History Matching

An Alternative Way of Inference for Biological Systems

Peter Challenor

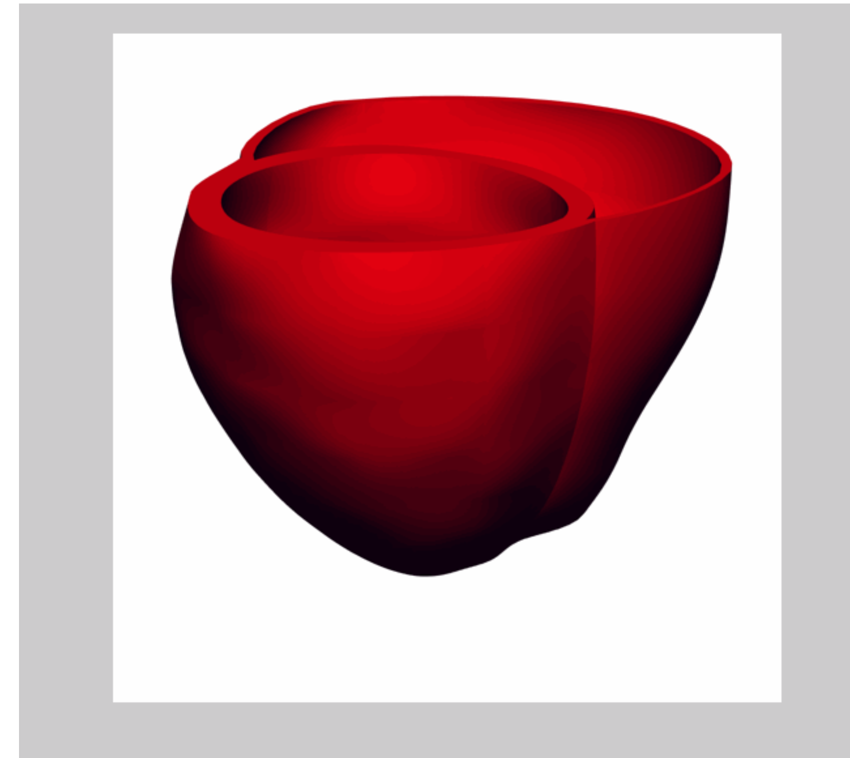
The Alan Turing Institute

University of Exeter

Complex Numerical Models

- Solve thousands of equations on very large computers

- Take many hours to run



- We cannot afford many runs

- But we want do inference

Complex Numerical Models

Real world Problem	Mathematical Model PDEs	Discretised model FE/FD	Computer code	Emulator

‘Black Box’ Model

- What is a black box model?
- We cannot change the model code
- (Non-intrusive methods)
- Work on propriety models or commercial codes

Building emulators
(Modelling Models)

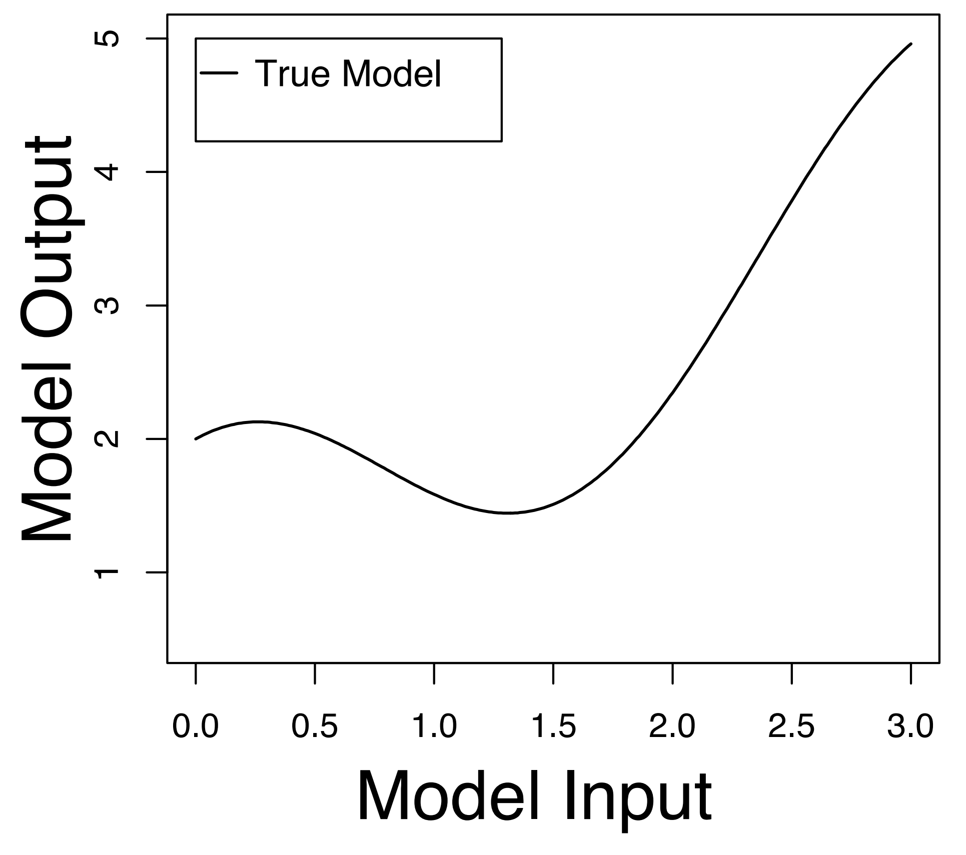
- Emulators are *surrogate* models with the addition of a measure of uncertainty.

- Use a Gaussian process (shallow learning)

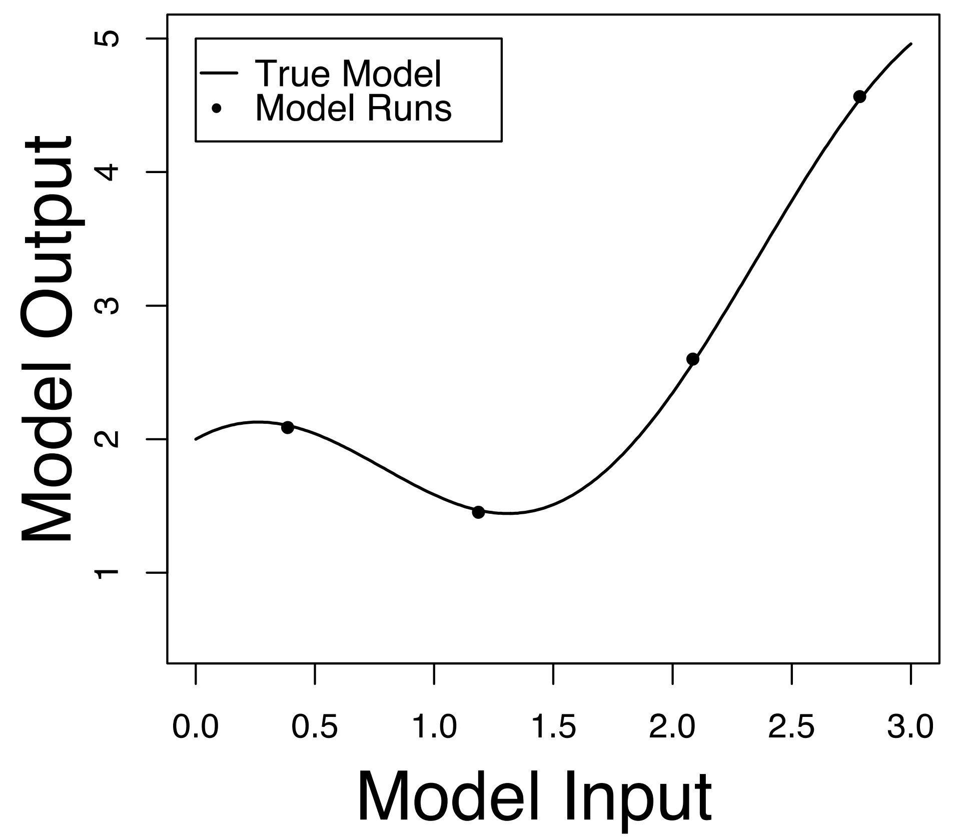
- Include mean term; low order polynomials

