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 perturbtation theory
5. A glimpse of applications
6. Glycolytic oscillator
7. Mitotic oscillator
8. Extensions, outlook, plan?

1. Scaling, perturbation methods, and singular limits

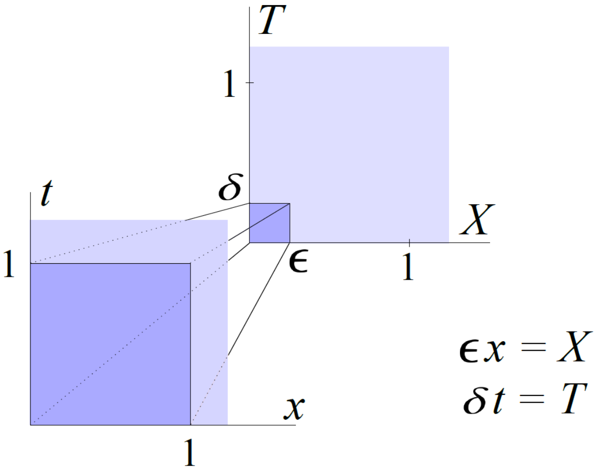
Scaling and perturbation arguments are crucial in applied mathematics

context: 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: $U(X,T)$

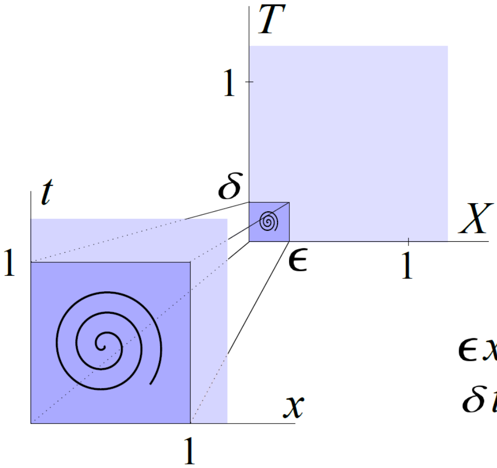


"micro" - state: $u(x,t)$

$\varepsilon \to 0,\ \delta \to 0$

Rescaling makes hidden details visible

"macro" - state: $U(X,T)$



$$\epsilon x = X$$
$$\delta t = T$$

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_ε, $\varepsilon \ll 1$
- 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_ε, $\varepsilon \ll 1$
- 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

singularly 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

$\Rightarrow$ boundary layers, internal layers

Rescaling gives another limit problem

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

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

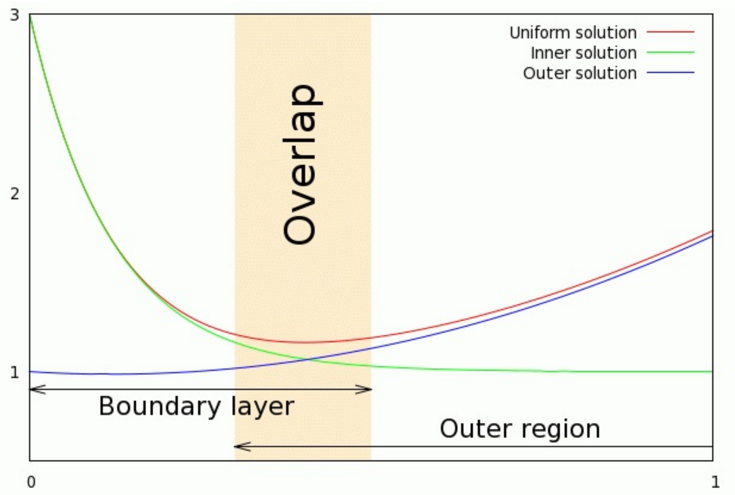
limit problem, first order ODE, simpler!

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

$\exists$ 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

singularly perturbed systems of ODEs in standard form

$$\begin{aligned} \varepsilon \dot{x} &= f(x,y,\varepsilon) \\ \dot{y} &= g(x,y,\varepsilon) \end{aligned} \qquad 0 \leq \varepsilon \ll 1$$

$x \in \mathbb{R}^m$ 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

$$
\begin{aligned}
u_t &= \varepsilon^2 \Delta u + f(u,v) \\
\delta v_t &= \Delta v + g(u,v)
\end{aligned}
$$

- $\varepsilon \in (0,\infty)$ 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

$u \in \mathbb{R}^n$, $x \in \mathbb{R}$, $t > 0$, (also $x \in \mathbb{R}^d$)

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

flux $f : \mathbb{R}^n \to \mathbb{R}^n$ smooth; diffusion matrix $B(u)$ smooth, positiv (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 $Re = UL/\nu$,
$\varepsilon := 1/Re \ll 1$

$$\begin{aligned} u_t + (u \cdot \nabla)u + \nabla p &= \varepsilon \Delta u \\ \nabla \cdot u &= 0 \end{aligned}$$

limit problem: Euler equations

$$\begin{aligned} u_t + (u \cdot \nabla)u + \nabla p &= 0 \\ \nabla \cdot u &= 0 \end{aligned}$$

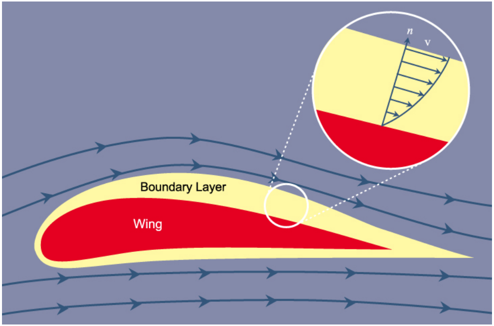
many deep results but also many open questions!

L. Prandtl created singular perturbation theory to explain boundary layers of fluids near walls (1904)

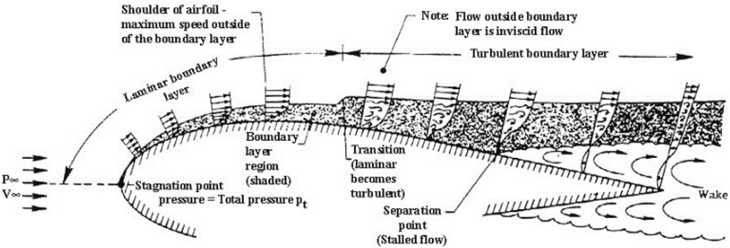
$x \in \Omega \subset \mathbb{R}^d$, boundary conditions at $\partial\Omega$

Navier Stokes: $u \,|_{\partial\Omega} = 0$, no slip at $\partial\Omega$

Euler equations: $u \cdot n \,|_{\partial\Omega} = 0$, no flow through $\partial\Omega$



Reality is much more multiscale!



