Delayed loss of stability in multiple time scale models of natural phenomena

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Summary. Numerous real-world phenomena exhibit mechanisms evolving on greatly different time scales. In this talk, we focus on delayed loss of stability in two classes of mathematical models, namely epidemics and neuroscience, specifically synaptic transmission, and comment on the possible asymptotic, and in one case transient, behaviour of such systems.

Introduction

Numerous natural phenomena exhibit mechanisms evolving on greatly different time scales, e.g. days against months or even years. The presence of multiple time scales gives rise to complex phenomenon, such as the focus of this talk, i.e. the so-called delayed loss of stability [1, 7]. Geometric Singular Perturbation Theory (GSPT) [2, 6] is a powerful tool to analyze such systems: by considering each time scale separately, GSPT allows to deduce information on the behaviour of the original model.
In this talk, we present various multiple time scale systems, both in standard and non-standard form [9], and describe their behaviour using different techniques from GSPT. In particular, we showcase the delayed loss of stability of orbits passing nearby critical manifolds (the sets of equilibria of the fast limit) of such systems. We focus on the entry-exit relation (also known as way-in/way-out, delayed loss of stability, or Pontryagin delay) which we use to analyze the passage of orbits near the critical manifolds.
In its simplest form, the entry-exit function is applied to planar systems of the form

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

with $0 < \epsilon \ll 1$, $x, z \in \mathbb{R}$, $f(x, 0, 0) > 0$ and $\text{sign}(g(x, 0, 0)) = \text{sign}(x)$.
As shown in Figure 1, one can derive a Poincaré map $x_0 \mapsto p_\epsilon(x_0)$ from a horizontal line $\{z = z_0\}$ to itself. The x-axis $z = 0$ changes stability, from attracting to repelling, at $x = 0$. Orbits which are attracted towards it at a point $(x, z) = (x_0, z_0)$, with $x_0 < 0$, will eventually leave a neighbourhood of the x-axis and re-intersect the line $\{z = z_0\}$ at a point with $(x, z) = (p_\epsilon(x_0), z_0)$, with $p_\epsilon(x_0) > 0$. As $\epsilon \to 0$, the exit point $p_\epsilon(x_0)$ approaches the value $p_0(x_0)$ given implicitly by the following integral:

$$\int_{x_0}^{p_0(x_0)} \frac{g(x, 0, 0)}{f(x, 0, 0)} \mathrm{d}x = 0.$$

Such a formula can be generalized to higher-dimensional systems, at the cost of additional assumptions which, as we explain, are not always trivially satisfied.

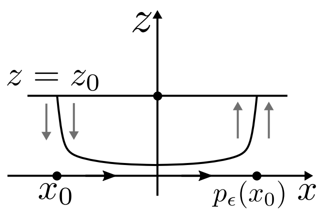

Figure 1: A visualization of the entry-exit map for a planar system.

The models

Compartmental epidemics models

The first models we present are the compartmental models, in non-standard GSPT form, studied in [3]. In all the models, the fast processes are the ones related to infection and recovery, whereas the slow processes are the ones related to loss of immunity or demography. The passage of an orbit close to the critical manifold, represented in all cases by the absence of infectious individuals in the population, allows us to bring the system in standard form through a rescaling of the variables, and to predict the beginning of another "wave" through the entry-exit function.
We analyzed three epidemics models given as slow-fast SIR (Susceptible-Infected-Recovered) and SIRS compartmental models, and proved that when the basic reproduction number R_0 is greater than 1, the system will converge to an endemic equilibrium characterized by an $\mathcal{O}(\epsilon)$ fraction of the population still in the infected compartment.
Then, we studied an SIRWS (where the "W" represents individuals in a Waning immunity phase), and we applied a geometrical argument, sketched in Figure 2, to prove the asymptotic convergence towards a unique endemic equilibrium or towards a limit cycle.

Finally, we present the SIRS compartmental model on homogeneous networks studied in [4]; one fundamental difference with the SIRS model studied in [3] is the existence of stable limit cycles. All the results obtained in the aforementioned papers heavily rely on the entry-exit function, and one critical assumption needed in order to use this tool (namely, separation of eigenvalues of the linearization of the systems along the critical manifold) is not always satisfied along solutions of the SIRS model on networks. We comment on such a limitation, and provide a possible solution to overcome such an issue.

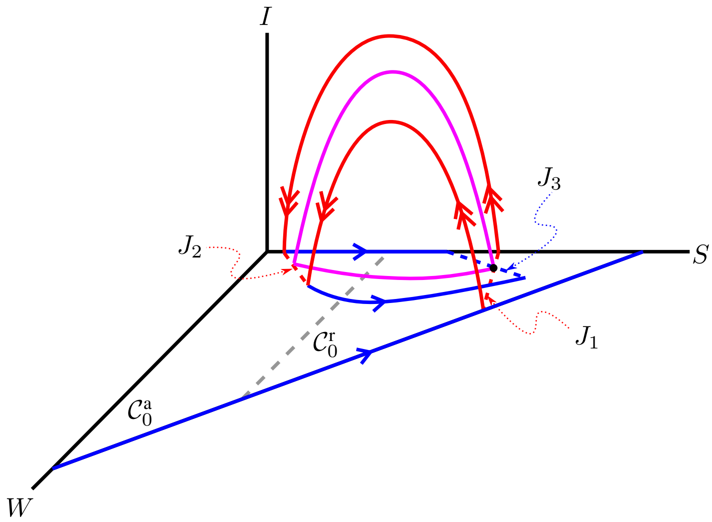

Figure 2: Concatenation of slow and fast orbits, giving rise to a limit cycle.

A short theoretical digression

As a follow-up to the criticality emerging from the model studied in [4], we shortly describe an ongoing project [5] which aims at generalizing the possibilities of application of the entry-exit function.

Specifically, we consider a class of 1-fast/2-slow systems of ODEs, and provide entry-exit relations for systems whose linearizations do not exhibit separation of eigenvalues on the critical manifold. We argue that such an approach could be generalized to higher-dimensional systems.

Synaptic transmission via neurotransmitter release

Then, we showcase the application of the entry-exit function to a planar system in standard GSPT form studied in [8]. The entry-exit function can be used, in this context, to compute the delay between subsequent spikes in the neural activity and capture possible response of a post-synaptic neuron to an input (formed by one or several spikes) received by a pre-synaptic neuron. This response always incurs a minimal delay (diffusion time to cross the synaptic cleft, the space in between the two neurons) but can increase substantially depending on the neural type and possible pathological behaviour of the underlying neural population. The entry-exit function hence allows to fine-tune the model so as to capture all these scenarios within a parsimonious framework, and fit to data of both excitatory and inhibitory synapses.

Lastly, we propose a generalization of the previous system, in which the quadratic component of the critical manifold is replaced with a quartic curve. We study how the shape of the quartic, as well as other parameters of the system, may affect both the transient and asymptotic behaviour of the system, since both are of interest in such applications.

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