- Could just use polynomials (lightweight emulators)

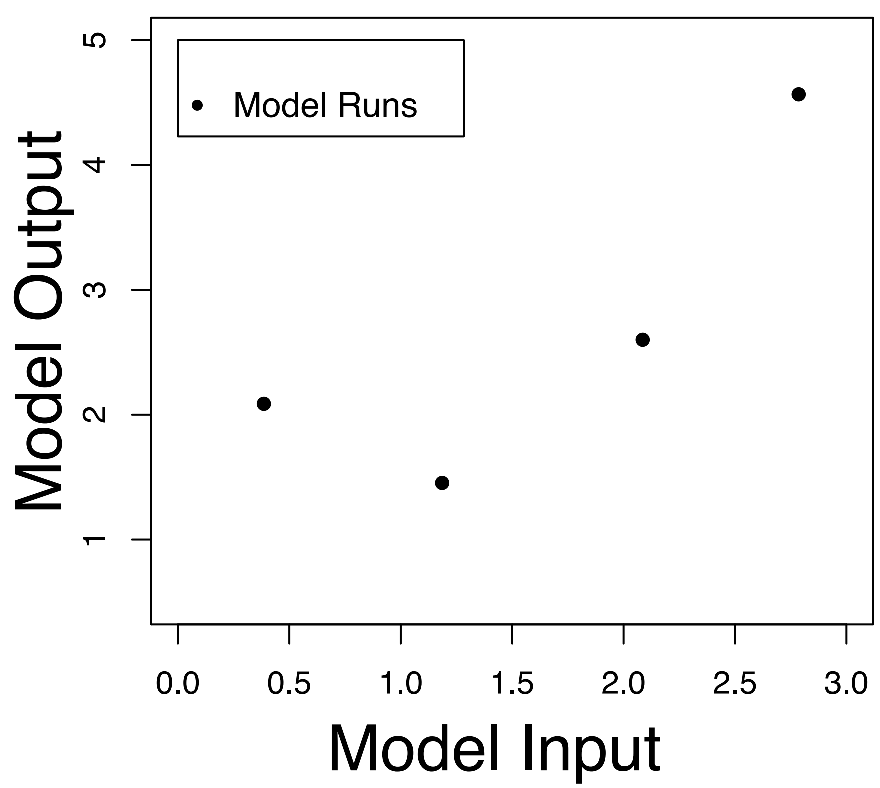
- Deep learning

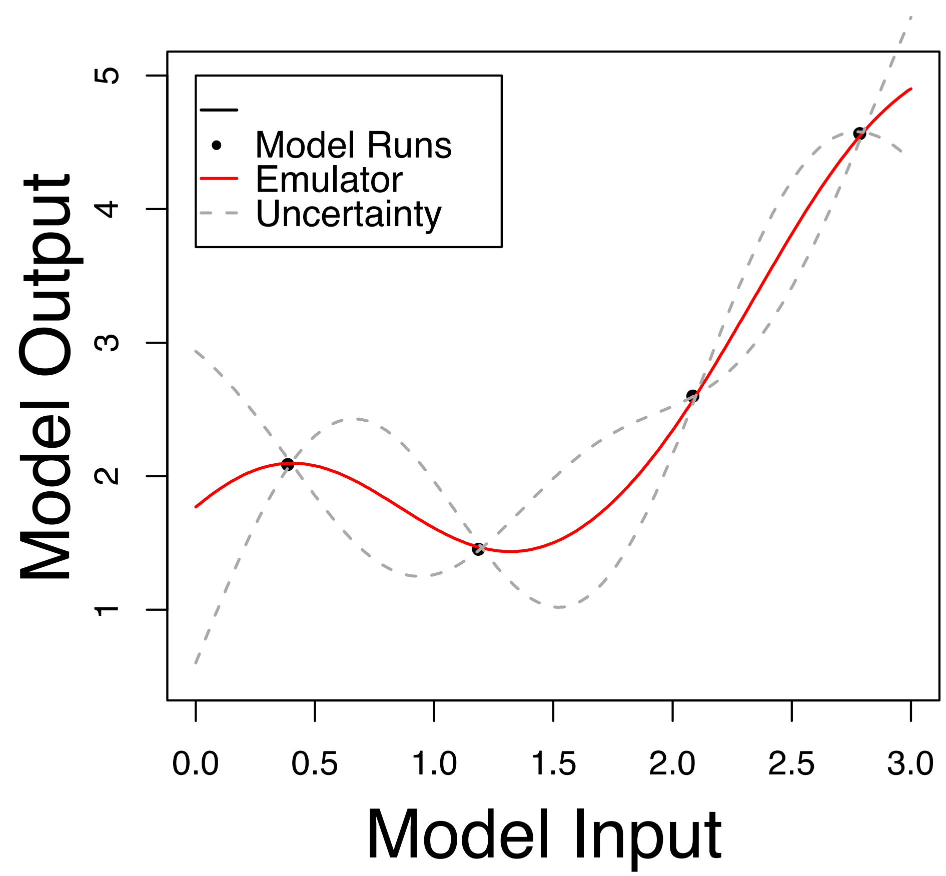


True Model
Model Output
Model Input
0.0
0.5
1.0
1.5
2.0
2.5
3.0
1
2
3
4
5

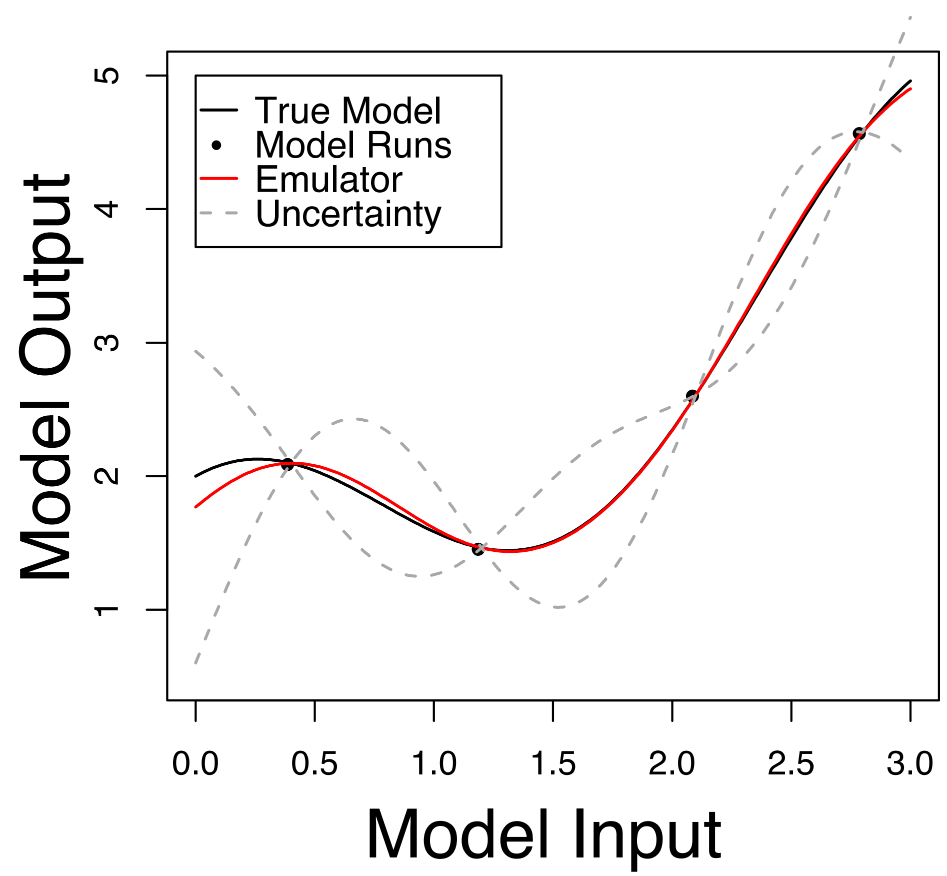


True Model
Model Runs
Model Output
Model Input
0.0
0.5
1.0
1.5
2.0
2.5
3.0
1
2
3
4
5


