u' + \varepsilon q(\varepsilon\tau)u = \varepsilon f(\varepsilon t) \]

limit problem, first order ODE, simpler!

\[ u'' + p(0)u' = 0, \quad u(\tau) \sim e^{-\lambda\tau} = e^{-\frac{\lambda t}{\varepsilon}} \]

\( \exists \) exponential decaying components, matched asymptotic expansion

\[ u(t, \varepsilon) = u_0(t) + u_0(\tau) + O(\varepsilon) \]
A boundary layer occurs...

http://www.scholarpedia.org/article/Singular_perturbation_theory
Example 2: fast-slow systems

singly perturbed systems of ODEs in standard form

\[ \begin{align*}
\varepsilon \dot{x} &= f(x, y, \varepsilon) \\
\dot{y} &= g(x, y, \varepsilon)
\end{align*} \quad 0 \leq \varepsilon \ll 1 \]

\(x \in \mathbb{R}^m\) fast, \(y \in \mathbb{R}^n\) slow, \(t \in \mathbb{R}\) time

mathematics: interesting and accessible dynamics

applications: biology, chemistry, electrical engineering, mechanics,...
Example 3: systems of singularly perturbed reaction diffusion equations

\[
\begin{align*}
u_t &= \varepsilon^2 \Delta u + f(u, v) \\
\delta v_t &= \Delta v + g(u, v)
\end{align*}
\]

- \( \varepsilon \in (0, \infty) \) different speeds of diffusion
- \( \delta \in (0, \infty) \) different reaction speeds
- pattern formation: travelling waves, spikes, spiral waves,...
- existence, stability, bifurcations,...
- stationary case in 1-d \( \Rightarrow \) back to fast-slow systems
Example 4: vanishing viscosity for hyperbolic conservation laws

\[ u \in \mathbb{R}^n, \quad x \in \mathbb{R}, \quad t > 0, \quad \text{also } x \in \mathbb{R}^d \]

\[ u_t + f(u)_x = \varepsilon (B(u)u_x)_x \]

flux \( f : \mathbb{R}^n \rightarrow \mathbb{R}^n \) smooth; diffusion matrix \( B(u) \) smooth, positive (semi)definit, \( \varepsilon \ll 1 \)

limit problem: hyperbolic conservation law

\[ u_t + f(u)_x = 0 \]

solutions develop singularities (shocks) in finite time

many deep results but also many open questions!
Example 5: Navier Stokes equations for large Reynolds number

velocity $u \in \mathbb{R}^3$, pressure $p \in \mathbb{R}$, $x \in \mathbb{R}^d$, $d = 2, 3$, $t \in \mathbb{R}$, Reynolds number $Re = UL/\nu$, $\varepsilon := 1/Re \ll 1$

\[ u_t + (u \cdot \nabla)u + \nabla p = \varepsilon \Delta u \]
\[ \nabla \cdot u = 0 \]

limit problem: Euler equations

\[ u_t + (u \cdot \nabla)u + \nabla p = 0 \]
\[ \nabla \cdot u = 0 \]

many deep results but also many open questions!
L. Prandtl created singular perturbation theory to explain boundary layers of fluids near walls (1904)

\[ x \in \Omega \subset \mathbb{R}^d, \quad \text{boundary conditions at } \partial \Omega \]

Navier Stokes: \( u \mid_{\partial \Omega} = 0 \), no slip at \( \partial \Omega \)

Euler equations: \( u \cdot n \mid_{\partial \Omega} = 0 \), no flow through \( \partial \Omega \)
Reality is much more multiscale!
Reality is much more multiscale!
Example 6: (semi)classical limit of Schrödinger equation

Wave function $\psi(t, x)$, potential $V(x)$

$$i\varepsilon \psi_t = -\varepsilon^2 \Delta \psi + V(x)\psi$$

Limit $\varepsilon \rightarrow 0$ corresponds to

Quantum mechanics $\rightarrow$ classical mechanics

Many deep results but also many open questions!
Schrödinger equation was (is!) very influential for development of singular perturbation theory.

Eigenvalue problem in 1-d, eigenvalue: energy $E$

$$\varepsilon^2 \psi_{xx} = (V(x) - E)\psi, \quad \psi(\pm\infty) = 0$$

- **Layer behaviour** for $V(x) > E$, classically forbidden region.
- **Fast oscillations** for $V(x) < E$, classically allowed region.
- **Turning points** at $V(x) = E$!
- Classical approach: WKB method
EVP for 1-d Schrödinger equation is a fast-slow problem

\[ \varepsilon^2 \psi_{xx} = (V(x) - E)\psi, \quad \psi(\pm\infty) = 0 \]

define

\[ u := \frac{\varepsilon \psi_x}{\psi} \]