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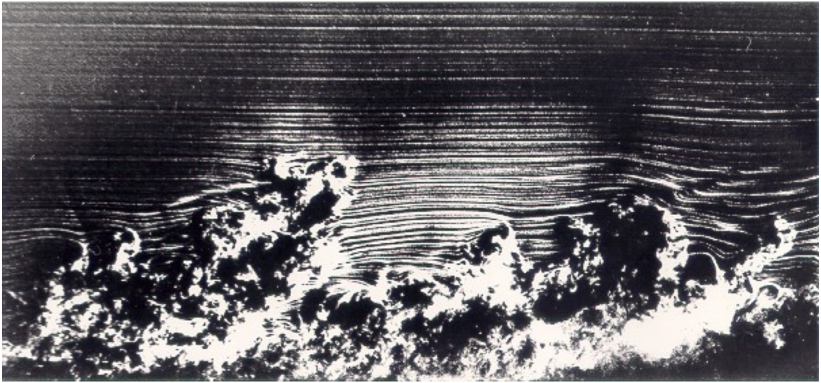


Example 6: (semi)classical limit of Schrödinger equation

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

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

limit $\varepsilon \to 0$ corresponds to

Quantum mechanics $\to$ classical mechanics

many deep results but also many open questions!

Schrödinger equation was (is!) very influential for development of singular perturbation theoy

eigenvalue problem in 1-d, eigenvalue: energy E

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

- 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

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

define

$$u := \frac{\varepsilon\psi_x}{\psi}$$

u satisfies fast-slow Riccati equation

$$\begin{aligned} \varepsilon\dot{u} &= V(x) - E - u^2 \\ \dot{x} &= 1 \end{aligned}$$

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

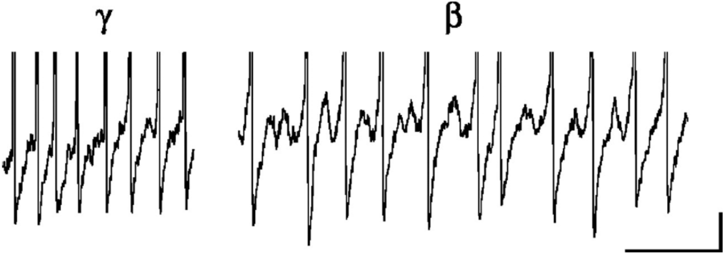
3. Fast-slow systems

Important biological processes are periodic on very different time scales

Rhythm	Period
Neural rhythms	0.01 - 1 s
Cardiac rhythm	1 s
Calzium-oszillations	1 s – min
Biochemical oscillations	1 min – 20 min
Mitotic cycle	10 min – 24 h
Hormonal rhythms	10 min – 24 h
Circadian rhythm	24 h
Ovarian cycle	28 days
Annual rhythms	1 year
Ecological oscillations	years

A. Goldbeter (1996)

Most of these processes show fast-slow dynamics



γ- and β - oscillations in human brain
38 Hz and 42Hz, units: 100 ms, 1mV

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

$$\begin{aligned} \varepsilon \dot{x} &= f(x, y, \varepsilon) \\ \dot{y} &= g(x, y, \varepsilon) \end{aligned} \qquad 0 \leq \varepsilon \ll 1$$

$x \in \mathbb{R}^n$ 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

$$\begin{aligned} \varepsilon\dot{x} &= f(x,y,\varepsilon) \\ \dot{y} &= g(x,y,\varepsilon) \end{aligned} \qquad (1)$$

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

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

$$\begin{aligned} x' &= f(x,y,\varepsilon) \\ y' &= \varepsilon g(x,y,\varepsilon) \end{aligned} \qquad (2)$$

Syst. (1) and Syst. (2) equivalent for $\varepsilon > 0$

There are two distinct limiting systems for $\varepsilon = 0$

- reduced problem
$$\begin{aligned} 0 &= f(x, y, 0) \\ \dot{y} &= g(x, y, 0) \end{aligned}$$

- layer problem
$$\begin{aligned} x' &= f(x, y, 0) \\ y' &= 0 \end{aligned}$$

critical manifold $\quad S := \{f(x, y, 0) = 0\}$

- 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_ε

- S_ε is invariant manifold
- S_ε is $O(\varepsilon)$ close to S
- S_ε depends smoothly on $O(\varepsilon)$
- S_ε inherits stablity properties from S
- flow on S_ε close to flow on S

The classical example: Van der Pol oscillator

$$\begin{aligned} \varepsilon\dot{x} &= y - \frac{x^3}{3} + x \\ \dot{y} &= a - x \end{aligned}$$

parameter a

reduced problem $S : y = \frac{x^3}{3} - x,\ x \in \mathbb{R}$

$$\begin{aligned} 0 &= y - \frac{x^3}{3} + x \\ \dot{y} &= a - x \end{aligned}$$

layer problem

$$\begin{aligned} x' &= y - \frac{x^3}{3} + x \\ y' &= 0 \end{aligned}$$

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 $x = a$
- $\dot{y} > 0$, $x < a$, $\qquad \dot{y} < 0$, $x > a$
- singular at $x = \pm 1$, $\qquad$ 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 Autocataltor

Olsen model describes oxidization of Nicotinamide Adenine Dinucleotide (NADH)

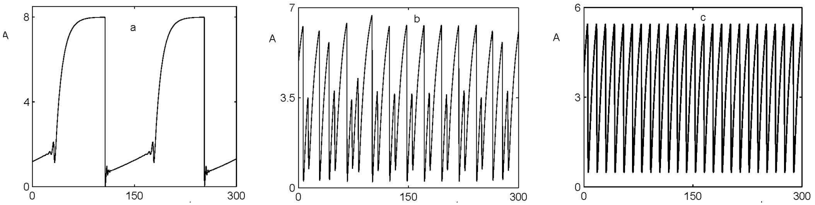
$$\begin{aligned}
\dot{A} &= k_7 - k_9 A - k_3 ABY \\
\dot{B} &= k_8 - k_1 BX - k_3 ABY \\
\dot{X} &= k_1 BX - 2k_2 X^2 + 3k_3 ABY - k_4 X + k_6 \\
\dot{Y} &= 2k_2 X^2 - k_3 ABY - k_5 Y
\end{aligned}$$

