Bayesian Statistical Parameter Synthesis for Linear Temporal Properties of Stochastic Models

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Outline

1. Introduction
   - Parametric Chemical Reaction Networks
   - Signal Temporal Logic
   - Verification: a statistical approach
2. Bayesian Threshold Synthesis Problem
   - Definition
   - Algorithm
3. Test Case and Results
4. Conclusions and Future Works

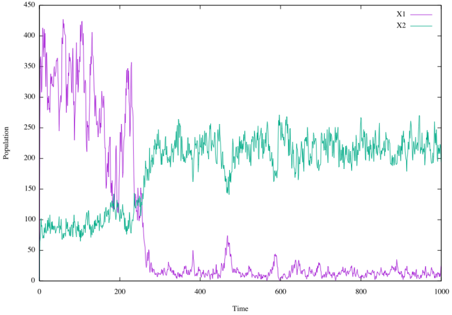
Models: Parametric Chemical Reaction Networks

Consider a Parametric Chemical Reaction Network (PCRN) as a tuple $\mathcal{M} = (\mathcal{S}, \mathbf{X}, D, \mathbf{x_0}, \mathcal{R}, \Theta)$

$$r_1 : S + I \xrightarrow{\alpha_1} 2I \qquad \alpha_1 = k_i \cdot \frac{X_s \cdot X_i}{N}$$

$$r_2 : I \xrightarrow{\alpha_2} R \qquad \alpha_2 = k_r \cdot X_i$$

- $\theta = (\theta_1, \ldots, \theta_k)$ is the vector of (kinetic) parameters, taking values in a compact hyperrectangle $\Theta \subset \mathbb{R}^k$
- a trajectory is a function $\mathbf{x}_\theta : T \to D$



The requirements: Signal Temporal Logic (STL)

Signal temporal logic is:

- a linear continuous time temporal logic.
- the atomic predicates are of the form $\mu(\mathbf{X}){:=}[g(\mathbf{X}) \geq 0]$ where $g : \mathbb{R}^n \to \mathbb{R}$ is a continuous function.
- the syntax is

$$\phi := \bot \mid \top \mid \mu \mid \neg\phi \mid \phi \vee \phi \mid \phi \mathbf{U}_{[T_1,T_2]}\phi, \tag{1}$$

Eventually and Globally Operators

$\mathbf{F}_{[T_1,T_2]}\phi \equiv \top\mathbf{U}_{[T_1,T_2]}\phi$ and $\mathbf{G}_{[T_1,T_2]}\phi \equiv \neg\mathbf{F}_{[T_1,T_2]}\neg\phi$

Interpretation (Boolean semantics)

$$(\mathbf{x}_\theta, 0) \models \mathbf{F}_{[0,50]}|X_1 - X_2| > 10$$

Verification

Problem

Which is the probability that a trajectory $\mathbf{x}_\theta$ generated by $\mathcal{M}_\theta$ satisfies $\phi \in \mathit{STL}$?

$$P_\phi(\theta) \equiv P(\phi \mid \mathcal{M}_\theta) := P(\{\mathbf{x}_\theta(t) \in \mathit{Path}^{\mathcal{M}_\theta} \mid (\mathbf{x}_\theta, 0) \models \phi\})$$

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$\Downarrow$

Classical Verification

compute or estimate the satisfaction probability $P_\phi(\theta)$ for a **fixed** θ

$\Downarrow$

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Parametric Verification

compute or estimate the satisfaction probability $P_\phi(\theta)$ **as a function of** $\theta \in \Theta$.

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compute or estimate the satisfaction probability $P_\phi(\theta)$ **as a function of** $\theta \in \Theta$.

Numerical approaches

Numerical Integration $\Rightarrow$ STATE SPACE EXPLOSION!