Model Runs
5
4
3
2
1
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Model Output
Model Input

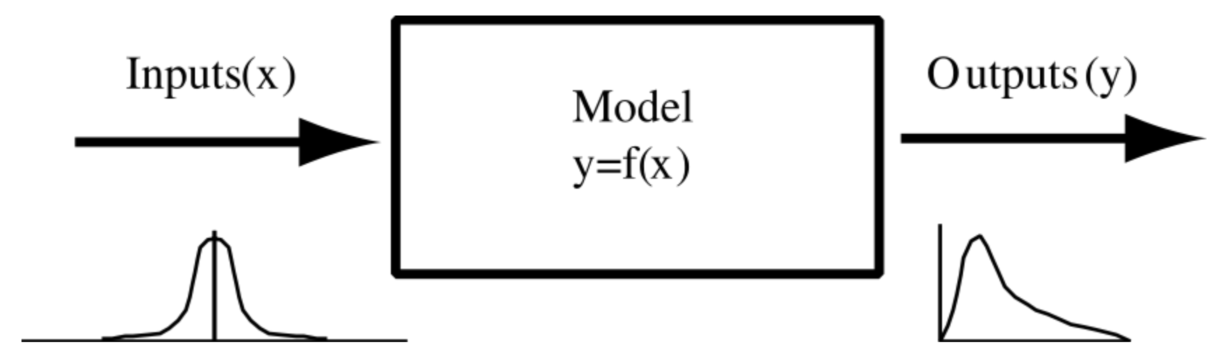


Model Runs
Emulator
Uncertainty
Model Output
Model Input
0.0
0.5
1.0
1.5
2.0
2.5
3.0
1
2
3
4
5


True Model
Model Runs
Emulator
Uncertainty
Model Output
Model Input
0.0
0.5
1.0
1.5
2.0
2.5
3.0
1
2
3
4
5

Where does the uncertainty come from?

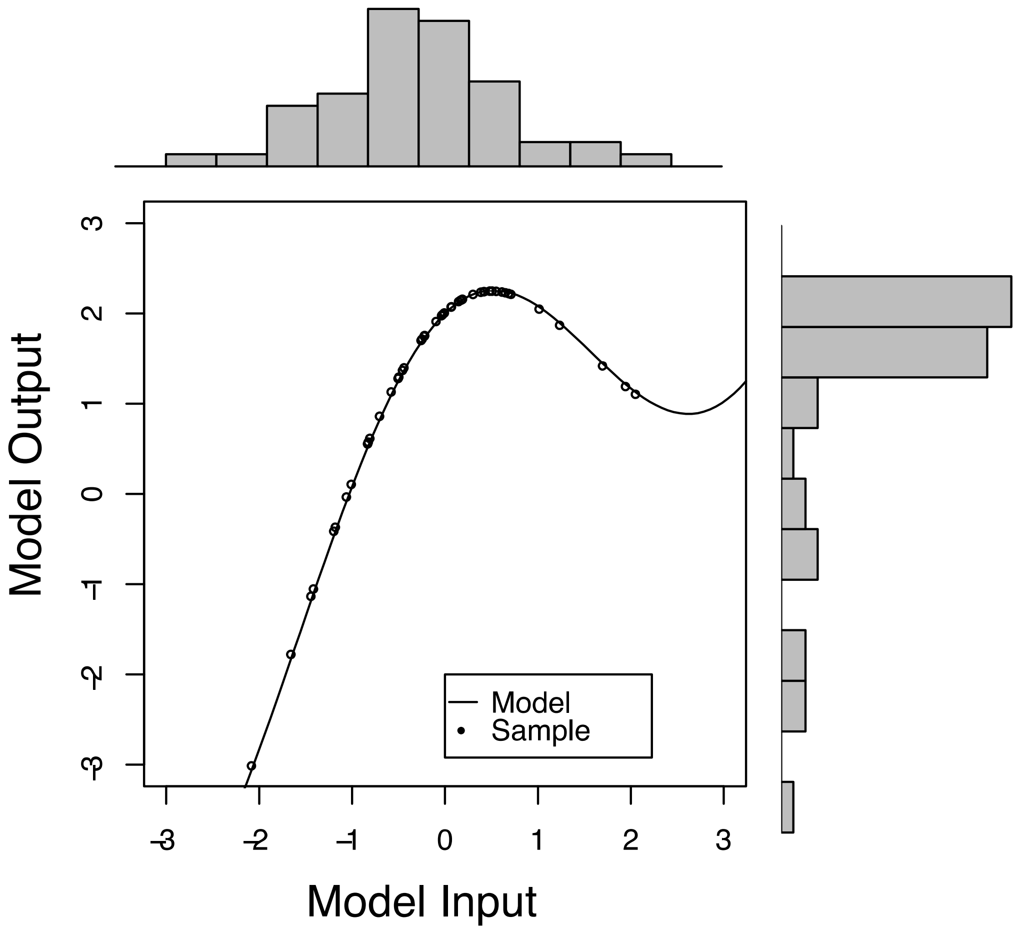
- Even for deterministic models
  - The model inputs are uncertain
  - The model structure is uncertain



- Some models are themselves stochastic (eg COVID)

Monte Carlo

- Classical method
- Requires many thousands of runs
- We cannot afford that



Inference

- Uncertainty quantification
- Sensitivity Analysis
- Uncertainty Analysis
- Inverse Modelling (calibration)

Two Levels of Inference

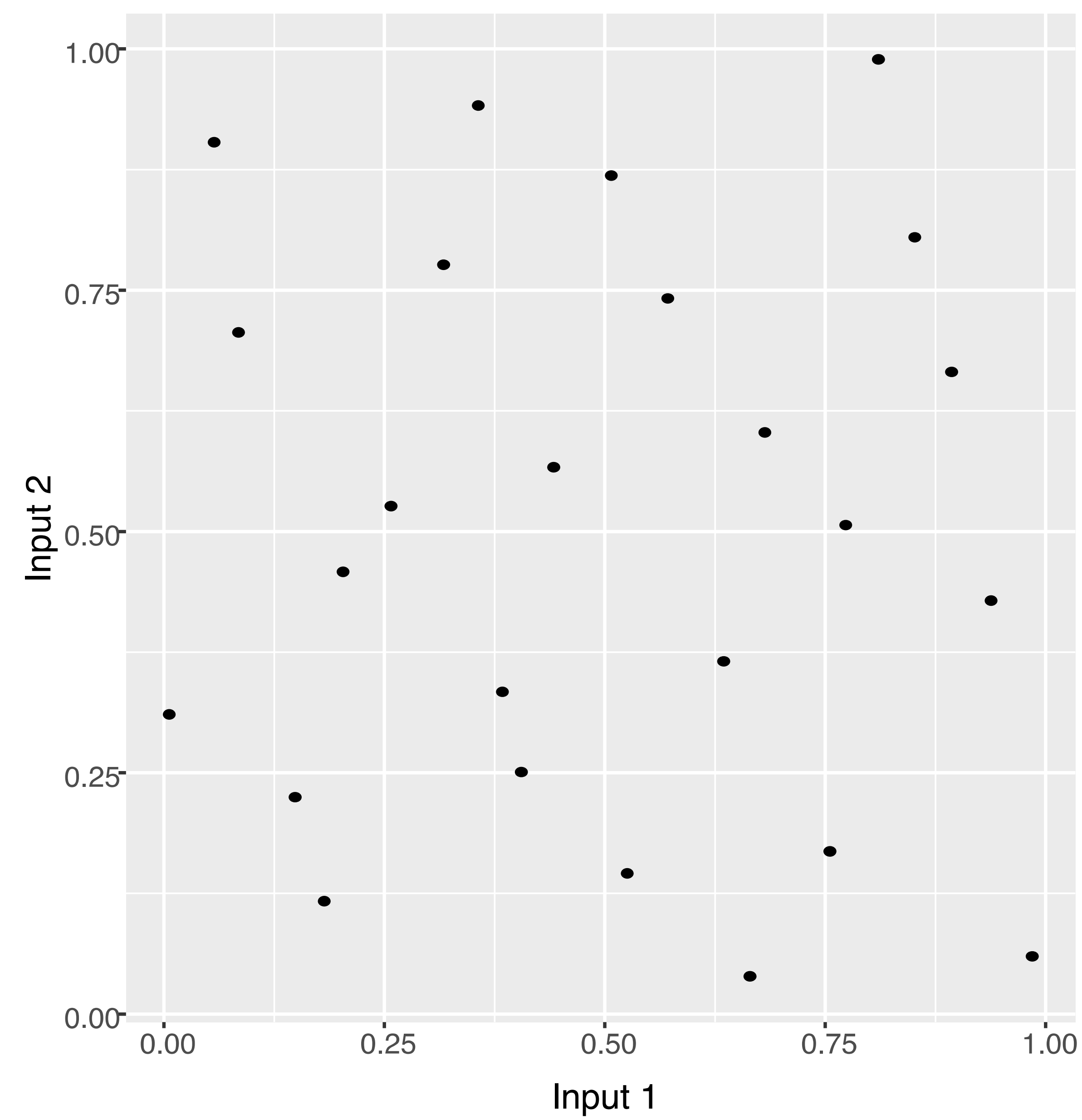
- Inference to build the emulator
- Inference to relate the numerical model to the real world (calibration, tuning, inverse modelling)