\( u \) satisfies fast-slow Riccati equation

\[ \varepsilon \dot{u} = V(x) - E - u^2 \]

\[ \dot{x} = 1 \]
Singular limits are important and interesting - also from the dynamical systems and geometric point of view

- shift from finding approximate solutions to qualitative understanding of patterns and dynamics
- difficult for numerics: stiffness, resolving small scales expensive
- accessible to formal and rigorous analysis
- analysis: difficulties but also advantages
- getting the geometry right helps
- lots of things to discover - even in fairly simple problems
3. Fast-slow systems
Important biological processes are periodic on very different time scales

<table>
<thead>
<tr>
<th>Rhythm</th>
<th>Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neural rhythms</td>
<td>0.01 - 1 s</td>
</tr>
<tr>
<td>Cardiac rhythm</td>
<td>1 s</td>
</tr>
<tr>
<td>Calzium-ozsillations</td>
<td>1 s – min</td>
</tr>
<tr>
<td>Biochemical oscillations</td>
<td>1 min – 20 min</td>
</tr>
<tr>
<td>Mitotic cycle</td>
<td>10 min – 24 h</td>
</tr>
<tr>
<td>Hormonal rhythms</td>
<td>10 min – 24 h</td>
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<tr>
<td>Circadian rhythm</td>
<td>24 h</td>
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<tr>
<td>Ovarian cycle</td>
<td>28 days</td>
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<td>Annual rhythms</td>
<td>1 year</td>
</tr>
<tr>
<td>Ecological oscillations</td>
<td>years</td>
</tr>
</tbody>
</table>

A. Goldbeter (1996)
Most of these processes show fast-slow dynamics

\[ \gamma \] - and \[ \beta \] - oscillations in human brain

38 Hz and 42 Hz, units: 100 ms, 1 mV

mixed mode oscillations and delay effects

mechanisms? classification? noise?
Modelling of processes on very different time scales leads to fast-slow dynamical systems

- slow processes coupled to fast processes
- singularly perturbed systems of ODEs

\[
\begin{align*}
\varepsilon \dot{x} &= f(x, y, \varepsilon) \\
\dot{y} &= g(x, y, \varepsilon) \\
0 &\leq \varepsilon \ll 1
\end{align*}
\]

\( x \in \mathbb{R}^n \) fast, \( y \in \mathbb{R}^m \) slow, \( t \in \mathbb{R} \) time

standard form, global splitting

- particularly relevant in biology
Singularly perturbed (fast-slow) ODEs in standard form require (at least) two scalings

\[ \varepsilon \dot{x} = f(x, y, \varepsilon) \]
\[ \dot{y} = g(x, y, \varepsilon) \]  \hspace{1cm} (1)

\( x \) fast, \( y \) slow, \( \varepsilon \ll 1 \), slow time scale \( t \),

transform to fast time scale \( \tau := t/\varepsilon \)

\[ x' = f(x, y, \varepsilon) \]
\[ y' = \varepsilon g(x, y, \varepsilon) \]  \hspace{1cm} (2)

Syst. \( (1) \) and Syst. \( (2) \) equivalent for \( \varepsilon > 0 \)
There are two distinct limiting systems for $\varepsilon = 0$

- **reduced problem**
  \[ 0 = f(x, y, 0) \]
  \[ \dot{y} = g(x, y, 0) \]

- **layer problem**
  \[ x' = f(x, y, 0) \]
  \[ y' = 0 \]

**critical manifold**
\[ S := \{ f(x, y, 0) = 0 \} \]

- **reduced problem** dynamical system on $S$
- $x$ slaved to $y$ through constraint $f(x, y, 0) = 0$

- $S$ “manifold” of equilibria for layer problem
- $y$ acts as parameter in layer problem
Two possible interpretations for $\varepsilon \ll 1$

main interest in slow process:

- $x$ fast process, which should be eliminated to obtain simpler model for $y$
- effects of fast processes?

main interest in fast process:

- $y$ slowly varying parameter
- effect of slow changes in $y$ on dynamics of $x$
- simplest case: $x' = f(x, y), y' = \varepsilon, y \in \mathbb{R}$
In “good” situations (pieces of) critical manifold $S$ persists as a slow manifold $S_\varepsilon$

- $S_\varepsilon$ is invariant manifold
- $S_\varepsilon$ is $O(\varepsilon)$ close to $S$
- $S_\varepsilon$ depends smoothly on $O(\varepsilon)$
- $S_\varepsilon$ inherits stability properties from $S$
- flow on $S_\varepsilon$ close to flow on $S$
The classical example: Van der Pol oscillator

\[ \varepsilon \dot{x} = y - \frac{x^3}{3} + x \]
\[ \dot{y} = a - x \]

reduced problem

\[ S : y = \frac{x^3}{3} - x, \quad x \in \mathbb{R} \]

layer problem

\[ x' = y - \frac{x^3}{3} + x \]
\[ y' = 0 \]
Van der Pol oscillator has folded critical manifold $S$

layer problem: $x' = y - \frac{x^3}{3} + x$

- $S$ attracting for $x < -1$ and $x > 1$
- $S$ repelling for $-1 < x < 1$
- fold points at $x = -1$ and $x = 1$

reduced problem

$$y = \frac{x^3}{3} - x \quad \Rightarrow \quad \dot{y} = (x^2 - 1) \dot{x} = a - x$$