A oxygen, B NADH, X, Y intermediate products

Reaction rates: $k_1 = 0.16, \quad 0.35, \quad 0.41$

$k_2 = 250$, $k_3 = 0.035$, $k_4 = 20$, $k_5 = 5.35$,
$k_6 = 10^{-5}$, $k_7 = 0.8$, $k_8 = 0.825$, $k_9 = 0.1$

The Olsen model has complicated dynamics

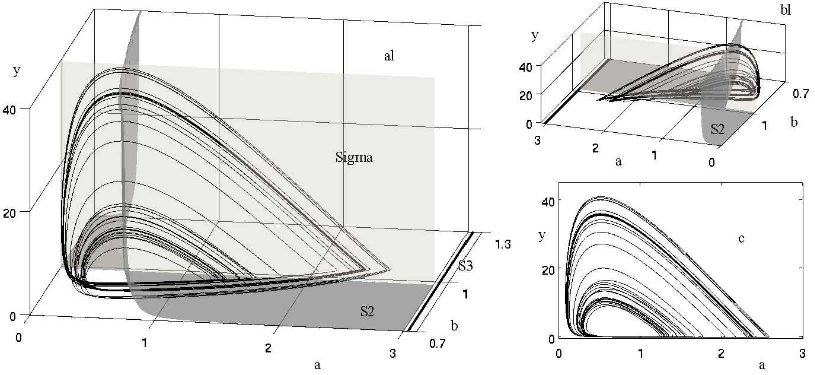


a) $k_1 = 0.16,$ b) $k_1 = 0.35,$ c) $k_1 = 0.41$

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

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

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

ε, ν determine time scales:
a, b slow variables 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

$$A = \frac{k_1 k_5}{k_3 \sqrt{2 k_2 k_8}} a, \qquad B = \frac{\sqrt{2 k_2 k_8}}{k_1} b$$

$$X = \frac{k_8}{2 k_2} x, \qquad Y = \frac{k_8}{k_5} y$$

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

phase space: $a, b, x, y \geq 0$

Olsen model has a complicated critical manifold

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

complicated critical manifold S

$$\begin{aligned}bx - x^2 + 3aby - \beta x + \delta &= 0 \\ x^2 - y - aby &= 0\end{aligned}$$

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

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

$$x = O(1) \Longrightarrow x' = -x + O(\varepsilon)$$

$$x = O(\varepsilon^{-1}),\ x = \frac{X}{\varepsilon} \Longrightarrow X' = -X + X^2 + O(\varepsilon)$$

4. Geometric Singular Perturbation Theory

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

$$\begin{aligned} \varepsilon \dot{x} &= f(x, y, \varepsilon) \\ \dot{y} &= g(x, y, \varepsilon) \end{aligned}$$

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

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

$$\begin{aligned} x' &= f(x, y, \varepsilon) \\ y' &= \varepsilon g(x, y, \varepsilon) \end{aligned}$$

systems equivalent for $\varepsilon > 0$

There are two distinct limiting systems for $\varepsilon = 0$

- reduced problem
$$\begin{aligned} 0 &= f(x,y,0) \\ \dot{y} &= g(x,y,0) \end{aligned}$$

- layer problem
$$\begin{aligned} x' &= f(x,y,0) \\ y' &= 0 \end{aligned}$$

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

$$x = h(y)$$

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

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 σ 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 $(h(y), y) \in S)$

$$\begin{array}{rcl} x' & = & f(x,y,0) \\ y' & = & 0 \end{array} \quad \text{is} \quad A := \begin{pmatrix} f_x & f_y \\ 0 & 0 \end{pmatrix}$$

$\exists$ trivial eigenvalue $\lambda = 0$, multiplicity (at least) n;
eigenspace is tangent space of S
Proof: $f(h(y), y) = 0$ differentiate

$$f_x h_y + f_y = 0 \quad \Rightarrow \begin{pmatrix} h_y \\ I_{n\times n} \end{pmatrix} \subset ker(A)$$

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

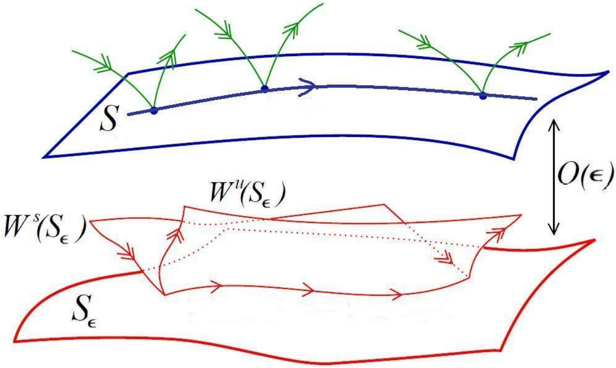
2) S_0 is compact

1) holds iff $f_x \mid_{S_0}$ 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_ε for ε small
N. Fenichel (1979)



The dynamics on the slow manifold is a smooth perturbation of the reduced problem

critical manifold S_0: graph $x = h_0(y)$

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

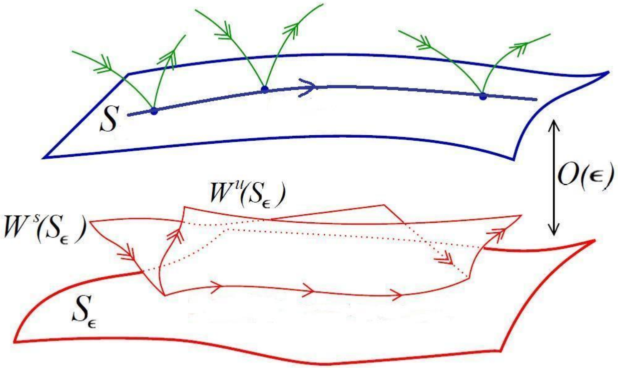
slow manifold S_ε: graph $x = h(y, \varepsilon)$, smooth expansion:

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

slow dynamics on S_ε

$$\dot{y} = g(h(y, \varepsilon), y, \varepsilon) = g(h_0(y), y, 0) + O(\varepsilon)$$

Slow manifold has stable and unstable manifolds



$W^s(S_\varepsilon)$ and $W^u(S_\varepsilon)$, smooth dependence on ε

In many applications critical manifolds are more complicated

- S has several normally hyperbolic branches separated by non-hyberbolic 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!)