Design

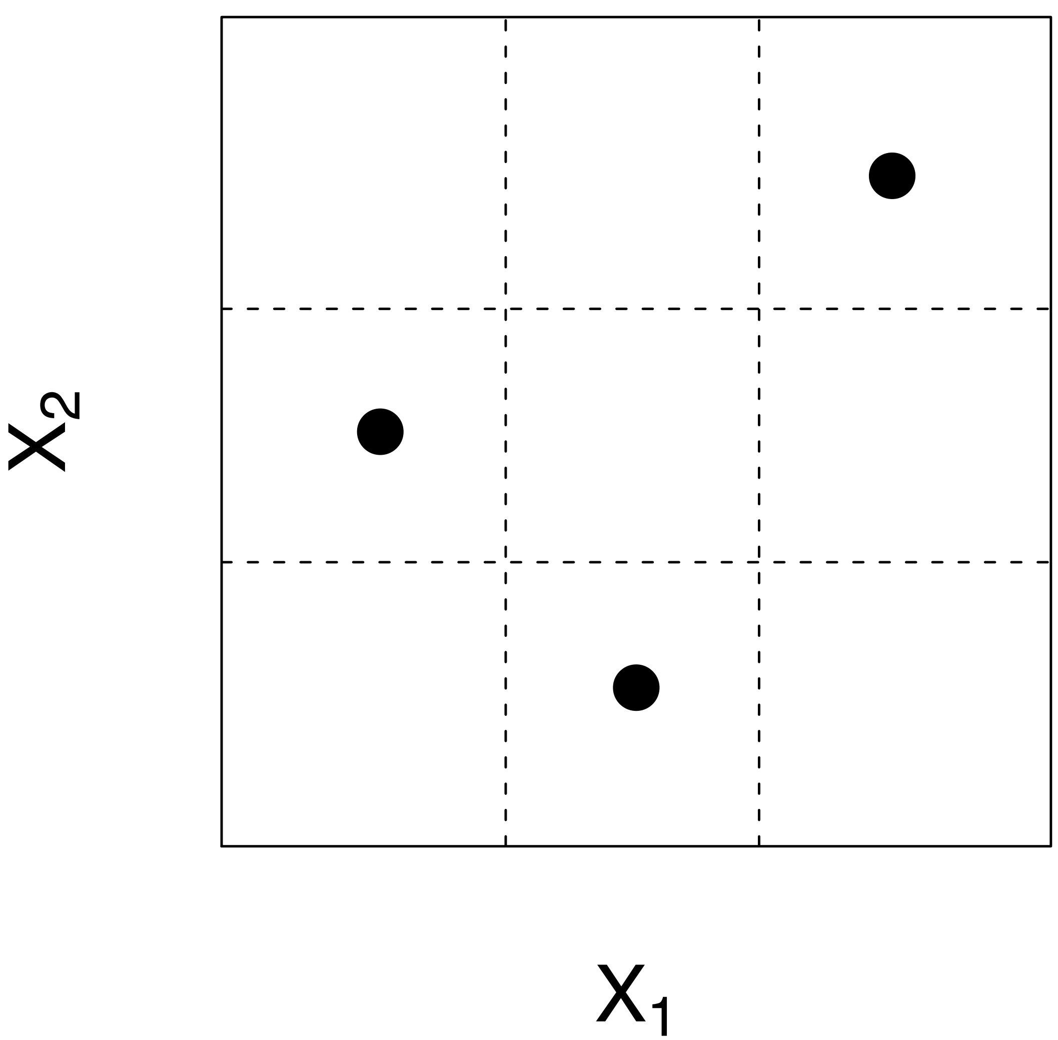
- Where do we do the model runs

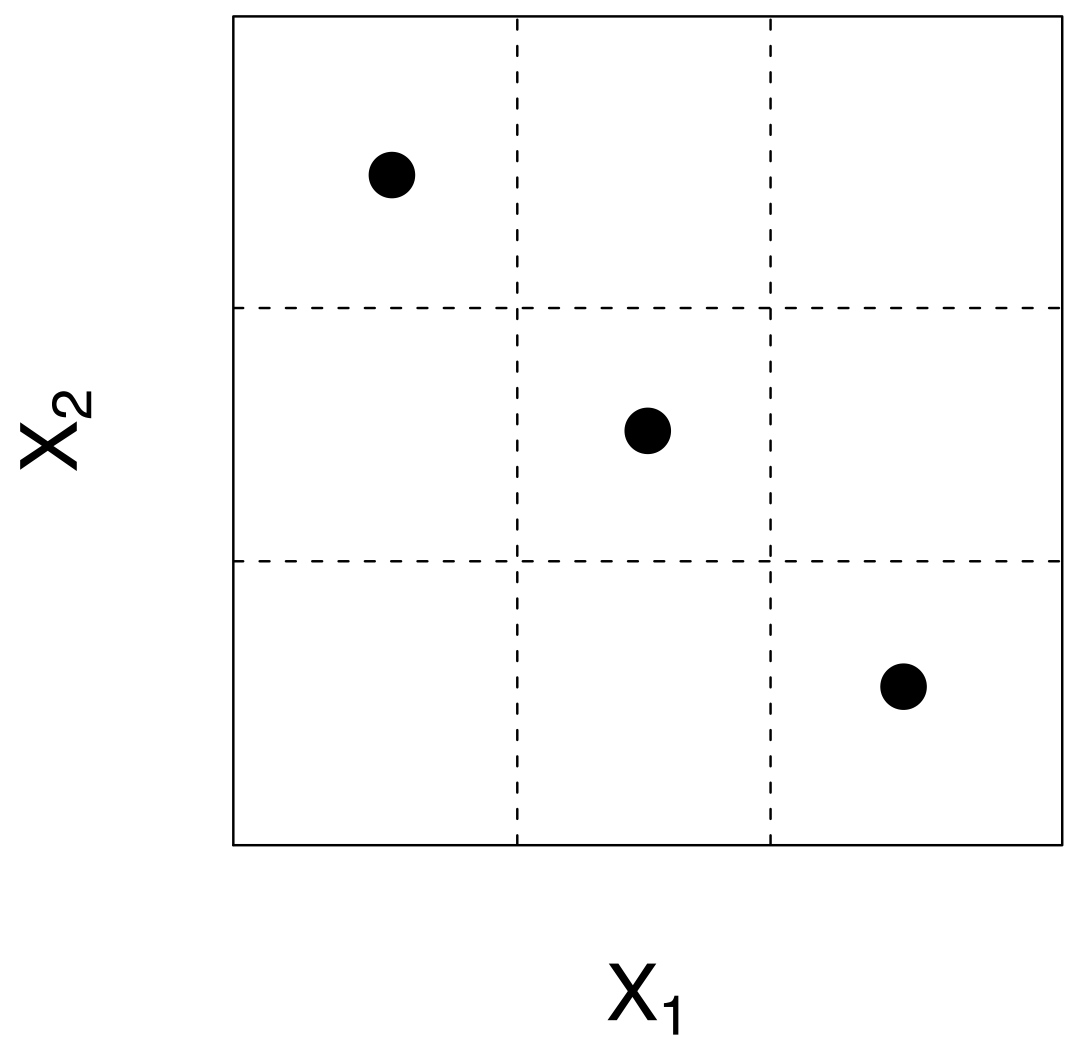
- Space filling

- Sequential design



The Latin Hypercube

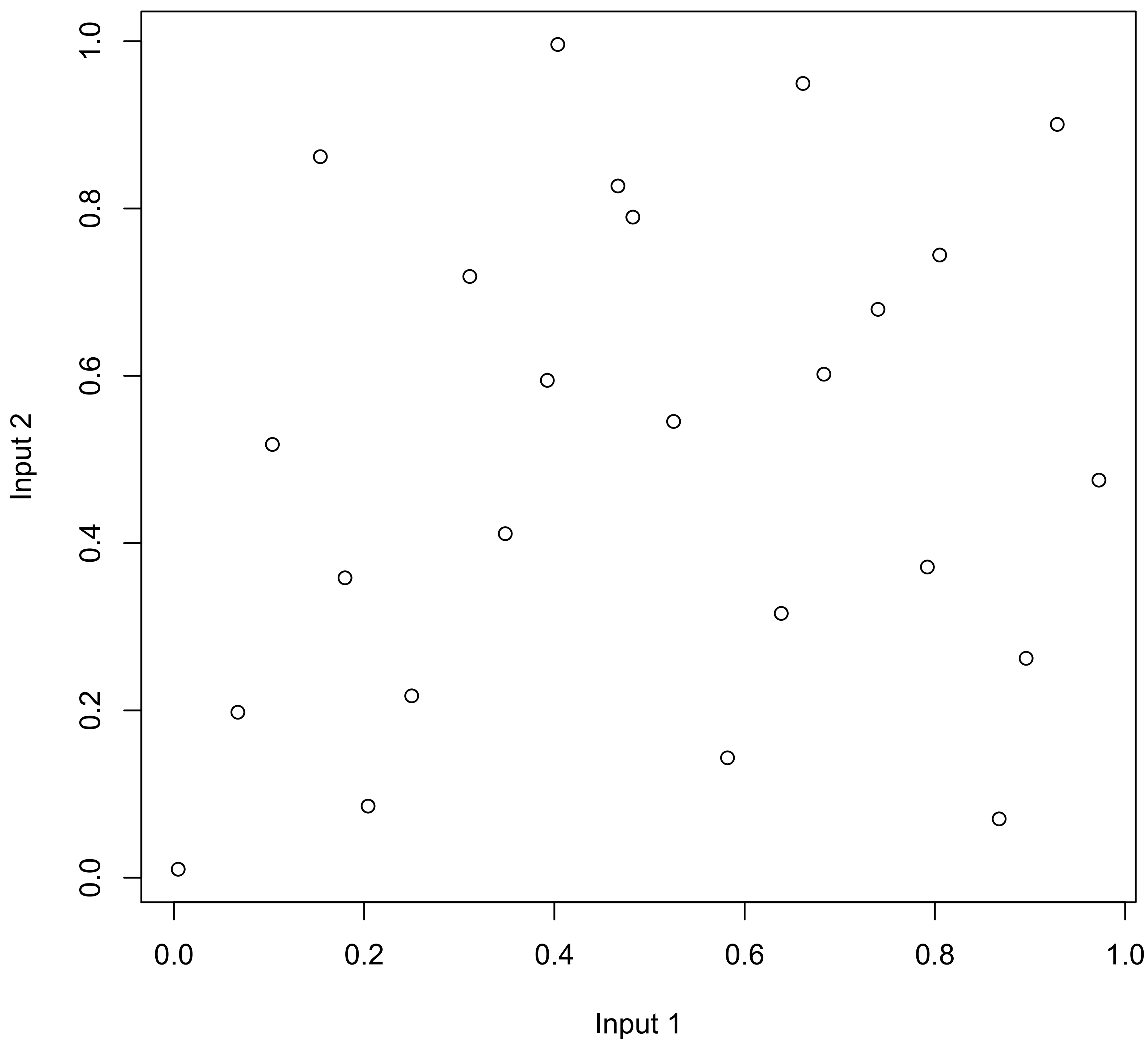