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Statistical Approaches

Statistical Model Checking (SMC)

Smoothed Model Checking (SmMC)

Gaussian Processes

Definition

A random variable $f(\theta), \theta \in \Theta$ is a GP

$$f \sim \mathcal{GP}(m, k) \iff (f(\theta_1), f(\theta_2), \dots, f(\theta_n)) \sim \mathcal{N}(\mathbf{m}, K)$$

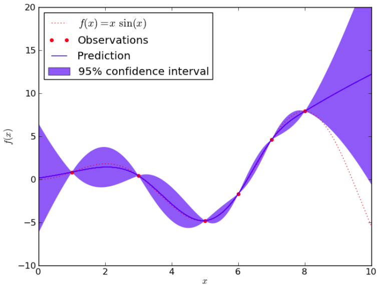
where $\mathbf{m} = (m(\theta_1; h_1), m(\theta_2; h_1), \dots, m(\theta_n; h_1))$ and $K_{ij} = k(f(\theta_i), f(\theta_j); h_2)$

Prediction

$$\{\underbrace{f(\theta_1), \dots, f(\theta_n)}_{\mathbf{f}}, f(\theta')\} \sim \mathcal{N}(\mathbf{m}', K')$$

$$\mathbb{E}(f(\theta')) = \underbrace{(k(\theta_1, \theta'), \dots, k(\theta_N, \theta',))}_{\mathbf{k}} \cdot K^{-1} \cdot \mathbf{f}$$

$$var(f(\theta')) = k(\theta', \theta') - \mathbf{k} \cdot K^{-1} \cdot \mathbf{k}^T$$



Smoothed Model Checking

Hypothesis: The reaction rate $\alpha_j(\mathbf{x}, \theta)$ depends smoothly on θ and polynomially on $\mathbf{x}$.

Goal: Approximate $\theta \to P_\phi(\theta)$ with a surrogate model $\theta \to \tilde{P}_\phi(\theta)$.

Problem: We cannot apply GP directly.

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Idea

Reconstructing a real-valued latent function $f(\theta)$, which is related to $P_\phi(\theta)$ and which can be approximated through GP regression.

$$f(\theta) = \underbrace{\Psi}_{probit}(P_\phi(\theta)) \iff P_\phi(\theta) = \int_{-\infty}^{f(\theta)} \mathcal{N}(0,1)$$

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Statistical Surrogates Model

From $\{P_\phi(\theta_\mathbf{1}), \ldots, P_\phi(\theta_\mathbf{n})\}$ we obtain $\tilde{P}_\phi(\theta)$ as a statistical surrogate models of $P_\phi(\theta)$.

- we can calculate: $p\left(\tilde{P}_\phi(\theta) \in [\lambda^-, \lambda^+]\right)$, mean, variance, etc.
- large training set $\Rightarrow$ a more accurate model.

Problem Definition

Partitioning the parameter space Θ in three classes $\mathcal{P}_\alpha$ (positive), $\mathcal{N}_\alpha$ (negative) and $\mathcal{U}_\alpha$ (undefined)

Threshold Synthesis Problem - Češka et al.[1]

- $\mathcal{P}_\alpha = \{\theta \in \Theta \mid P_\phi(\theta) > \alpha\}$
- $\mathcal{N}_\alpha = \{\theta \in \Theta \mid P_\phi(\theta) < \alpha\}$
- $\mathcal{U}_\alpha = \Theta \setminus (\mathcal{P}_\alpha \cup \mathcal{N}_\alpha)$, $\frac{vol(U_\alpha)}{vol(\Theta)} < \epsilon$.

[1] M. Češka, F. Dannenberg, N. Paoletti, M. Kwiatkowska and L. Brim, Precise parameter synthesis for stochastic biochemical systems, Acta Informatica 56(6), 2017, 589 - 623.

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Bayesian Threshold Synthesis Problem

- $\mathcal{P}_\alpha = \{\theta \in \Theta \mid p(\tilde{P}_\phi(\theta) > \alpha) > \delta\}$
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$\delta \in (0, 1)$ is the confidence probability.

Lower and Upper Bound functions

$$p\left(\tilde{P}_\phi(\theta) < \lambda^+(\theta, \delta)\right) > \delta$$
$$p\left(\tilde{P}_\phi(\theta) > \lambda^-(\theta, \delta)\right) > \delta$$