$$\begin{aligned} \varepsilon\dot{x} &= f(x,y,\mu,\varepsilon) \\ \dot{y} &= g(x,y,\mu,\varepsilon) \\ \dot{\mu} &= 0 \end{aligned}$$

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 — Freistühler + Sz. (2002, 2010)

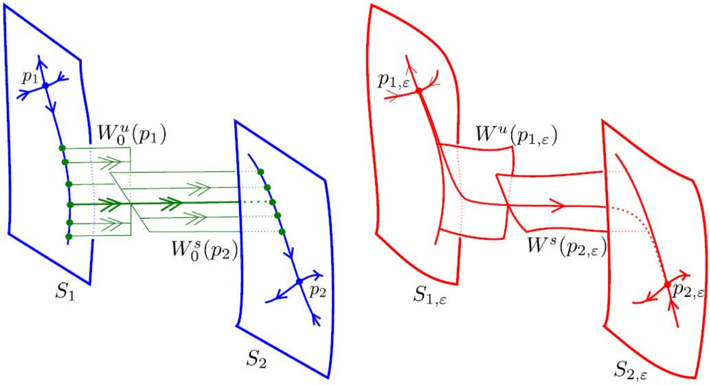
issues: existence, stability and bifurcations

Fenichel theory can be used for three types of problems

- reduction to a single normally hyperbolic slow manifold (often attracting); stucturally stable properties of reduced flow persist.
- connections between invariant objects contained in two different normally hyberbolic 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 $0 < \varepsilon \ll 1$



$\varepsilon = 0$ $\qquad$ $\varepsilon > 0$

Sz. (1991)

Pulse propagation in Fitzhugh-Nagumo equation

$$
\begin{aligned}
u_t &= u_{xx} + f(u) - w \\
v_t &= \varepsilon(u - \gamma w)
\end{aligned}
$$

- $w = f(u)$ S-shaped $\quad f(u) = u(u-a)(1-u)$
- Reststate $(u, v) = (0, 0)$
- travelling wave $(u, w)(x, t) = (u, w)(\underbrace{x + ct}_{:=\tau})$,
- speed c
- $\lim_{\tau \to \pm\infty} (u, w)(\tau) = (0, 0)$
- existence, stability

Pulse is homoclinic orbit of fast-slow system

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

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

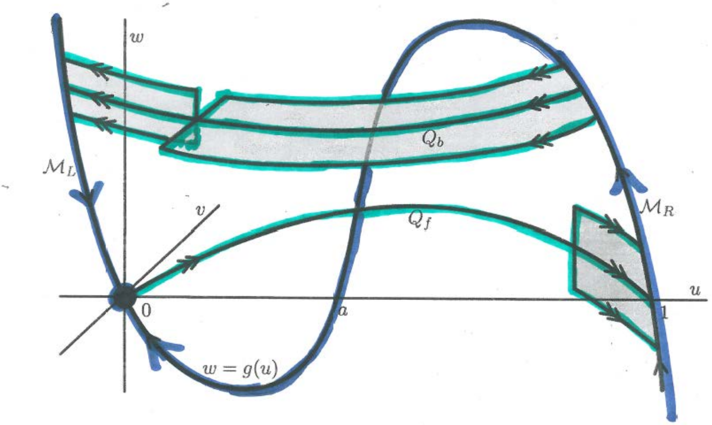
Reduced problem and layer problem

$$\begin{aligned} 0 &= v \\ 0 &= cv - f(u) + w \\ \dot{w} &= (u - \gamma w)/c \end{aligned}$$

one dimensional S $\quad w = f(u), \quad v = 0$

$$\begin{aligned} u' &= v \\ v' &= cv - f(u) + w \\ w' &= 0 \end{aligned}$$

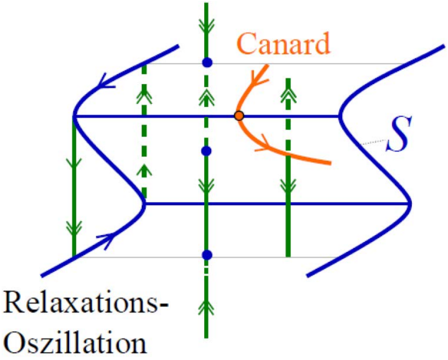
Singular homoclinic orbit of travelling wave problem for Fitzhugh-Nagumo equation



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



singularities of S: folds, bifurcation points, poles,...

$\Rightarrow \frac{\partial f}{\partial x}$ 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.

Dumortier + Roussarie (1996), Krupa + Sz. (2001)

The 3-d autocatalator has complicated fast-slow dynamics

$$\begin{aligned} \dot{a} &= \mu + c - a - ab^2 \\ \varepsilon \dot{b} &= a - b + ab^2 \\ \dot{c} &= b - c \end{aligned}$$

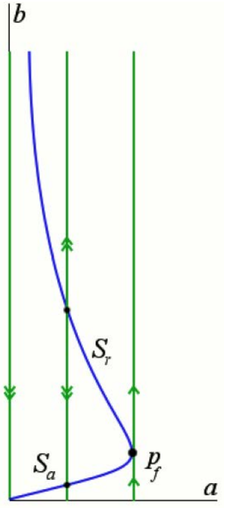
2-dim folded critical manifold S

$a - b + ab^2 = 0$

$S = S_a \cup p_f \cup S_r$

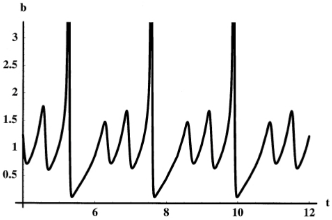
S_a attracting

S_r repelling

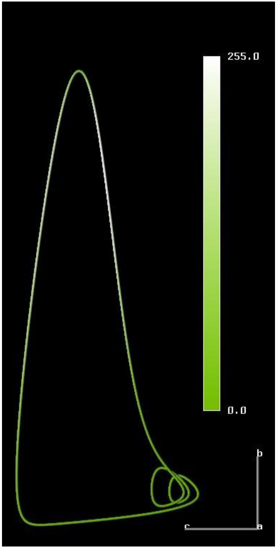


Mixed mode oscillations are complicated periodic solutions containing large and small oscillations

$$\begin{aligned}\dot{a} &= \mu + c - a - ab^2\\ \varepsilon\dot{b} &= a - b + ab^2\\ \dot{c} &= b - c\end{aligned}$$