- equilibrium at $x = a$
- $\dot{y} > 0$, $x < a$, $\dot{y} < 0$, $x > a$
- singular at $x = \pm 1$, except for $a = \pm 1!$
Much of this persists for $0 < \varepsilon \ll 1$

- relaxation oscillations for $-1 < a < 1$
- excitability for $a < -1$ and $a > 1$
- canards and canard cycles for special values of $a$ close to $a = \pm 1$
In higher dimensions fast-slow systems can be more complicated

- a “terrible” problem: Olsen model
- a “good” problem: 3-d and 2-d Autocatalator
Olsen model describes oxidization of Nicotinamide Adenine Dinucleotide (NADH)

\[
\begin{align*}
\dot{A} &= k_7 - k_9 A - k_3 ABY \\
\dot{B} &= k_8 - k_1 BX - k_3 ABY \\
\dot{X} &= k_1 BX - 2k_2 X^2 + 3k_3 ABY - k_4 X + k_6 \\
\dot{Y} &= 2k_2 X^2 - k_3 ABY - k_5 Y \\
\end{align*}
\]

\(A\) oxygen, \(B\) NADH, \(X, Y\) intermediate products

Reaction rates: \(k_1 = 0.16, 0.35, 0.41\)

\(k_2 = 250, k_3 = 0.035, k_4 = 20, k_5 = 5.35, k_6 = 10^{-5}, k_7 = 0.8, k_8 = 0.825, k_9 = 0.1\)
The Olsen model has complicated dynamics

- a) $k_1 = 0.16$
- b) $k_1 = 0.35$
- c) $k_1 = 0.41$

**Slow-fast dynamics:** a) and b) mixed-mode oscillations or chaotic, c) relaxation oscillations

**Goal:** understand mechanisms of these patterns and bifurcations, very sensitive parameter dependence
Visualization in phase space shows more details

slow dynamics in $A, B$ close to $X, Y \approx 0$,
fast dynamics in $A, B, X, Y$ away from $X, Y \approx 0$, 
Scaling $A$, $B$, $X$, and $Y$ gives a slow-fast system

\[ \begin{align*}
\dot{a} &= \theta - \alpha a - aby \\
\dot{b} &= \nu(1 - bx - aby) \\
\varepsilon^2 \dot{x} &= bx - x^2 + 3aby - \beta x + \delta \\
\varepsilon^2 \dot{y} &= x^2 - y - aby
\end{align*} \]

\[ \nu \approx 10^{-1}, \quad \theta, \alpha, \beta \approx 1, \quad \varepsilon \approx 10^{-2}, \quad \delta \approx 10^{-5} \]

$\varepsilon, \nu$ determine time scales:
- $a, b$ slow variables  \quad $x_2, y_2$ fast variables;
- $\nu \ll 1 \Rightarrow b$ is slower than $a$

$\alpha \sim k_1$, $\delta \sim k_6$, bifurcation parameters
Finding the scaling is not easy

\[ A = \frac{k_1 k_5}{k_3 \sqrt{2} k_2 k_8} a, \quad B = \frac{\sqrt{2} k_2 k_8}{k_1} b \]

\[ X = \frac{k_8}{2k_2} x, \quad Y = \frac{k_8}{k_5} y \]

\[ T = \frac{k_1 k_5}{k_3 k_8 \sqrt{2} k_2 k_8} t \]

phase space: \( a, b, x, y \geq 0 \)
Olsen model has a complicated critical manifold

\[ \dot{a} = \theta - \alpha a - aby \]
\[ \dot{b} = \nu(1 - bx - aby) \]
\[ \varepsilon^2 \dot{x} = bx - x^2 + 3aby - \beta x + \delta \]
\[ \varepsilon^2 \dot{y} = x^2 - y - aby \]

complicated critical manifold \( S \)

\[ bx - x^2 + 3aby - \beta x + \delta = 0 \]
\[ x^2 - y - aby = 0 \]

further complications:
- impact of \( \delta \neq 0 \) versus \( \delta = 0 \)
- for \( x, y \) large different scaling needed
Good scaling is a bit like magic