Problem Definition

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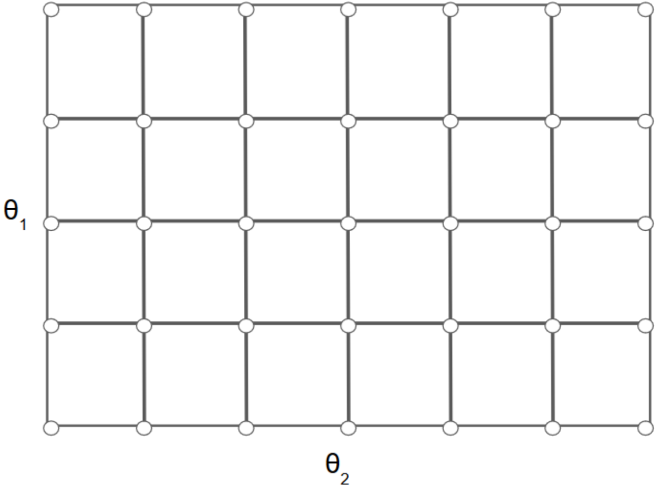
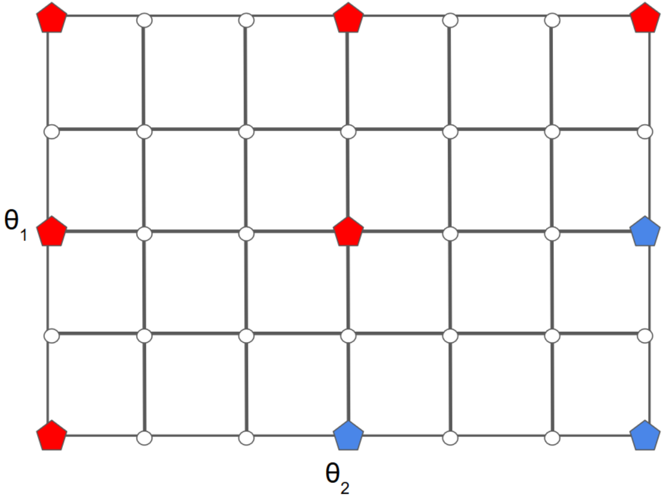
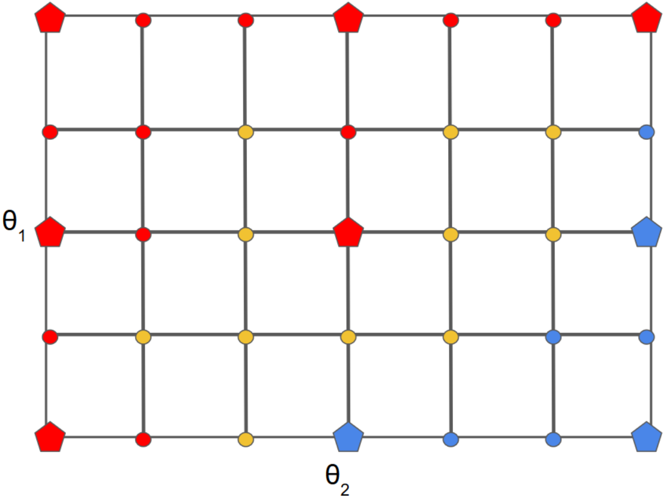
Algorithm I - Grid