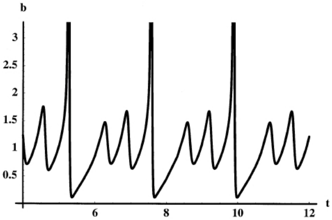


1^2 periodische Lösung

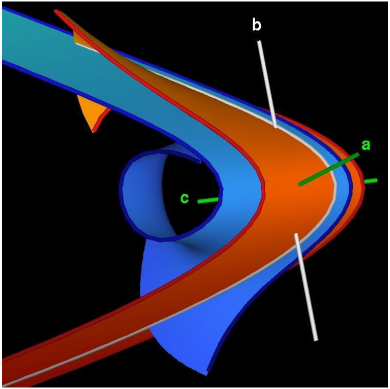


Intersection of attracting and repelling slow manifolds generates canards und mixed mode oscillations

$$\begin{aligned}\dot{a} &= \mu + c - a - ab^2\\ \varepsilon\dot{b} &= a - b + ab^2\\ \dot{c} &= b - c\end{aligned}$$



1^2 periodische Lösung



Details of generic planar fold point are fairly complicated

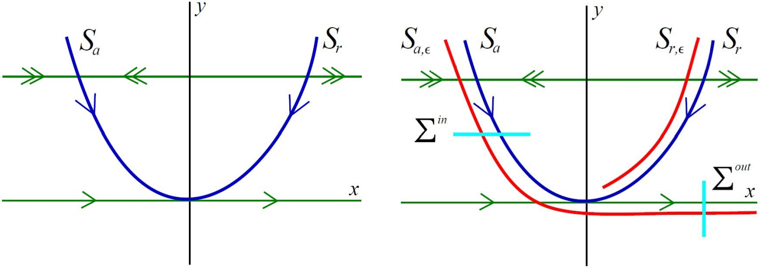
- normal hyperbolicity breaks down at fold point
- reduced flow singular at fold pint
- important for relaxation oscillations
- classical problem, many approaches and results
- blow-up method

  Dumortier + Roussarie (1996), Krupa + Sz. (2001)

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

Krupa, Sz. (2001)

$$x' = -y + x^2 + \cdots$$
$$y' = -\varepsilon + \cdots$$



- asymptotics of $S_{a,\varepsilon} \cap \Sigma^{out}$
- map: $\pi : \Sigma^{in} \to \Sigma^{out}$ contraction, rate $e^{-C/\varepsilon}$

One has to consider the extended system

$$\begin{aligned} x' &= f(x, y, \varepsilon) \\ y' &= \varepsilon g(x, y, \varepsilon) \\ \varepsilon' &= 0 \end{aligned}$$

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 nondegenarate
- $f_{xx} \neq 0$, $f_y \neq 0$
- $\Rightarrow$ saddle node bifurcation in $f = 0$

It is straightforward to transform to normal form

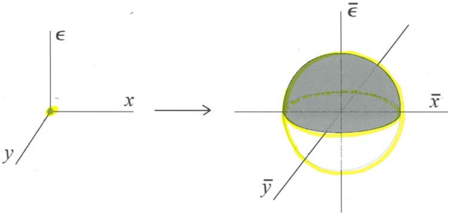
$$
\begin{aligned}
x' &= -y + x^2 + O(\varepsilon, xy, y^2, x^3) \\
y' &= \varepsilon(-1 + O(x, y, \varepsilon)) \\
\varepsilon' &= 0
\end{aligned}
$$

- $(0, 0, 0)$ is a very degenerate equilibrium
- eigenvalue $\lambda =$, multiplicity three
- blow-up the singularity

Blow-up corresponds to using (weighted) spherical coordinates for (x, y, ε)

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

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



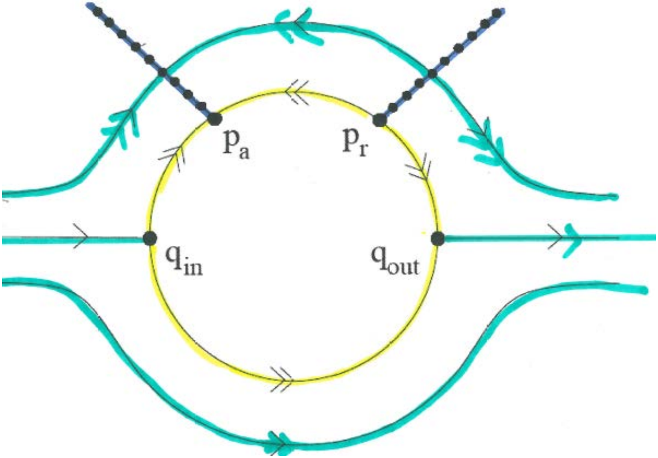
singularity at origin is blown up to **sphere** $r = 0$

Blow-up makes hidden details visible and accessible to analysis

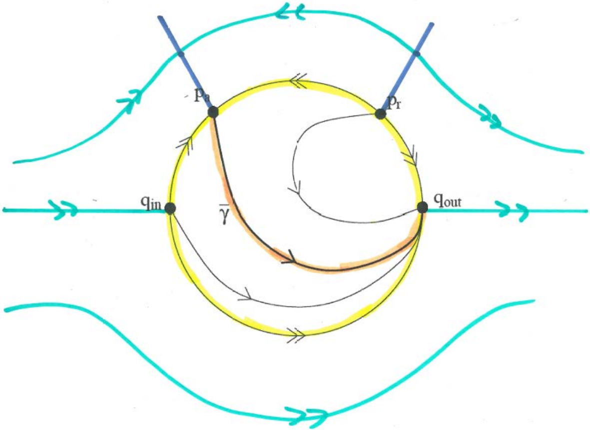
blow-up is

- **clever rescaling**
- **zooming into singularity**
- and **compactification** (of things that are pushed to “infinity” by zooming in)