- large terms dominate small terms
- finding a good scaling is nontrivial!
- what is a good scaling?
- nonlinear problem \( \Rightarrow \) good scaling depends on position in phase space
- often there exist several good scalings

\[
x' = -x + \varepsilon x + \varepsilon x^2, \quad x \in \mathbb{R}, \quad \varepsilon \ll 1
\]

\[
x = O(1) \implies x' = -x + O(\varepsilon)
\]

\[
x = O(\varepsilon^{-1}), \quad x = \frac{X}{\varepsilon} \implies X' = -X + X^2 + O(\varepsilon)
\]
4. Geometric Singular Perturbation Theory
Singularly perturbed (fast-slow) ODEs in standard form require (at least) two scalings

\[ \varepsilon \dot{x} = f(x, y, \varepsilon) \]
\[ \dot{y} = g(x, y, \varepsilon) \]

\( x \) fast, \( y \) slow, \( \varepsilon \ll 1 \), slow time scale \( t \),

transform to fast time scale \( \tau := t/\varepsilon \)

\[ x' = f(x, y, \varepsilon) \]
\[ y' = \varepsilon g(x, y, \varepsilon) \]

systems equivalent for \( \varepsilon > 0 \)
There are two distinct limiting systems for $\varepsilon = 0$

- **reduced problem**
  
  \[
  \begin{align*}
  0 &= f(x, y, 0) \\
  y &= g(x, y, 0)
  \end{align*}
  \]

- **layer problem**
  
  \[
  \begin{align*}
  x' &= f(x, y, 0) \\
  y' &= 0
  \end{align*}
  \]

**critical manifold**

\[ S := \{ f(x, y, 0) = 0 \} \]

**reduced problem** is a dynamical system on $S$.

$S$ is a “manifold” of equilibria for layer problem.
Large pieces of critical manifold $S$ can be described as a graph

Solve $f(x, y, 0) = 0$ by implicit function theorem for

$$x = h(y)$$

when $\frac{\partial f}{\partial x}(x, y, 0)$ regular

Reduced problem is essentially

$$\dot{y} = g(h(y), y, 0)$$

lifted to $S$ via $x = h(y)$
Spectrum of linearization of layer problem determines stability of $S$

$(x_0, y_0) \in S$, $x_0$ equilibrium of $x' = f(x, y_0, 0)$

linearization $A_0 := \frac{\partial f}{\partial x}(x_0, y_0, 0)$, spectrum $\sigma$

splits according to

$$\Re \lambda^s < 0, \quad \Re \lambda^c = 0, \quad \Re \lambda^u > 0$$

in

$$\sigma = \sigma^s \cup \sigma^c \cup \sigma^u$$

with stable, center, and unstable eigenspaces $E^s$, $E^c$, and $E^u$

$$\mathbb{R}^m = E^s \oplus E^c \oplus E^u$$

$x_0$ hyperbolic iff $E^c = 0$
Invariant manifold theory provides nonlinear analogs to stable-, center-, unstable spaces

- stable and unstable manifolds $W^s(x_0)$ and $W^u(x_0)$ at hyperbolic equilibria $x_0$
- center-stable, center- and center-unstable manifolds at non-hyperbolic equilibria $x_0$
- stable- and unstable manifolds are unique and robust under perturbation
- center manifolds more not unique; more delicate
- local bifurcations take place within center manifolds
Individual points of a critical manifolds are not hyperbolic

Assume that $S_0 \subset S$ is given as a graph $x = h(y)$

Linearization of layer problem at point $(h(y), y) \in S$)

\[
x' = f(x, y, 0) \\
y' = 0
\]

is $A := \begin{pmatrix} f_x & f_y \\ 0 & 0 \end{pmatrix}$

$\exists$ trivial eigenvalue $\lambda = 0$, multiplicity (at least) $n$; eigenspace is tangent space of $S$

Proof: $f(h(y), y) = 0$ differentiate

\[
f_x h_y + f_y = 0 \quad \Rightarrow \quad \begin{pmatrix} h_y \\ I_{n \times n} \end{pmatrix} \subset ker(A)$
Pieces of critical manifolds can be normally hyperbolic

Assume that $S_0 \subset S$ is given as a graph $x = h(y)$

**Definition:** $S_0$ is normally hyperbolic iff:
1) linearization $A$ no eigenvalues $Re\lambda = 0$, except trivial eigenvalue $\lambda = 0$ with multiplicity $n$
2) $S_0$ is compact

1) holds iff $f_x |_{S_0}$ has no eigenvalues $Re\lambda = 0$
2) is a uniformity condition
GSPT based on invariant manifold theory allows to go from $\varepsilon = 0$ to $0 < \varepsilon \ll 1$

**Theorem**: $S_0 \subset S$ normally hyperbolic $\Rightarrow S_0$ perturbs **smoothly** to slow manifold $S_\varepsilon$ for $\varepsilon$ small