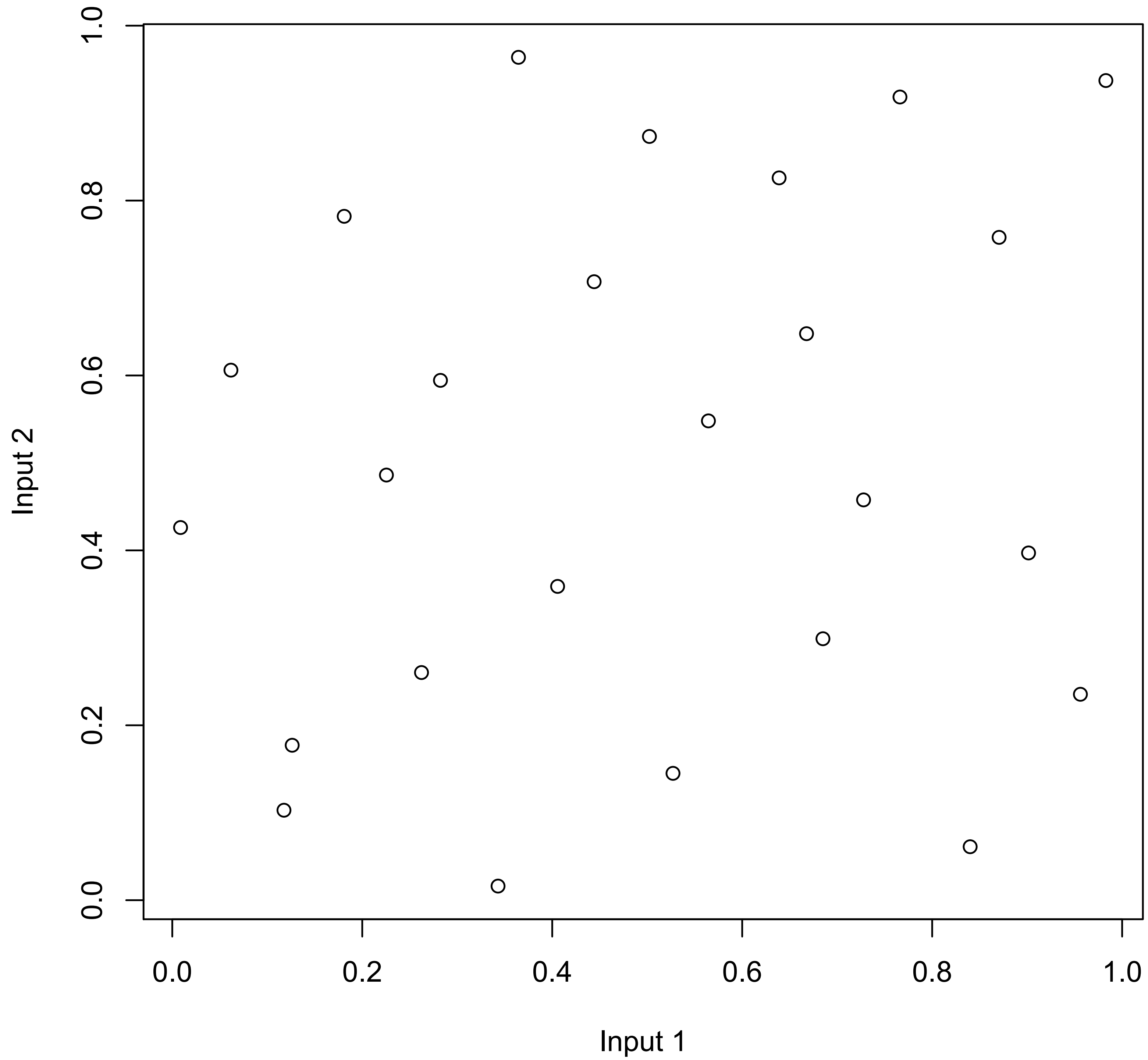
The Latin Hypercube

- We don’t have an algorithm for the optimal Latin hypercube
- What is a good Latin hypercube?
- Maximin
- Orthogonal designs