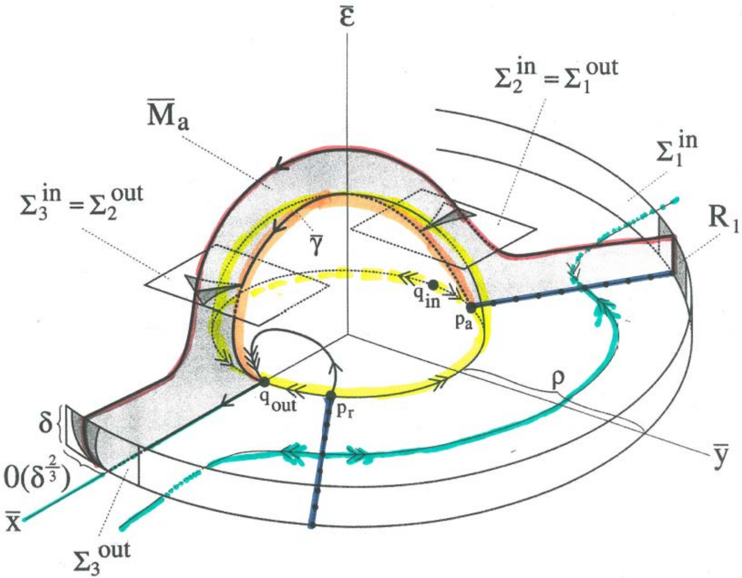
Blow-up of layer problem shows some details



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:

sugar $\rightarrow$ water + CO_2 + energy

subprocess: glucose α $\rightarrow$ pyruvat β + energy

$$\begin{aligned} \dot{\alpha} &= \mu - \phi(\alpha,\beta) \\ \dot{\beta} &= \lambda\phi(\alpha,\beta) - \beta \end{aligned}$$

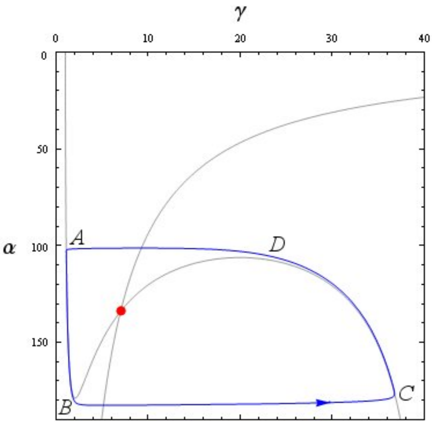
$$\phi(\alpha,\beta) = \frac{\alpha^2\beta^2}{L+\alpha^2\beta^2}$$

$$L, \lambda \gg 1, \quad 0 < \mu < 1$$

L. Segel, A. Goldbeter, Scaling in biochemical kinetics: dissection of a relaxation oscillator, J. Math. Bio. (1994)

$$\sqrt{\lambda/L} \ll 1/\sqrt{\lambda} \ll 1 \overset{\text{formally}}{\Longrightarrow} \text{periodic solution}$$

Numerical simulation for $L = 5 \times 10^6, \lambda = 40, \mu = 0.15$ shows limit cycle



- L large, λ fixed: classical relaxation oscillations
- L, λ both large: more complicated

For $\lambda, L \to \infty$ the variables α, β are large $\Rightarrow$ rescaling

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

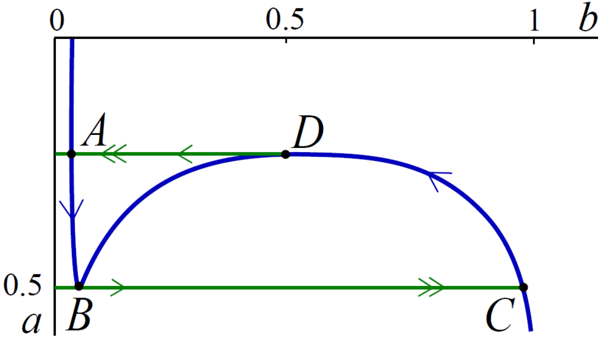
$$a' = \varepsilon\left(\mu - \frac{a^2b^2}{\delta^2 + a^2b^2}\right)$$

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

- a slow, b fast with respect to ε
- Goldbeter-Segel condition: $\varepsilon \ll \delta \ll 1$
- $\varepsilon \to 0$ **"standard"** , $\delta \to 0$ **"singular"** ?

Critical manifold has two folds for $\delta > 0$, $\varepsilon = 0$

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



$\Longrightarrow$ relaxation oscillations $\exists$ for $\delta > 0$ and $\varepsilon \ll 1$

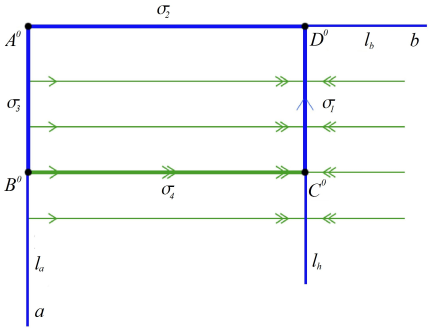
Critical manifold S^{δ} is singular for $\delta \to 0$

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

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

$a = 0, \; b = 0$
non-hyperbolic

$b = 1$ hyperbolic

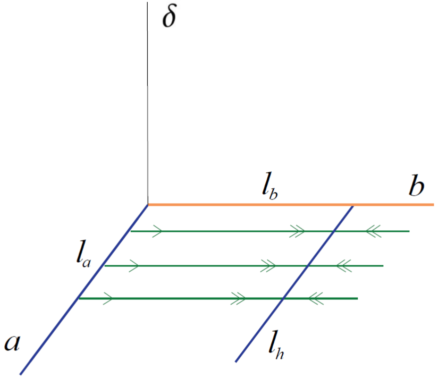


desingularization: **blow-up** (with respect to δ)

Consider the extended system in (a, b, δ) space

vector field X_ε

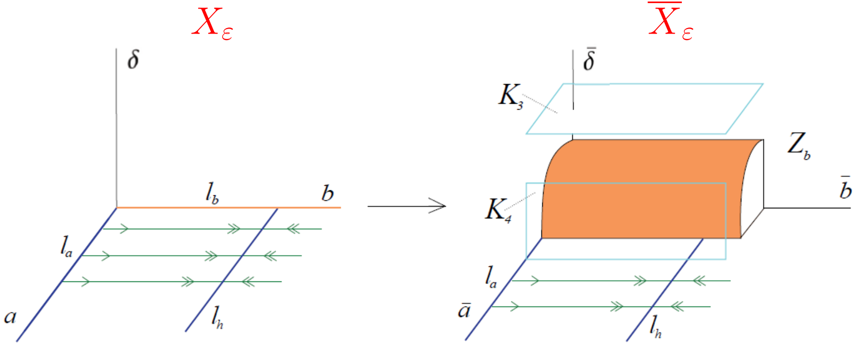
$$a' = \varepsilon f(a, b, \delta)$$
$$b' = g(a, b, \delta)$$
$$\delta' = 0$$