N. Fenichel (1979)
The dynamics on the slow manifold is a smooth perturbation of the reduced problem

**critical manifold** $S_0$: \( \text{graph } x = h_0(y) \)

**reduced problem**: \( \dot{y} = g(h_0(y), y, 0) \)

**slow manifold** $S_\varepsilon$: \( \text{graph } x = h(y, \varepsilon), \) smooth expansion:

\[
h(y, \varepsilon) = h_0(y) + \varepsilon h_1(y) + \varepsilon^2 h_2(y) + \cdots
\]

**slow dynamics on** $S_\varepsilon$

\[
\dot{y} = g(h(y, \varepsilon), y, \varepsilon) = g(h_0(y), y, 0) + O(\varepsilon)
\]
Slow manifold has stable and unstable manifolds

$W^s(S_\varepsilon)$ and $W^u(S_\varepsilon)$, smooth dependence on $\varepsilon$
In many applications critical manifolds are more complicated

- $S$ has several normally hyperbolic branches separated by non-hyperbolic submanifolds, e.g. folds
- $S$ has bifurcation points or singularities
- layer problem allows jumps (fast transitions) between these branches
- parameters $\mu \in \mathbb{R}^p$ can be included as “trivial” slow variables (with nontrivial effects!)

\[
\begin{align*}
\varepsilon \dot{x} &= f(x, y, \mu, \varepsilon) \\
\dot{y} &= g(x, y, \mu, \varepsilon) \\
\dot{\mu} &= 0
\end{align*}
\]
5. A glimpse of applications and things to come
Fenichel’s normally hyperbolic GSPT explains many phenomena and has many applications.

- **nerve pulses**  
  Jones (1986, 1990)

- **pulses and other patterns in reaction diffusion equations**  
  A. Doelman, B. Gardner, T. Kaper, B. Sandstede, S. Schecter, A. Scheel,...(1990,...)

- **detonation waves**  
  Gasser + Sz. (1993)

- **viscous shock waves**  

Issues: existence, stability and bifurcations
Fenichel theory can be used for three types of problems

- reduction to a single normally hyperbolic slow manifold (often attracting); structurally stable properties of reduced flow persist.
- connections between invariant objects contained in two different normally hyperbolic slow manifolds, i.e. heteroclinic orbits; needs transversality arguments
- connections involving additional passages close to slow manifolds of saddle type; needs transversality and “Exchange Lemma”

C. Jones, N. Kopell, T. Kaper,...
Singular heteroclinic orbits perturb to heteroclinic orbits for $0 < \varepsilon \ll 1$

\[
\begin{align*}
&\varepsilon = 0 \\
&\varepsilon > 0
\end{align*}
\]

Sz. (1991)
Pulse propagation in Fitzhugh-Nagumo equation

\[ u_t = u_{xx} + f(u) - w \]
\[ v_t = \varepsilon (u - \gamma w) \]

- \( w = f(u) \) \textit{S}-shaped \quad \quad f(u) = u(u - a)(1 - u)
- Reststate \( (u, v) = (0, 0) \)
- travelling wave \( (u, w)(x, t) = (u, w)(x + ct), \quad : = \tau \)
- speed \( c \)
- \( \lim_{\tau \to \pm \infty} (u, w)(\tau) = (0, 0) \)
- existence, stability
Pulse is homoclinic orbit of fast-slow system

\begin{align*}
u' &= v \\
v' &= cv - f(u) + w \\
w' &= \varepsilon (u - \gamma w)/c
\end{align*}

- equilibrium \((0, 0, 0)\), hyperbolic
- one-dimensional unstable manifold \(W^u\)
- two-dimensional stable manifold \(W^s\)
- pulse: homoclinic orbit \(\omega \subset W^u \cap W^s\)
- homoclinic \(\exists \iff c = c(\varepsilon)\)
- \(u, v\) fast, \(w\) slow, add \(c' = 0\) as slow
Reduced problem and layer problem

\[ 0 = v \]
\[ 0 = cv - f(u) + w \]
\[ w = (u - \gamma w)/c \]

one dimensional

\[ S \quad w = f(u), \quad v = 0 \]

\[ u' = v \]
\[ v' = cv - f(u) + w \]
\[ w' = 0 \]
Singular homoclinic orbit of travelling wave problem for Fitzhugh-Nagumo equation
Particularly successful in “low” dimensions

- $m = 1, n = 1$, one slow and one fast variable
- $m = 2, n = 1$, two fast variables and one slow variable
- $m = 1, n = 2$, one fast variable and two slow variables
- $m = 2, n = 2$, two fast variables and two slow variables
- $m$ large, $n = 1, 2, 3$ global reduction to single critical manifold
Singularities of $S$ cause loss of normal hyperbolicity

$\frac{\partial f}{\partial x}$ singular!  
loss of normal hyperbolicity  
Fenichel theory does not apply!

