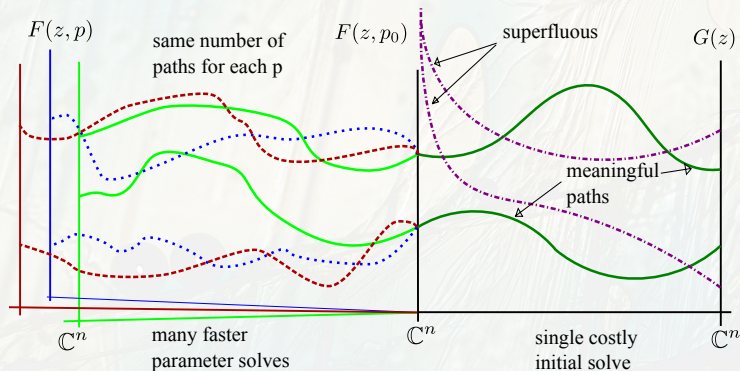


Using polynomial systems to study biochemical reaction networks

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Coefficient-Parameter Homotopy



A reminder about parameter homotopy.

Paramotopy

- ▶ Command-line software which enables rapid investigations into parametrized polynomial systems.
- ▶ Uses *Bertini* to perform solves, under the hood.
- ▶ Numeric-menu driven interface which simplifies and automates Bertini functions.
- ▶ Open source, free.

The ‘Alicia’ system

$$x_0 + x_1 + x_2 + y_1 + y_2 + y_3 + y_4 = k_1,$$

$$e + y_1 + y_2 = k_2,$$

$$f + y_3 + y_4 = k_3,$$

$$-a_1 * x_0 * e + b_1 * y_1 + c_4 * y_4 = 0,$$

$$c_2 * y_2 - a_3 * x_2 * f + b_3 * y_3 = 0,$$

$$a_1 * x_0 * e - (b_1 + c_1) * y_1 = 0,$$

$$a_2 * x_1 * e - (b_2 + c_2) * y_2 = 0,$$

$$a_3 * x_2 * f - (b_3 + c_3) * y_3 = 0,$$

$$a_4 * x_1 * f - (b_4 + c_4) * y_4 = 0.$$

The system has 9 variables, 9 equations, and 15 parameters. The parameters in the problem are a_i, b_i, c_i, k_j , for $i \in \{1, 2, 3, 4\}$, and $j \in \{1, 2, 3\}$.

Starting Point

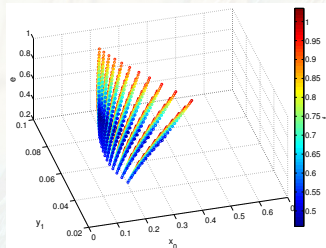
[The parameters] are all assumed to be positive. For some of them, the system has only one positive solution (i.e., all coordinates are real and positive) and for the others, it has three. How can numerical methods help us determining values, regions, etc., for this to happen?

Initial answer

To start answering questions about this system:

- ▶ Perform grid-sample solves across the unit cube $[0, 1]^{15}$, to find the number of solutions

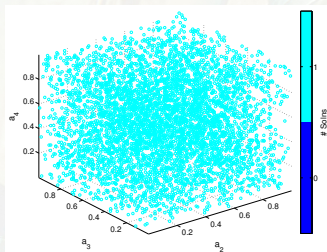
Found only points with a single positive real equilibrium.



- ▶ Perform positive-dimensional numerical irreducible decomposition for random point in parameter space
Only solutions are ‘isolated’ solutions – just points.

Monte Carlo sampling

Grid-sampling the unit cube provided only single-equilibria points – maybe Monte Carlo sampling will help? Randomly sampling 10^5 times in all parameters yielded the same picture:

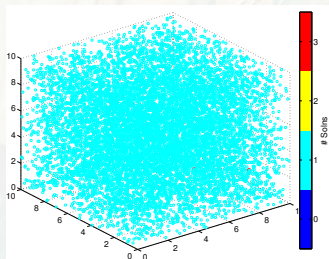


Monte carlo sampling of the unit cube seemed to lend itself to the conjecture that this portion of parameter space is devoid of points at which multiple positive equilibria exist. Perhaps the unit cube has only unique equilibria?