$(\varepsilon, \delta) = (0, 0)$ degenerate

lines l_a and l_b of **non-hyperbolic** equilbria

Line l_b is desingularized by first blow-up

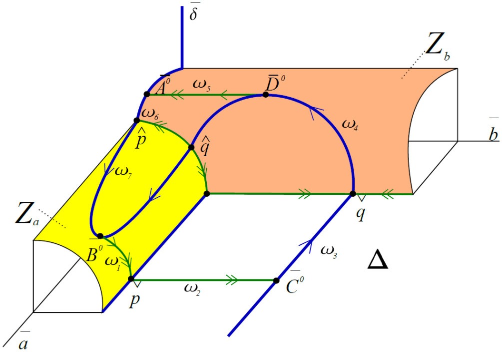


$$a = r\overline{a},\ \delta = r\overline{\delta}, \quad (\overline{a}, \overline{\delta}) \in \mathbb{S}^1,\ r \in \mathbb{R}, \quad b = \overline{b} \in \mathbb{R}$$

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

line $\overline{l}_a$ is still **degenerate**

Line $\bar{l}_a$ is desingularized by second blow-up

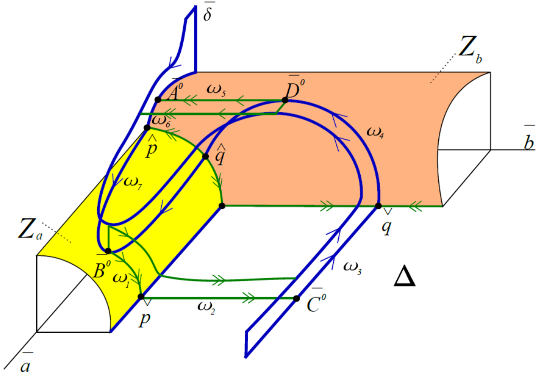


$$\bar{b} = \rho\bar{\bar{b}},\ \bar{\delta} = \rho^2\bar{\bar{\delta}}, \quad (\bar{\bar{b}}, \bar{\bar{\delta}}) \in \mathbb{S}^1, \rho \in \mathbb{R}, \quad \bar{a} = \bar{\bar{a}} \in \mathbb{R}$$

vector field $\bar{\bar{X}}_\varepsilon$ is desingularized with respect to δ

for $\varepsilon = 0$ $\exists$ smooth critical manifold $\bar{\bar{S}}$

GSPT is applicable with respect to ε uniformly with respect to δ



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

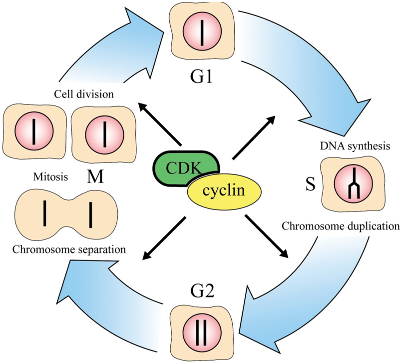
I. Kosiuk + Sz., SIAM J. Appl. Dyn. Systems (2011)

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



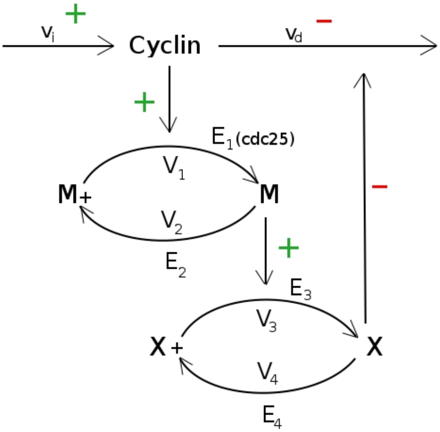
Paul Nurse, Lee Hartwell,
Tim Hunt

Nobel-Prize in medicine (2001)

cell-cycle: periodic sequence of cell divisions

- crucial players: **Cyclin**, **Cyclin-dependent kinase (Cdk)**
- driven by an oscillator?

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 $M_+ \longrightarrow M$
M activates $X_+ \longrightarrow X$
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 $C \geq 0$

aktive Cdk $M \geq 0$

active Cyklin-protease $X \geq 0$

$$\begin{aligned} \dot{C} &= v_i - v_d X \frac{C}{K_d + C} - k_d C \\ \dot{M} &= V_1 \frac{C}{K_c + C} \frac{1 - M}{K_1 + 1 - M} - V_2 \frac{M}{K_2 + M} \\ \dot{X} &= V_3 M \frac{1 - X}{K_3 + 1 - X} - V_4 \frac{X}{K_4 + X} \end{aligned}$$

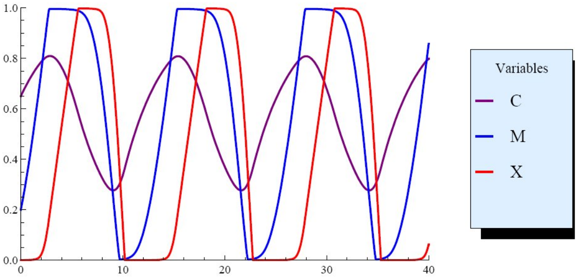
Michaelis constants K_j

small Michaelis constants

$\varepsilon \ll 1$

$$\frac{X}{\varepsilon + X} = \begin{cases} \approx 1, & X = O(1) \\ \frac{x}{1+x}, & X = \varepsilon x \\ \approx 0, & X = o(\varepsilon) \end{cases}$$

The mitotic oscillator has a periodic solution



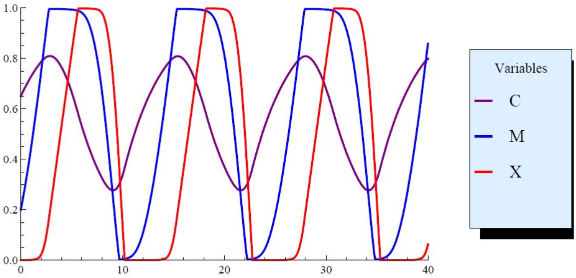
parameter

$$
\begin{aligned}
k_d &= 0.25\\
v_i &= 0.25\\
K_c &= 0.5\\
K_d &= 0\\
V_1 &= 3\\
V_2 &= 1.5\\
V_3 &= 1\\
V_4 &= 0.7
\end{aligned}
$$