**Blow-up method:**
- “clever” rescalings near singularities of $S$
- singularities are “blown-up” to spheres, cylinders, etc.

The $3$-$d$ autocatalator has complicated fast-slow dynamics

\[
\begin{align*}
\dot{a} &= \mu + c - a - ab^2 \\
\varepsilon \dot{b} &= a - b + ab^2 \\
\dot{c} &= b - c
\end{align*}
\]

2-dim folded critical manifold $S$

\[a - b + ab^2 = 0\]

$S = S_a \cup p_f \cup S_r$

$S_a$ attracting

$S_r$ repelling
Mixed mode oscillations are complicated periodic solutions containing large and small oscillations

\[
\begin{align*}
\dot{a} &= \mu + c - a - ab^2 \\
\varepsilon\dot{b} &= a - b + ab^2 \\
\dot{c} &= b - c
\end{align*}
\]

$1^2$ periodische Lösung
Intersection of attracting and repelling slow manifolds generates canards und mixed mode oscillations

\[ \dot{a} = \mu + c - a - ab^2 \]
\[ \varepsilon \dot{b} = a - b + ab^2 \]
\[ \dot{c} = b - c \]

\[ 1^2 \text{ periodische Lösung} \]
Details of generic planar fold point are fairly complicated

- normal hyperbolicity breaks down at fold point
- reduced flow singular at fold point
- important for relaxation oscillations
- classical problem, many approaches and results
- blow-up method

Fold point: \((0, 0)\) nonhyperbolic, blow-up method

Krupa, Sz. (2001)

\[
\begin{align*}
x' &= -y + x^2 + \cdots \\
y' &= -\varepsilon + \cdots
\end{align*}
\]

- asymptotics of \(S_{a,\varepsilon} \cap \Sigma^{out}\)
- map: \(\pi : \Sigma^{in} \rightarrow \Sigma^{out}\) contraction, rate \(e^{-C/\varepsilon}\)
One has to consider the extended system

\[ x' = f(x, y, \varepsilon) \]
\[ y' = \varepsilon g(x, y, \varepsilon) \]
\[ \varepsilon' = 0 \]

defining conditions of generic fold at origin \((x, y, \varepsilon) = (0, 0, 0)\)

- \( f = 0, f_x = 0 \), origin non-hyperbolic
- \( g(0, 0, 0) \neq 0 \), reduced flow nondegenerate
- \( f_{xx} \neq 0, f_y \neq 0 \)
- \( \Rightarrow \) saddle node bifurcation in \( f = 0 \)
It is straightforward to transform to normal form

\[ x' = -y + x^2 + O(\varepsilon, xy, y^2, x^3) \]
\[ y' = \varepsilon(-1 + O(x, y, \varepsilon)) \]
\[ \varepsilon' = 0 \]

- \((0, 0, 0)\) is a very degenerate equilibrium
- eigenvalue \(\lambda = \), multiplicity three
- blow-up the singularity
Blow-up corresponds to using (weighted) spherical coordinates for \((x, y, \varepsilon)\)

\[
x = r\bar{x}, \quad y = r^2\bar{y}, \quad \varepsilon = r^3\bar{\varepsilon}
\]

\((\bar{x}, \bar{y}, \bar{\varepsilon}) \in S^2, \quad r \in \mathbb{R}\)

singularity at origin is blown up to sphere \(r = 0\)
Blow-up makes hidden details visible and accessible to analysis

blow-up is
- clever rescaling
- zooming into singularity
- and compactification (of things that are pushed to “infinity” by zooming in)
Blow-up of layer problem shows some details
More details live on the sphere
The full dynamics of the blown up fold point
Many details have to be filled in

- computations in suitable charts
- charts correspond to asymptotic regimes
- gain hyperbolicity
- gain transversality
- invariant manifold theory, center manifolds, Fenichel theory
- local and global bifurcations
- special functions: here Airy equation
- regular perturbation arguments
Many applications need GSPT beyond the standard

- no global separation into slow and fast variables
- loss of normal hyperbolicity
- dynamics on more than two distinct time-scales
- several scaling regimes with different limiting problems are needed
- singular or non-uniform dependence on several parameters
- lack of smoothness

Motivation: applications from biology, chemistry, and mechanics
6. Glycolytic oscillator
Singular dependence on two parameters in a model of glycolytic oscillations

- existence of a complicated limit cycle
- desingularization by GSPT + blow up method
- many time scales
Glycolysis is a complicated enzyme reaction:

\[
\text{sugar} \rightarrow \text{water} + CO_2 + \text{energy}
\]

subprocess: \( \text{glucose} \alpha \rightarrow \text{pyruvat} \beta + \text{energy} \)

\[
\dot{\alpha} = \mu - \phi(\alpha, \beta) \\
\dot{\beta} = \lambda \phi(\alpha, \beta) - \beta
\]

\[
\phi(\alpha, \beta) = \frac{\alpha^2 \beta^2}{L + \alpha^2 \beta^2}
\]