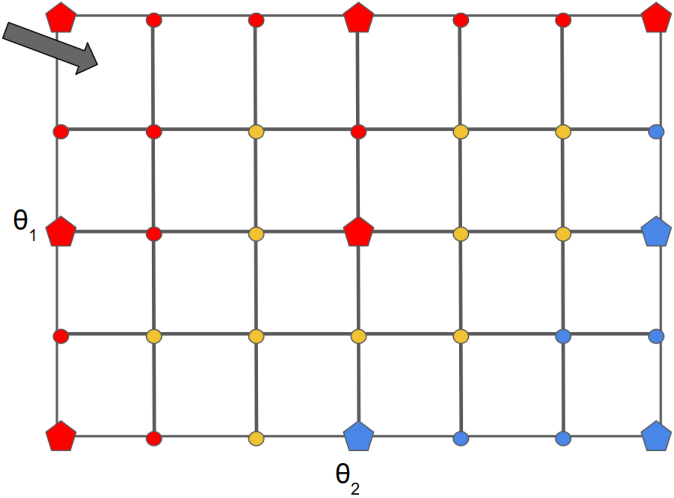
Algorithm II - Training Set



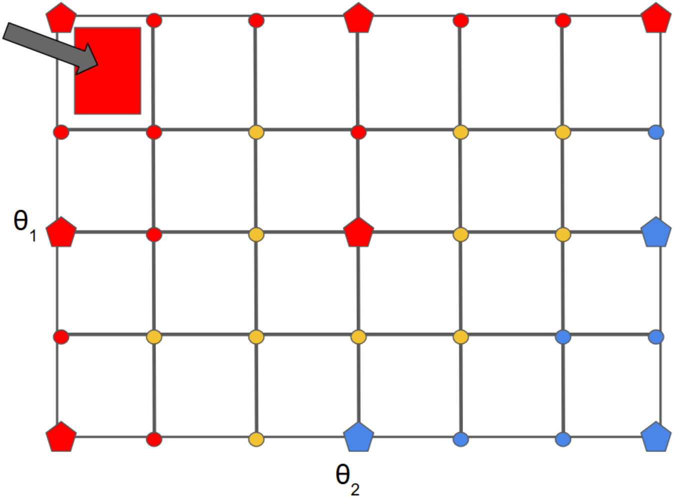
Algorithm III - Prediction



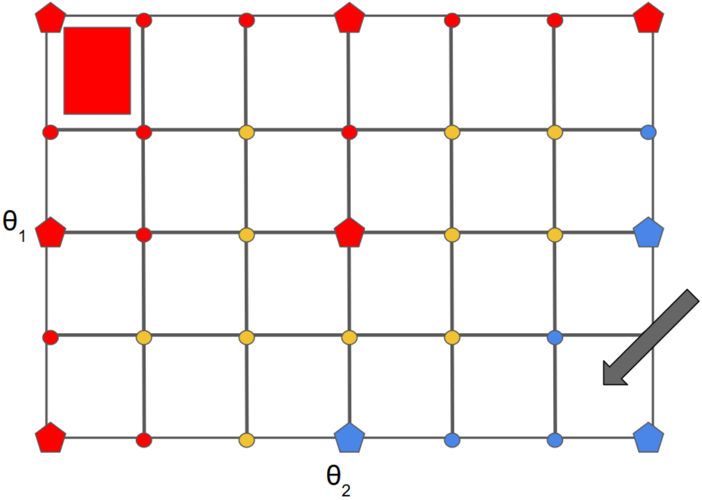
Algorithm IV - Tessellation



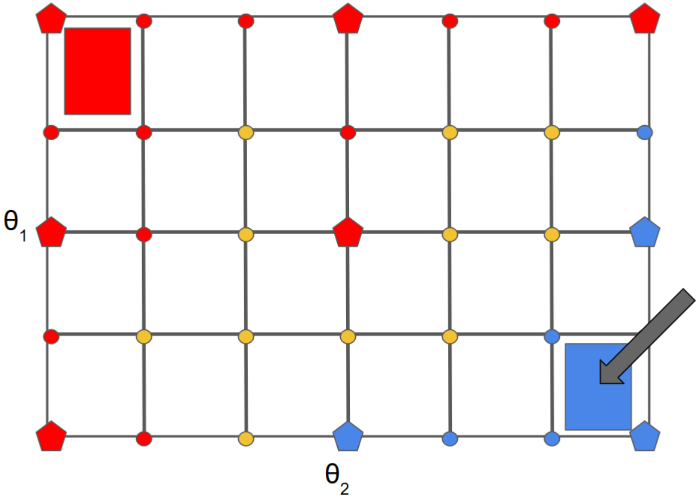
Algorithm V - Tessellation