A Latin Hypercube



A maximin LHC



Estimation for Emulation

- Either MLE or Bayes
- Non-linear parameters (length scales, nuggets) either plug in or full Bayes

- Likelihood surface complex
- Other maxima/posteriors
-

Relationship between models and the real world

- Models are designed to inform us about the real world
- They are not the same as the real world
- The real world is not a set of equations
- The discretised equations are not the continuum equations
- The code is not the discretised equations

All models are wrong, but some are useful

George Box

Model Discrepancy

- It is important to take model discrepancy into account
- Least squares or Bayesian calibration will give the wrong answer
- And the uncertainty will go to zero as you increase the amount of dat

Kennedy and O’Hagan (2001)

- Kennedy and O’Hagan came up with an ingenious solution

- Model the difference between the model and reality as the sum of two GPs

- One is the emulator of the model and the other is the discrepancy

Identifiability

- This fine for prediction (we know the sum of the GPs)
- But suffers from identifiability problems
- Strong priors
- Constrain the discrepancy or the emulator

An Alternative

- Don’t try to find the ‘best’ set of inputs (x)
- Find inputs (x) that are *implausible* given the data (y)
- This is a lot easier
- No optimisation
- No sampling posterior

History Matching

- Set up a measure of the distance between the data and the model prediction

$$Imp = \sqrt{\frac{E(y - f(x))^2}{V(y - f(x))}}$$

- If this distance is too far. That value of $\boldsymbol{x}$ is implausible

- We can expand the variance term to give

$$Imp = \sqrt{\frac{(y - E(f(x)))^2}{V_y + V_{f(x)}}}$$

- Where V_y is the variance of y

- and $V_{f(x)}$ is the variance of $f(x)$

- For Imp >3 we say that the inputs (x) are implausible (Pukelsheim (1994))

- but could be expensive to run in which case we can only compute Imp in a small number of places

- Replace $f(x)$ with our emulator $f^*(x)$

- Expanding the variance as before gives

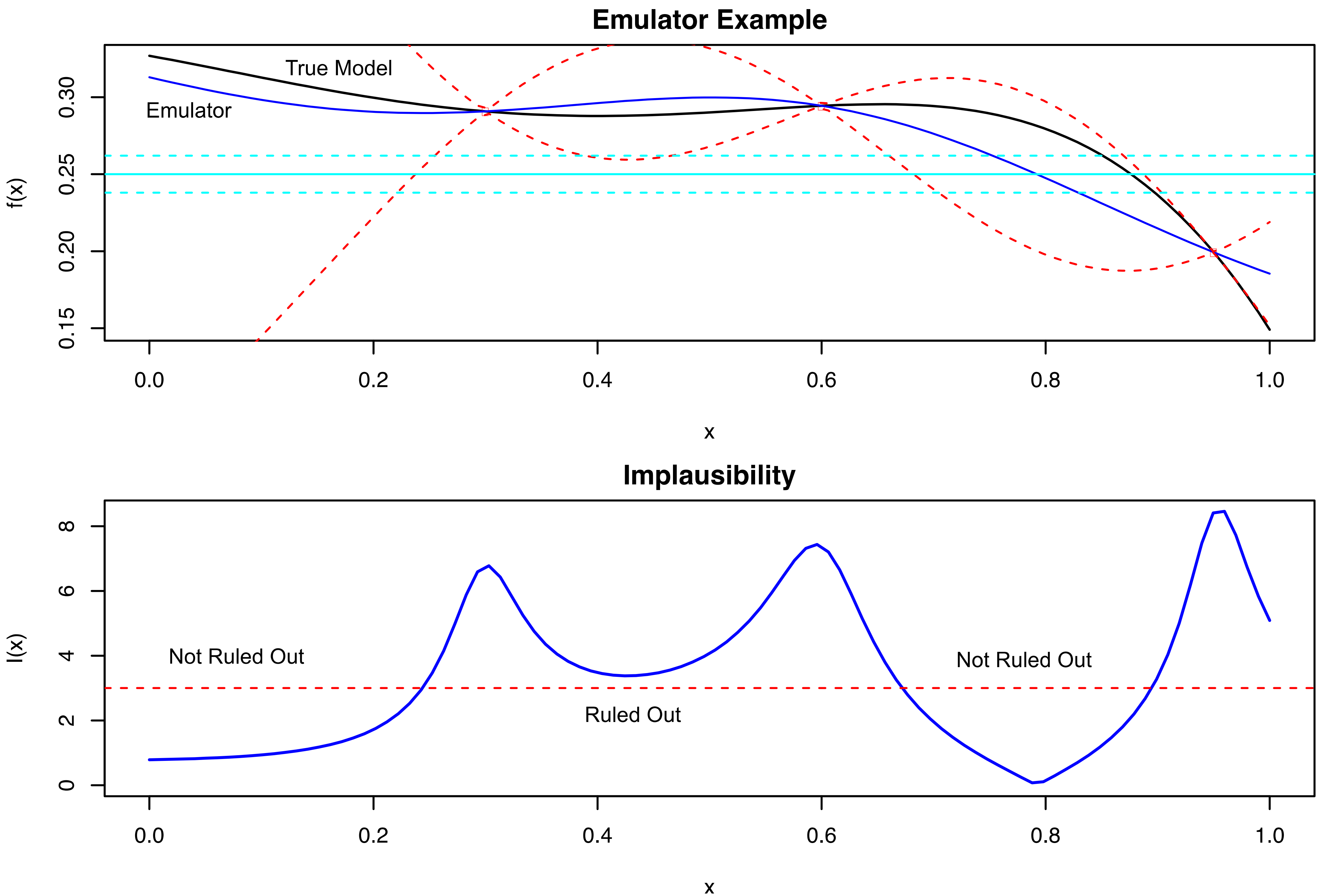
$$Imp = \sqrt{\frac{y - E(f(x))^2}{V_y + V_{emul} + V_{disc}}}$$

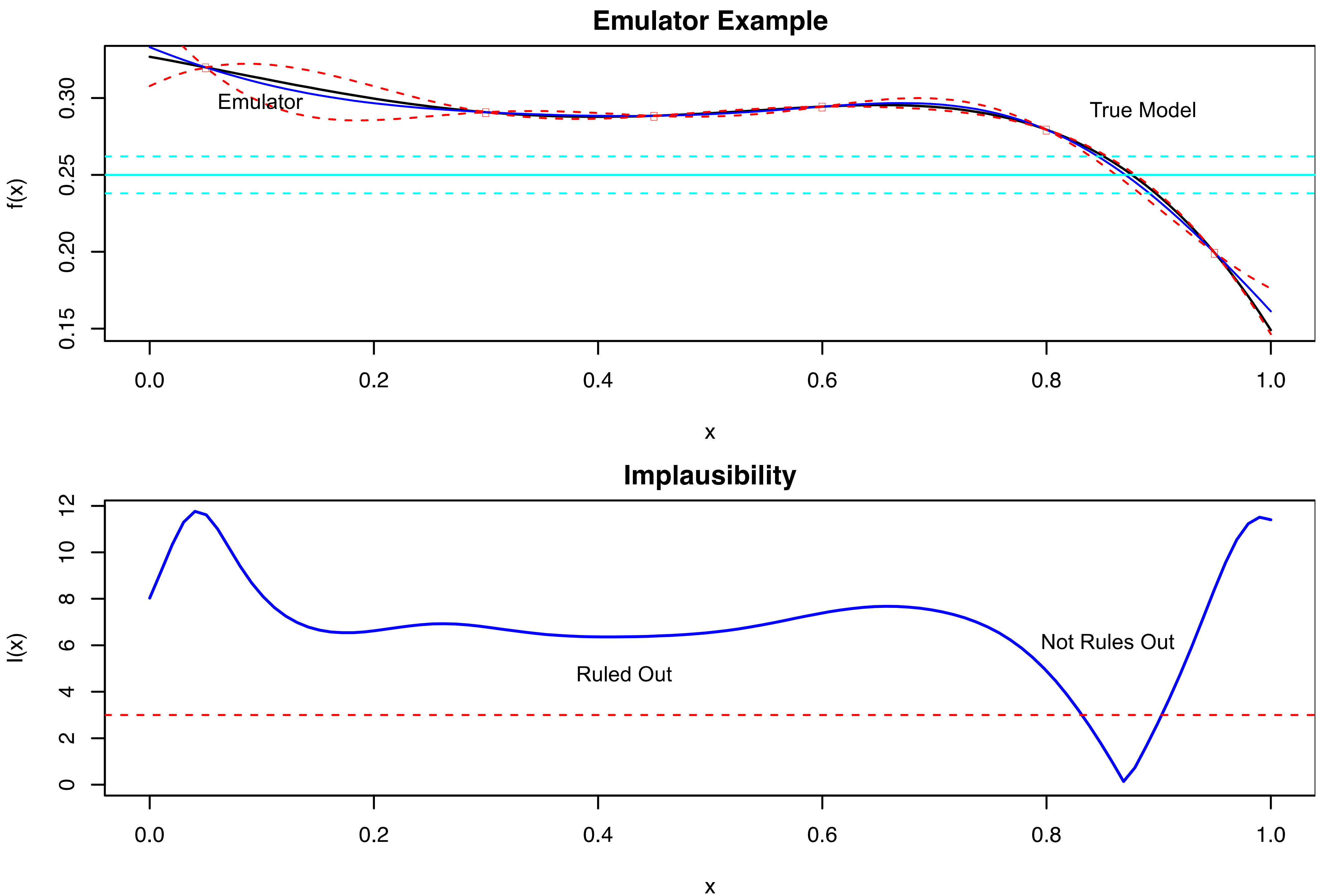
- V_y is the variance of the data y
- V_{emul} is the emulator variance
- V_{disc} is the model discrepancy