\( L, \lambda \gg 1, \quad 0 < \mu < 1 \)


\[
\sqrt{\lambda/L} \ll 1/\sqrt{\lambda} \ll 1 \quad \text{formally} \quad \xrightarrow{\text{periodic solution}}
\]
Numerical simulation for $L = 5 \times 10^6$, $\lambda = 40$, $\mu = 0.15$ shows limit cycle

- $L$ large, $\lambda$ fixed: classical relaxation oscillations
- $L$, $\lambda$ both large: more complicated
For $\lambda, L \to \infty$ the variables $\alpha, \beta$ are large $\Rightarrow$ rescaling

\[ \varepsilon := \sqrt{\lambda/L}, \quad \delta := 1/\sqrt{\lambda}, \quad a := \varepsilon \alpha, \quad b = \delta^2 \beta \]

\[ a' = \varepsilon \left( \mu - \frac{a^2 b^2}{\delta^2 + a^2 b^2} \right) \]

\[ b' = \frac{a^2 b^2}{\delta^2 + a^2 b^2} - b + \delta^2 \]

- $a$ slow, $b$ fast with respect to $\varepsilon$
- Goldbeter-Segel condition: $\varepsilon \ll \delta \ll 1$
- $\varepsilon \to 0$ “standard”, $\delta \to 0$ “singular”? 
Critical manifold has two folds for $\delta > 0$, $\varepsilon = 0$

$$S^\delta = \{(a, b) : a^2b^2(1 - b) + \delta^2(a^2b^2 - b + \delta^2) = 0\}$$

$\Rightarrow$ relaxation oscillations $\exists$ for $\delta > 0$ and $\varepsilon \ll 1$
Critical manifold $S^\delta$ is singular for $\delta \to 0$

$$S^\delta : \quad a^2 b^2 (1 - b) + \delta^2 (a^2 b^2 - b + \delta^2) = 0$$

$$S^0 : \quad a^2 b^2 (1 - b) = 0$$

$a = 0, b = 0$

non-hyperbolic

$b = 1$ hyperbolic

desingularization: blow-up (with respect to $\delta$)
Consider the extended system in \((a, b, \delta)\) space

vector field \(X_\varepsilon\)

\[
\begin{align*}
a' &= \varepsilon f(a, b, \delta) \\
b' &= g(a, b, \delta) \\
\delta' &= 0
\end{align*}
\]

\((\varepsilon, \delta) = (0, 0)\) degenerate lines \(l_a\) and \(l_b\) of non-hyperbolic equilibria
Line $l_b$ is desingularized by first blow-up

$$a = r\bar{a}, \quad \delta = r\bar{\delta}, \quad (\bar{a}, \bar{\delta}) \in S^1, \quad r \in \mathbb{R}, \quad b = \bar{b} \in \mathbb{R}$$

**line** $l_b \rightarrow$ **surface of cylinder** $r = 0$

**line** $\bar{l}_a$ **is still degenerate**
Line $\overline{l}_a$ is desingularized by second blow-up

$$\overline{b} = \rho \overline{b}, \quad \overline{\delta} = \rho^2 \overline{\delta}, \quad (\overline{b}, \overline{\delta}) \in S^1, \rho \in \mathbb{R}, \quad \overline{a} = \overline{a} \in \mathbb{R}$$

vector field $\overline{X}_\varepsilon$ is desingularized with respect to $\delta$

for $\varepsilon = 0 \exists$ smooth critical manifold $\overline{S}$
GSPT is applicable with respect to $\varepsilon$ uniformly with respect to $\delta$

Theorem: $\varepsilon \ll \delta \ll 1 \implies \exists$ periodic solution

7. Mitotic Oscillator
Singular behaviour in a model of the cell cycle

- existence of a complicated limit cycle
- singular behaviour as $\varepsilon \to 0$
- very different from standard form
- desingularization by GSPT + blow-up
The mitotic oscillator is a simple model related to the dynamics of the cell-cycle.

Cell-cycle: periodic sequence of cell divisions
- crucial players: Cyclin, Cyclin-dependent kinase (Cdk)
- driven by an oscillator?