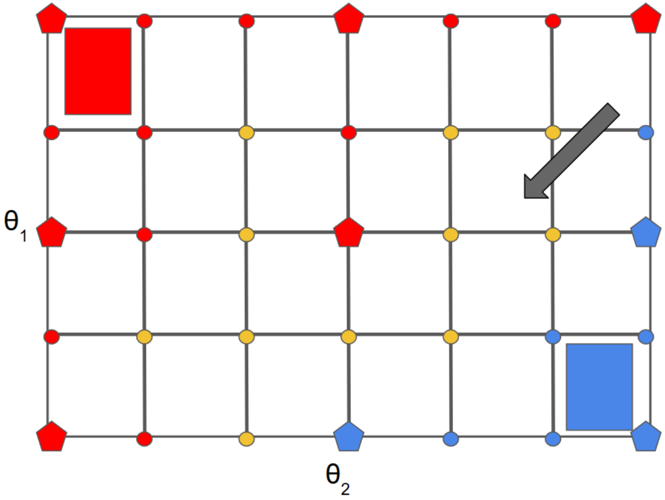
Algorithm VI - Tessellation



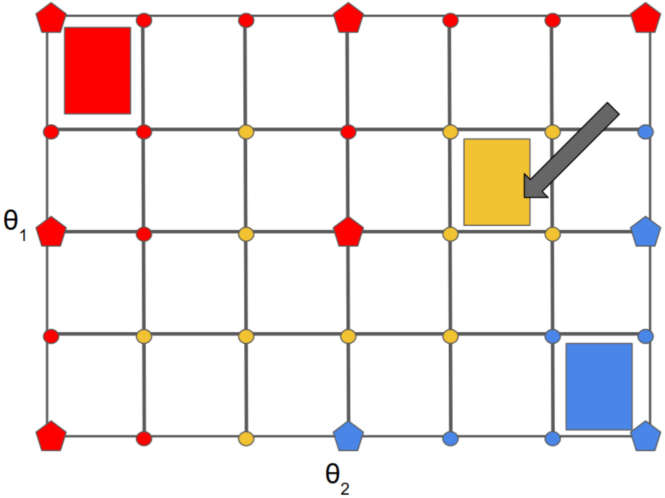
Algorithm VII - Tessellation



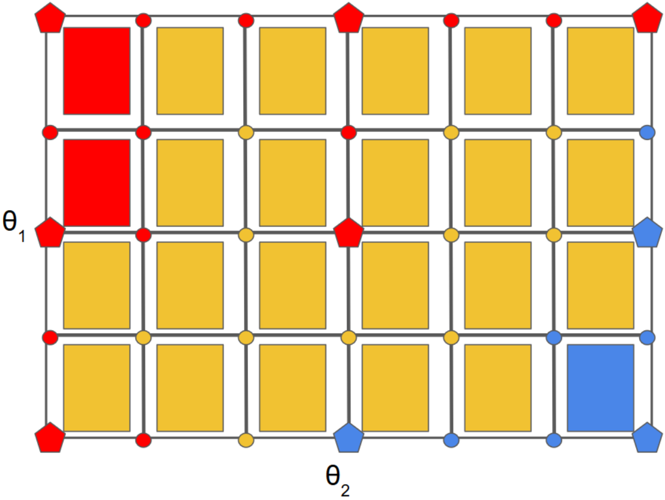
Algorithm VIII - Tessellation



Algorithm IX - Tessellation

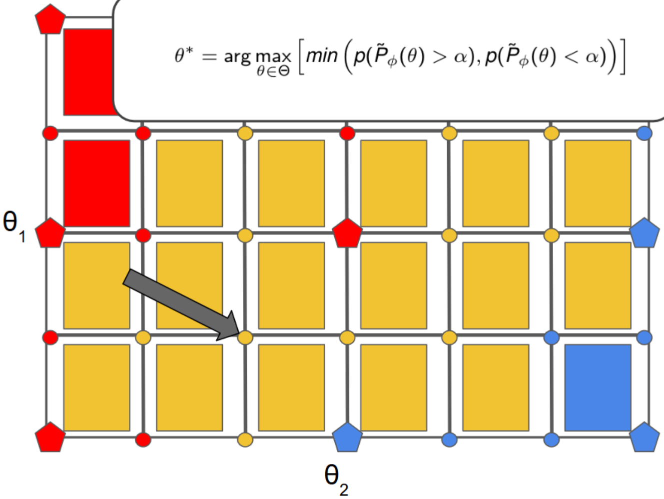