Procedure

- Collect data
- Run designed experiment
- Build emulator
- Perform history matching
- All points with Imp <3 deemed *not implausible*
- If we have many metrics take $max(Imp)$
- These constitute the *Not Ruled Out Yet* (NROY) space

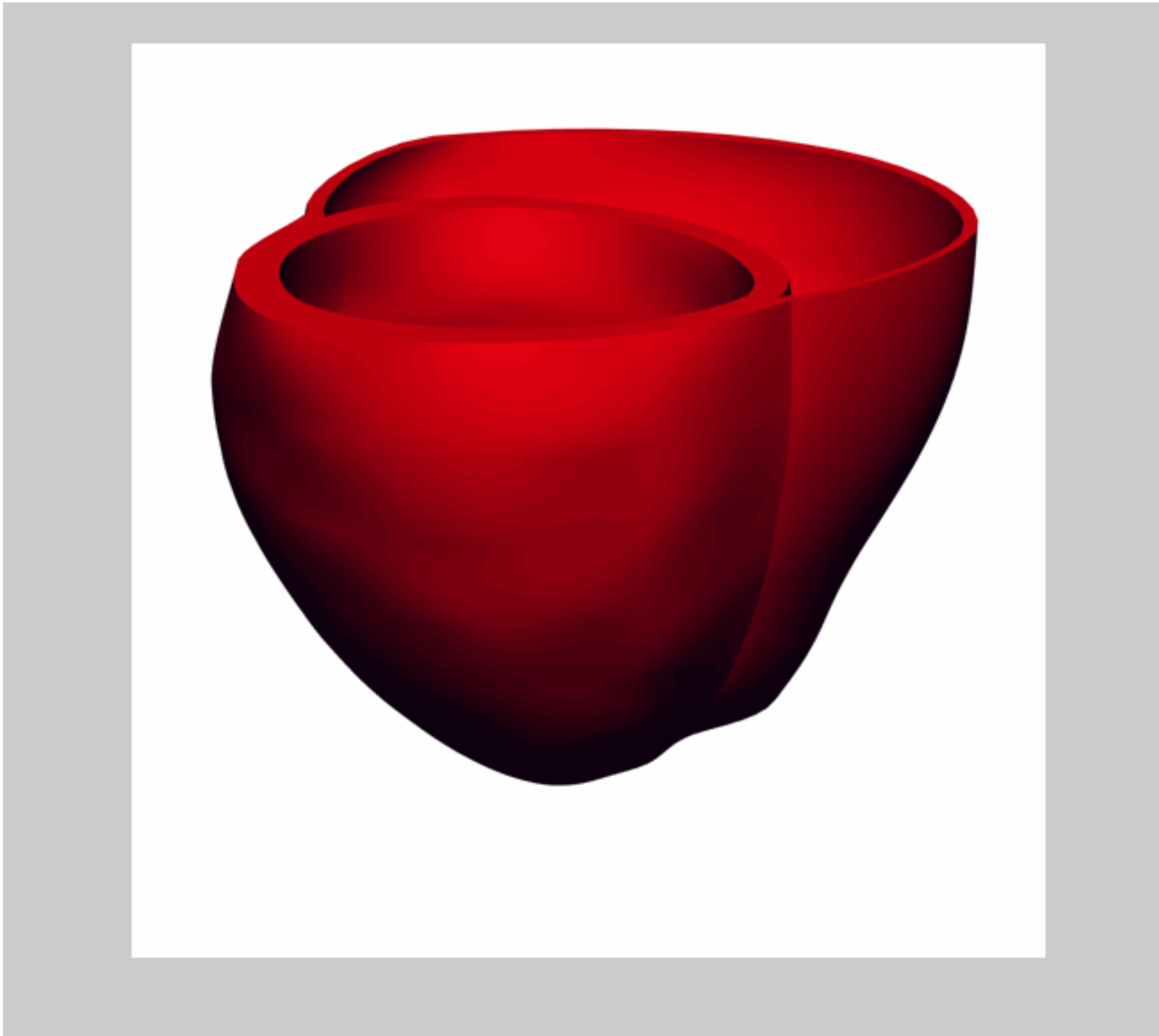
- Design additional experiment within NROY space (wave 2)
- Rebuild emulator
- History match
- Repeat until NROY is either small enough or does not shrink
- At which point we may need more data


Emulator Example
True Model
Emulator
f(x)
0.15
0.20
0.25
0.30
0.0
0.2
0.4
0.6
0.8
1.0
x
Implausibility
Not Ruled Out
Ruled Out
Not Ruled Out
I(x)
0
2
4
6
8
0.0
0.2
0.4
0.6
0.8
1.0
x