Beyond the Unit Cube

Let's move out a 10 units – the 10-cube, $[0, 10]^{15}$

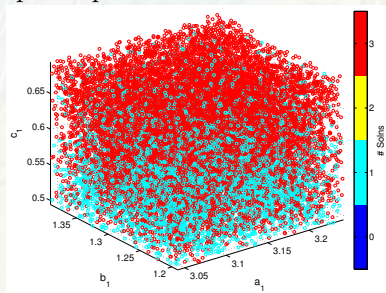
Randomly sampling can be quite fruitful for system with large numbers of parameters, with estimates on numbers (such as volumes) converging as the square root.



My first pass at sampling, using only 10^4 points, produced *two* parameter points with non-unique equilibria. See the red points?

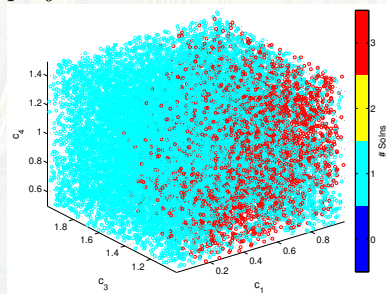
Zooming In

First zoom in around one of the special points.



Definite space containing multiple different numbers of positive real equilibria.

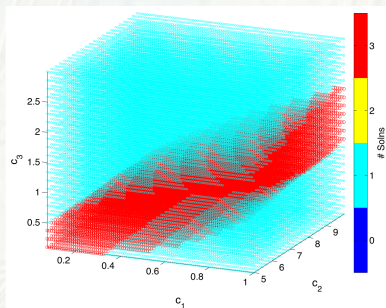
Second zoom, different projection.



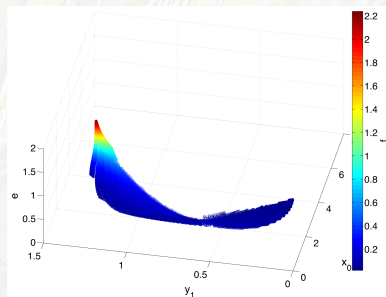
Structure begins to emerge.

Structure Emerges

Having seen a separation of the number of posreal equilibria depending on what looks like c_1, c_3 , I chose to run a mesh around the point of interest.



Number of solutions - vs
parameter point.



Solution set structure.

Stucture Emerges



Play

Paramotopy – Recent Advancements

Since performing this investigation, I have made the following improvements:

- ▶ Added Search method
 - ▶ Can search for a specific number of positive real solutions, or a range of values, from 0 to ∞ .
 - ▶ Search a maximum number of test points.
 - ▶ Accumulate a minimum number of desired parameter points, or a target number of total solutions.
- ▶ Reorganized code, and menu structures, to allow further expansion in the future.

Summary

How can numerical methods help investigate a dynamical system?

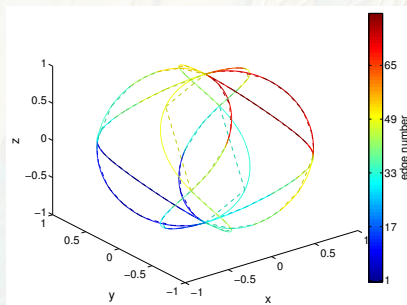
- ▶ Provide numerical description to equilibria.
- ▶ Visualize to gain intuition.
- ▶ Search for anomalous points.
- ▶ Fix some parameters, vary others.
- ▶ Break down solution set in terms of dimensions and components.

Real Embedded Sets

- ▶ Paramotopy was designed to solve ‘square’ systems – where the number of equations $\geq$ number of variables. This is where we expect ‘isolated’ solutions.
- ▶ Many systems, including some square systems, have positive dimensional components of the solution set. Finding the *real* parts of these complex components is hard.
- ▶ The Bertini team and I have been implementing *cellular decomposition* methods for providing a completed description of real embedded components.
- ▶ So far, we have curves completed, and are working on surfaces.

Bertini Real

Perhaps a chemical system has a non-square system, or has a positive dimensional component. Bertini Real could provide a way to visualize the interaction between parameters and variables, in a different way from Paramotopy.



Thank you for your kind attention.

- ▶ Paramotopy is joint work with Matt Niemerg
- ▶ We have been graciously funded by the NSF, and DARPA.