Algorithm X - Tessellation

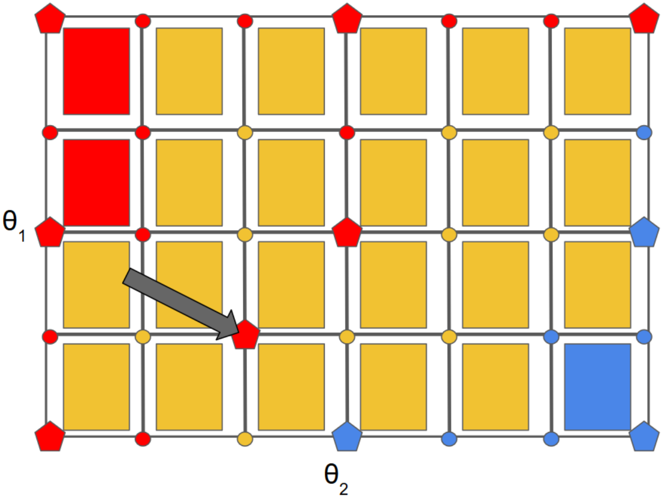


Algorithm XI - Active Learning Step

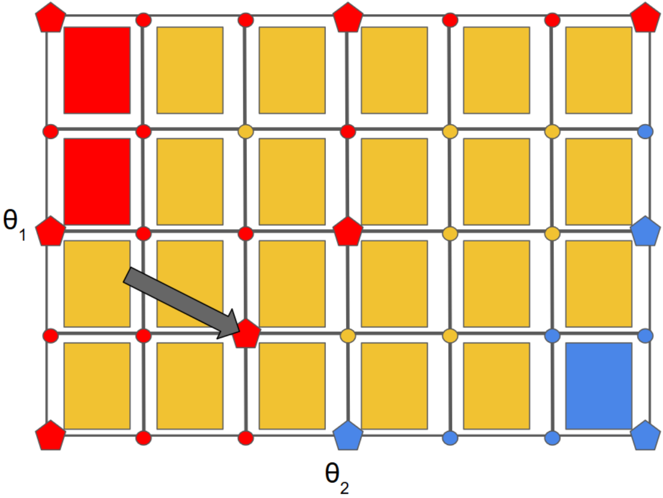
$$\theta^* = \arg\max_{\theta \in \Theta} \left[min \left(p(\tilde{P}_\phi(\theta) > \alpha), p(\tilde{P}_\phi(\theta) < \alpha) \right) \right]$$