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

$$\varepsilon = 10^{-3}$$

The mitotic oscillator has a periodic solution



parameter

$$\begin{aligned} k_d &= 0.25 \\ v_i &= 0.25 \\ K_c &= 0.5 \\ K_d &= 0 \\ V_1 &= 3 \\ V_2 &= 1.5 \\ V_3 &= 1 \\ V_4 &= 0.7 \end{aligned}$$

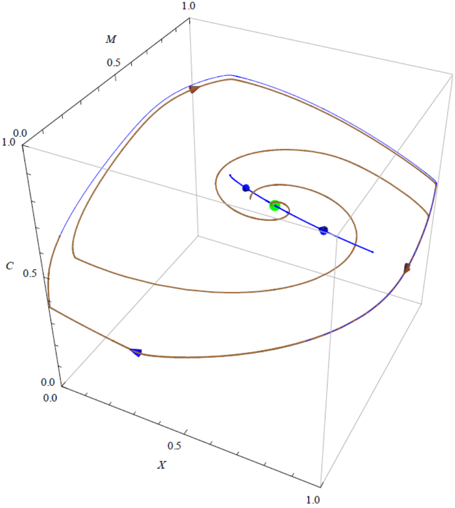
$$\begin{aligned} \dot{C} &= \frac{1}{4}(1 - X - C) \\ \dot{M} &= \frac{6C}{1+2C}\frac{1-M}{\varepsilon + 1 - M} - \frac{3}{2}\frac{M}{\varepsilon + M} \\ \dot{X} &= M\frac{1-X}{\varepsilon + 1 - X} - \frac{7}{10}\frac{X}{\varepsilon + X} \end{aligned}$$

$$\varepsilon = 10^{-3}$$

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 Γ_ε
Kosiuk + Sz. (2011)



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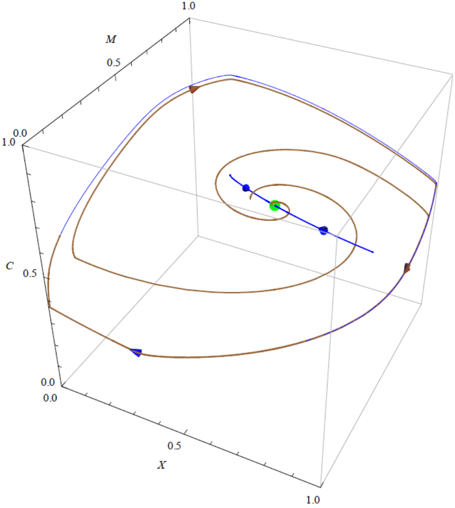
exists periodic orbit Γ_ε
Kosiuk + Sz. (2011)

singular perturbation?



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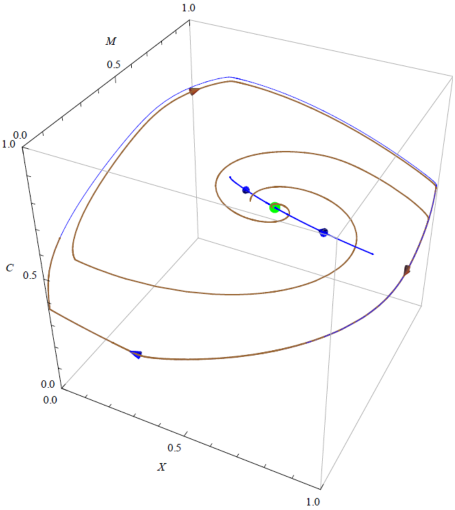
partly very close to
$M = 0$, $X = 0$, $M = 1$,
$X = 0$

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

singular perturbation? **no**

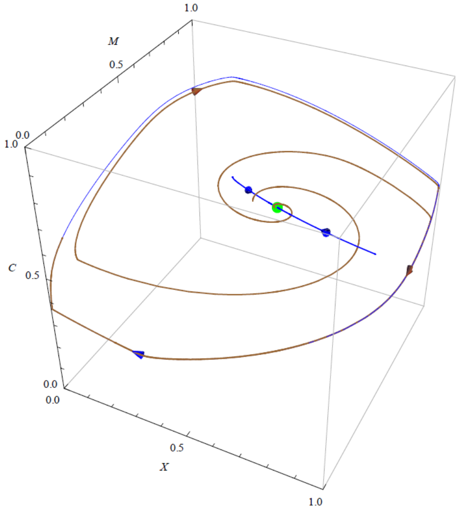


The periodic orbit lies in the cube $[0,1]^3 \subset \mathbb{R}^3$

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

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

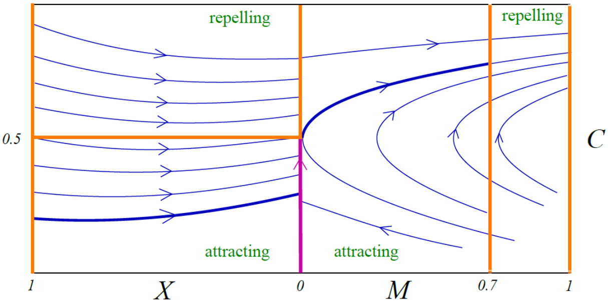
singular perturbation?
at least not in standard form!



Proof uses GSPT and blow-up

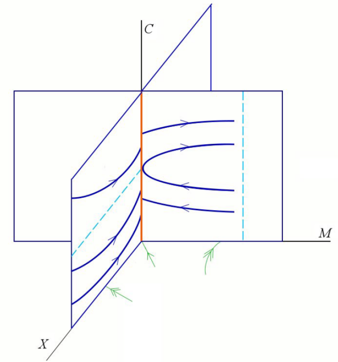
Sliding on **sides** corresponds to slow motion on critical manifolds $M = 0$ and $X = 0$

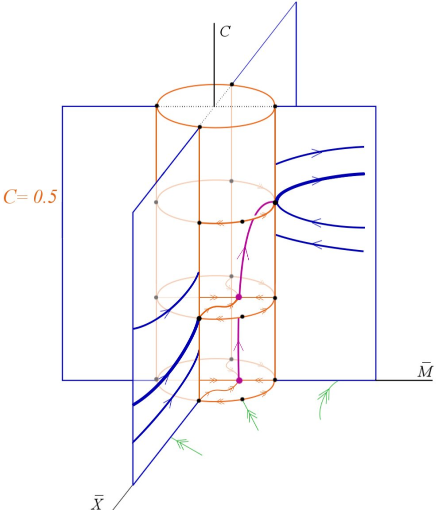
$M = 0$ $X = 0$



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