Paul Nurse, Lee Hartwell, Tim Hunt
Nobel-Prize in medicine (2001)
The mitotic oscillator has the following components:

Cyklin $C$
active Cdk $M$
inactive Cdk $M_+$
active C-protease $X$
inactive C-protease $X_+$

$C$ activates $M_+ \rightarrow M$
$M$ activates $X_+ \rightarrow X$
$X$ degrades $C$

A. Goldbeter, PNAS (1991); more realistic larger models contain subsystems similar to the Goldbeter model.
Dynamics is governed by Michaelis-Menten kinetics

cyklin \( C \geq 0 \)
\[
\dot{C} = v_i - v_d X \frac{C}{K_d + C} - k_d C
\]

aktive Cdk \( M \geq 0 \)
\[
\dot{M} = V_1 \frac{C}{K_c + C} \frac{1 - M}{K_1 + 1 - M} - V_2 \frac{M}{K_2 + M}
\]

active Cyklin-protease \( X \geq 0 \)
\[
\dot{X} = V_3 M \frac{1 - X}{K_3 + 1 - X} - V_4 \frac{X}{K_4 + X}
\]

Michaelis constants \( K_j \)

small Michaelis constants
\[
\frac{X}{\varepsilon + X} = \left\{ \begin{array}{ll}
\approx 1, & X = O(1) \\
\frac{x}{1+x}, & X = \varepsilon x \\
\approx 0, & X = o(\varepsilon)
\end{array} \right.
\]
The mitotic oscillator has a periodic solution

\[ \dot{C} = \frac{1}{4} (1 - X - C) \]

\[ \dot{M} = \frac{6C}{1 + 2C \varepsilon + 1 - M} \frac{1 - M}{2 \varepsilon + M} - \frac{3}{2} \frac{M}{\varepsilon + M} \frac{1}{\varepsilon + 1 - X} \]

\[ \dot{X} = M \frac{1 - X}{\varepsilon + 1 - X} - \frac{7}{10} \frac{X}{\varepsilon + X} \]

Variables:
- C
- M
- X

Parameter values:
- \( k_d = 0.25 \)
- \( v_i = 0.25 \)
- \( K_c = 0.5 \)
- \( K_d = 0 \)
- \( V_1 = 3 \)
- \( V_2 = 1.5 \)
- \( V_3 = 1 \)
- \( V_4 = 0.7 \)
- \( \varepsilon = 10^{-3} \)
The mitotic oscillator has a periodic solution

\[
\begin{align*}
\dot{C} &= \frac{1}{4}(1 - X - C) \\
\dot{M} &= \frac{6C}{1 + 2C \varepsilon + 1 - M} - \frac{3M}{2 \varepsilon + M} \\
\dot{X} &= M \frac{1 - X}{\varepsilon + 1 - X} - \frac{7X}{10 \varepsilon + X}
\end{align*}
\]

Variables:
- \(C\)
- \(M\)
- \(X\)

Parameter:
- \(k_d = 0.25\)
- \(v_i = 0.25\)
- \(K_c = 0.5\)
- \(K_d = 0\)
- \(V_1 = 3\)
- \(V_2 = 1.5\)
- \(V_3 = 1\)
- \(V_4 = 0.7\)
- \(\varepsilon = 10^{-3}\)
The periodic orbit lies in the cube $[0, 1]^3 \subset \mathbb{R}^3$

partly very close to $M = 0, X = 0, M = 1, X = 0$

Theorem: $\varepsilon \ll 1 \Rightarrow$ exists periodic orbit $\Gamma_\varepsilon$

Kosiuk + Sz. (2011)
The periodic orbit lies in the cube $[0, 1]^3 \subset \mathbb{R}^3$

partly very close to $M = 0, X = 0, M = 1, X = 0$

**Theorem:** $\varepsilon \ll 1 \Rightarrow$ exists periodic orbit $\Gamma_{\varepsilon}$

Kosiuk + Sz. (2011)

**singular perturbation?**
The periodic orbit lies in the cube \([0, 1]^3 \subset \mathbb{R}^3\)

partly very close to 
\(M = 0, \ X = 0, \ M = 1, \ X = 0\)

**Theorem:** \(\varepsilon \ll 1 \Rightarrow \exists \text{ periodic orbit } \Gamma_\varepsilon\)

Kosiuk + Sz. (2011)

singular perturbation? no
The periodic orbit lies in the cube $[0, 1]^3 \subset \mathbb{R}^3$

partly very close to $M = 0, X = 0, M = 1, X = 0$

**Theorem:** $\varepsilon \ll 1 \Rightarrow$ exists periodic orbit $\Gamma_\varepsilon$
Kosiuk + Sz. (2011)

**singular perturbation?**
at least not in standard form!
Proof uses GSPT and blow-up

Sliding on sides corresponds to slow motion on critical manifolds $M = 0$ and $X = 0$
Proof uses GSPT and blow-up

Sliding on **edge** corresponds to slow motion on one-dimensional critical manifold in blown-up edge.
8. Conclusion, outlook and program

- overview and two case studies
- identify fastest time-scale and corresponding scale of dependent variables, rescale
- often the limiting problem has a (partially) non-hyperbolic critical manifold
- use (repeated) blow-ups to desingularize
- identify relevant singular dynamics
- carry out perturbation analysis
- approach useful in other multi-parameter singular perturbation problems