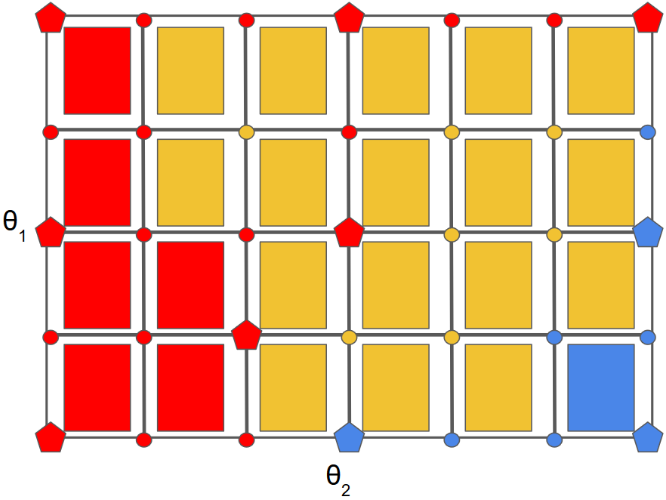
Algorithm XII - Update



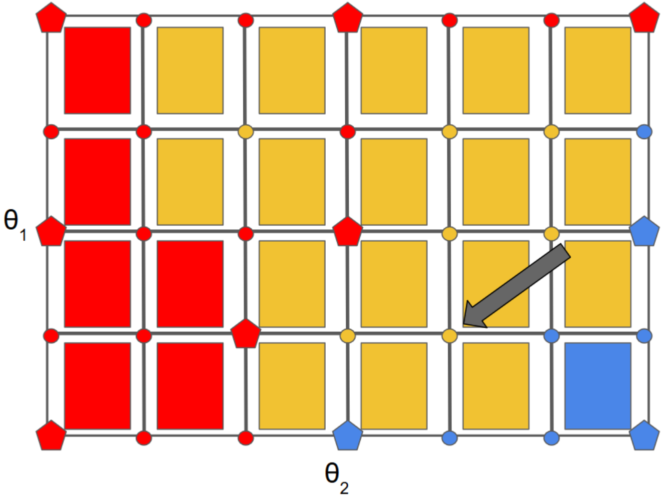
Algorithm XIII - Update



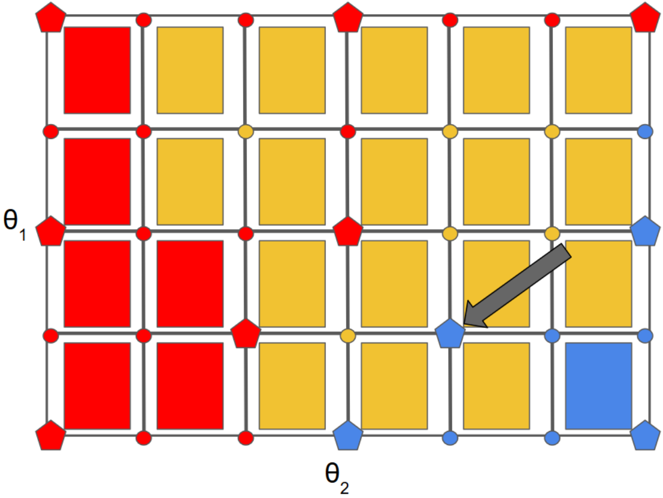
Algorithm XIV - Update



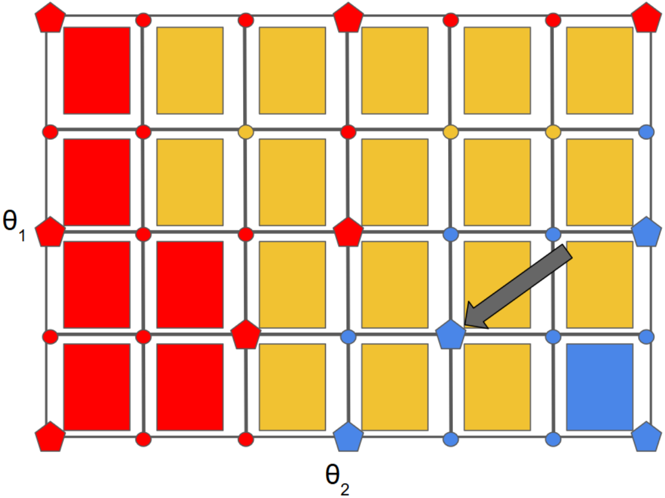
Algorithm XV - Active Learning Step



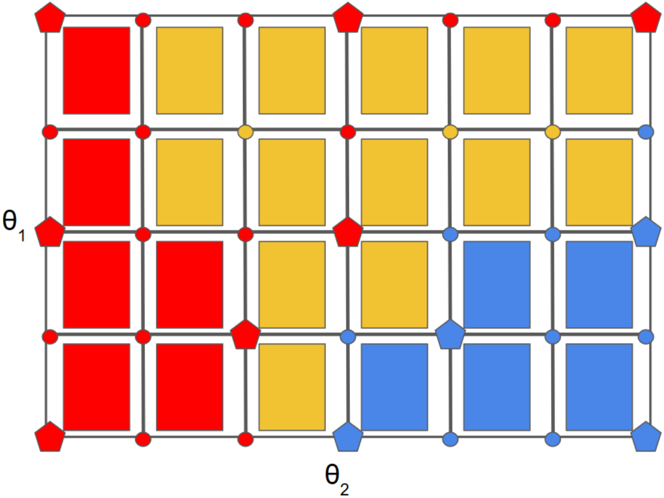
Algorithm XVI- Update



Algorithm XVII - Update

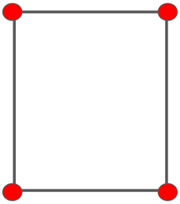


Algorithm XVIII - Update



Problem: the guarantees

A guarantee Problem



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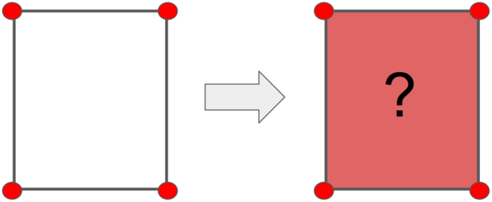

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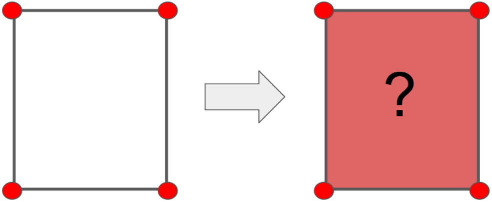

Solution

Continuity of Gaussian Processes.

Problem: the guarantees

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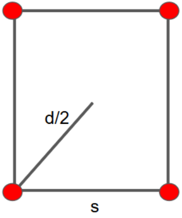

- global/local Lipschitz approach: $\left(\hat{p} - L * \frac{d}{2}\right) > \alpha$
- Heuristic Approach: $s \ll$ GP length scale and $\delta = 0.99$

Solution

Continuity of Gaussian Processes.

Epidemic Model: SIR

SIR Model

$$
\begin{aligned}
r_1 : S + I &\xrightarrow{\alpha_1} 2I \qquad \alpha_1 = k_i \cdot \frac{X_s \cdot X_i}{N} \\
r_2 : I &\xrightarrow{\alpha_2} R \qquad \alpha_2 = k_r \cdot X_i
\end{aligned}
$$

Disease Extinction

$$\phi = (I > 0)\,\mathcal{U}_{[100,120]}\,(I = 0)$$

Results

Bayesian Threshold Synthesis Problem

- volume tolerance: $\epsilon = 0.1$
- threshold: $\alpha = 0.1$

Case	$k_i \times k_r$	**h**-grid	Time (sec)
1	$[0.005, 0.3] \times 0.05$	0.0007	17.92 ± 2.61
2	$0.12 \times [0.005, 0.2]$	0.0005	4.87 ± 0.01
3	$[0.005, 0.3] \times [0.005, 0.2]$	(0.003,0.002)	116.4 ± 4.06

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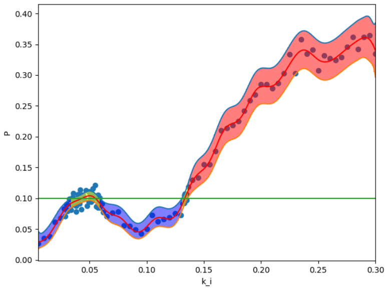

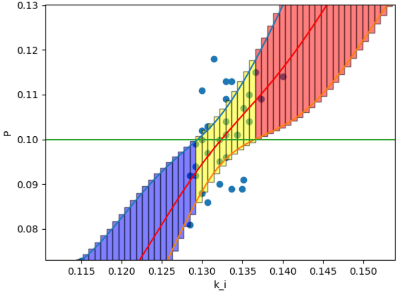

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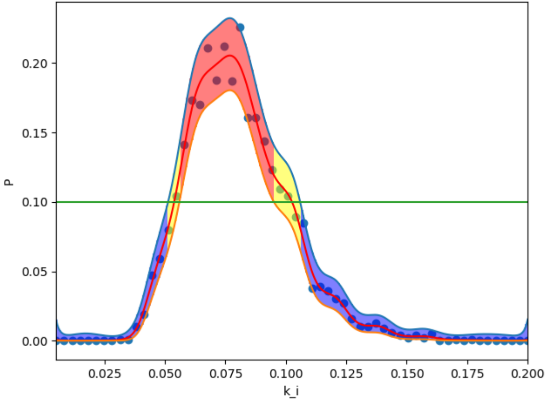

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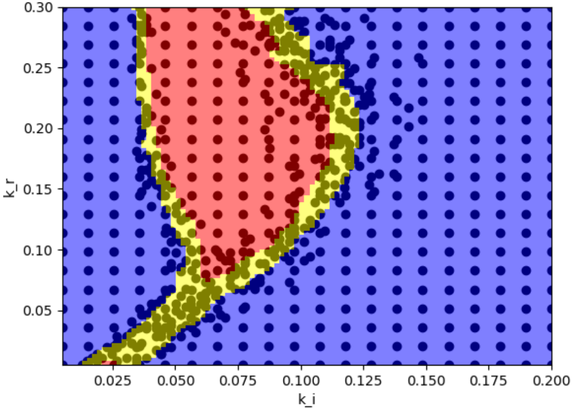

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Conclusions

- Bayesian version of the Threshold Synthesis Problem
- Smoothed Model Checking + Active Learning Approach
- good performance in terms of execution time w.r.t [Češka et al.][2], retaining good accuracy **at the price of having only statistical guarantees**.

[2] M. Češka, F. Dannenberg, N. Paoletti, M. Kwiatkowska and L. Brim, Precise parameter synthesis for stochastic biochemical systems, Acta Informatica 56(6), 2017, 589 - 623.

Future Works

- leveraging GPU Computing
- adaptive grid approach to tessellate the parameter space
- use GP reconstruction tailored for grid dataset
- combined approach with numerical methods of [Češka et al.]

Thank You