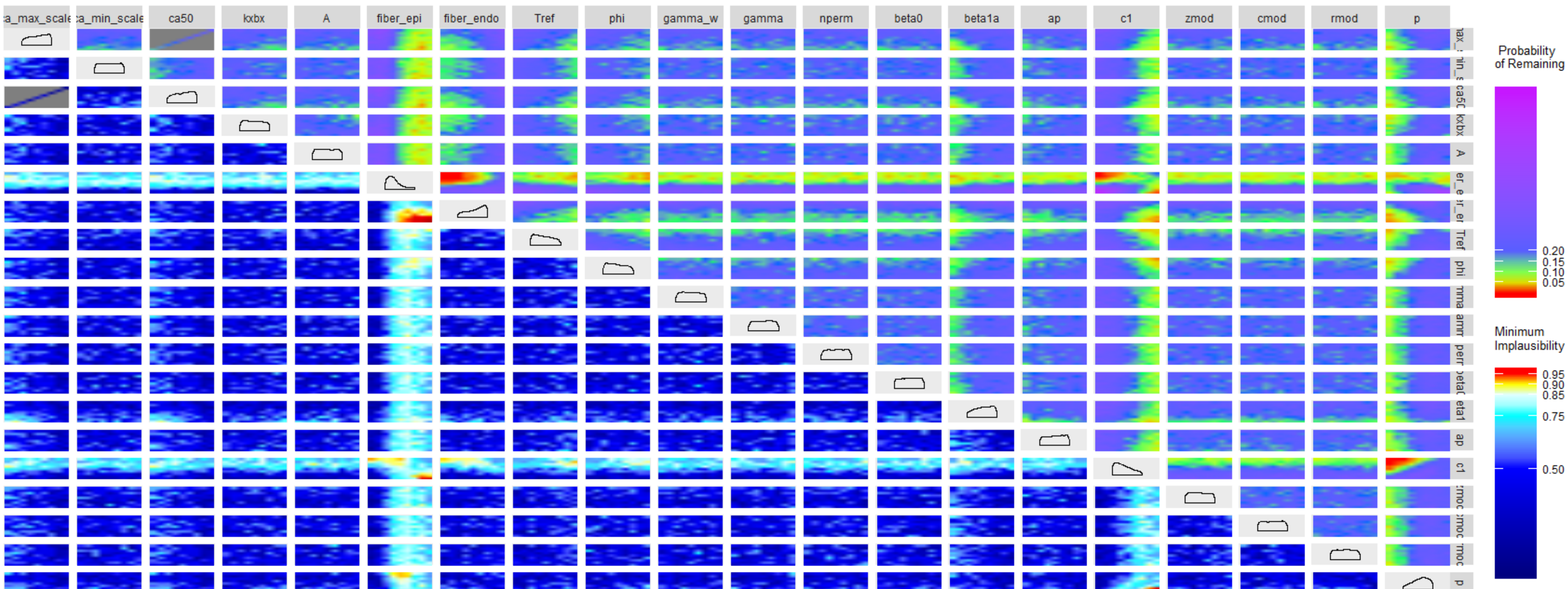
Emulator Example
f(x)
0.15
0.20
0.25
0.30
Emulator
True Model
0.0
0.2
0.4
0.6
0.8
1.0
x
Implausibility
I(x)
0
2
4
6
8
10
12
Ruled Out
Not Rules Out
0.0
0.2
0.4
0.6
0.8
1.0
x

A Cardiac Model

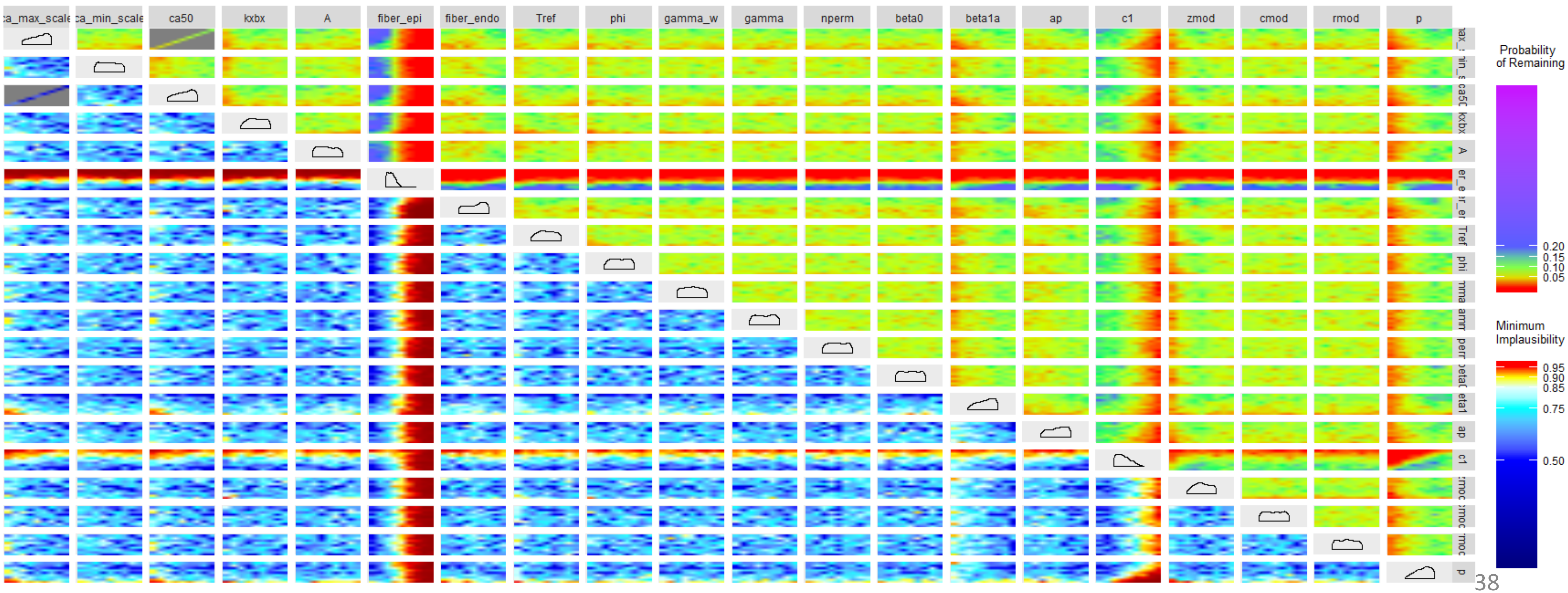


Thanks to Steve Neiderer, KCL/St Thomas

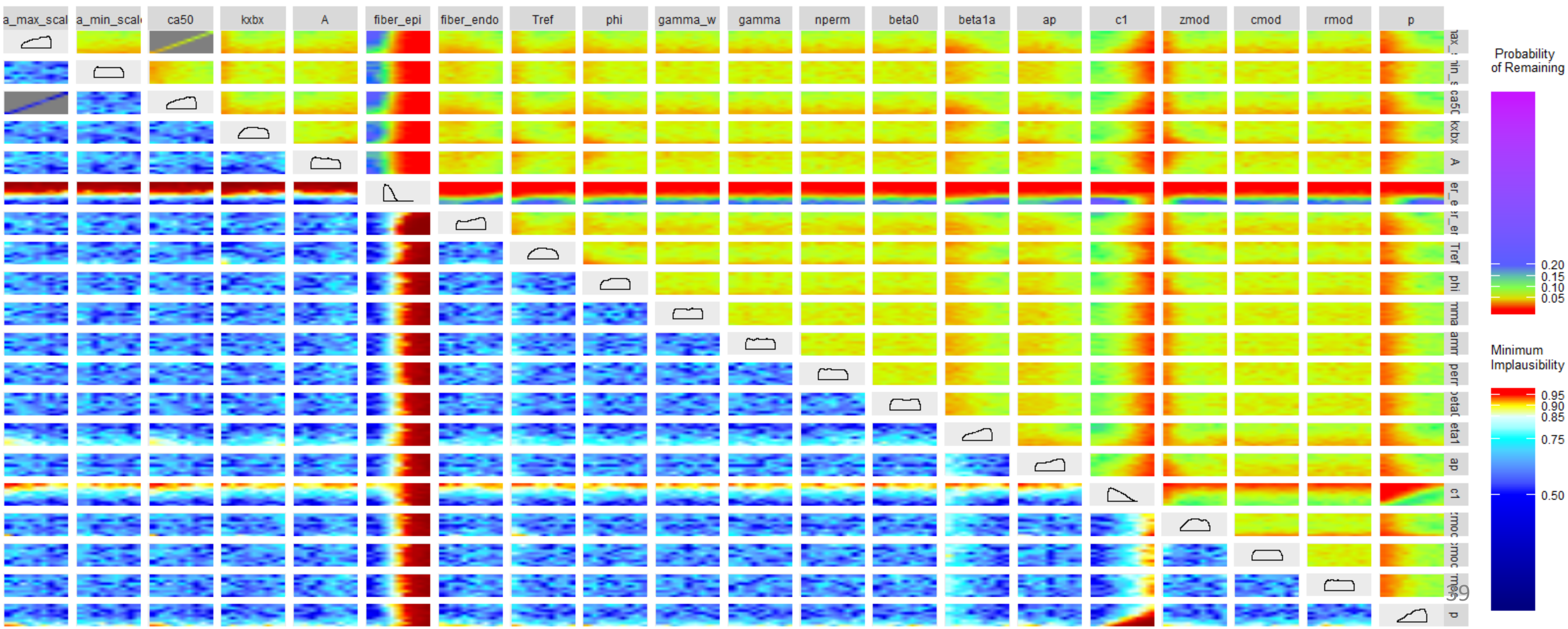
Wave 1: 25% of the parameter space remains

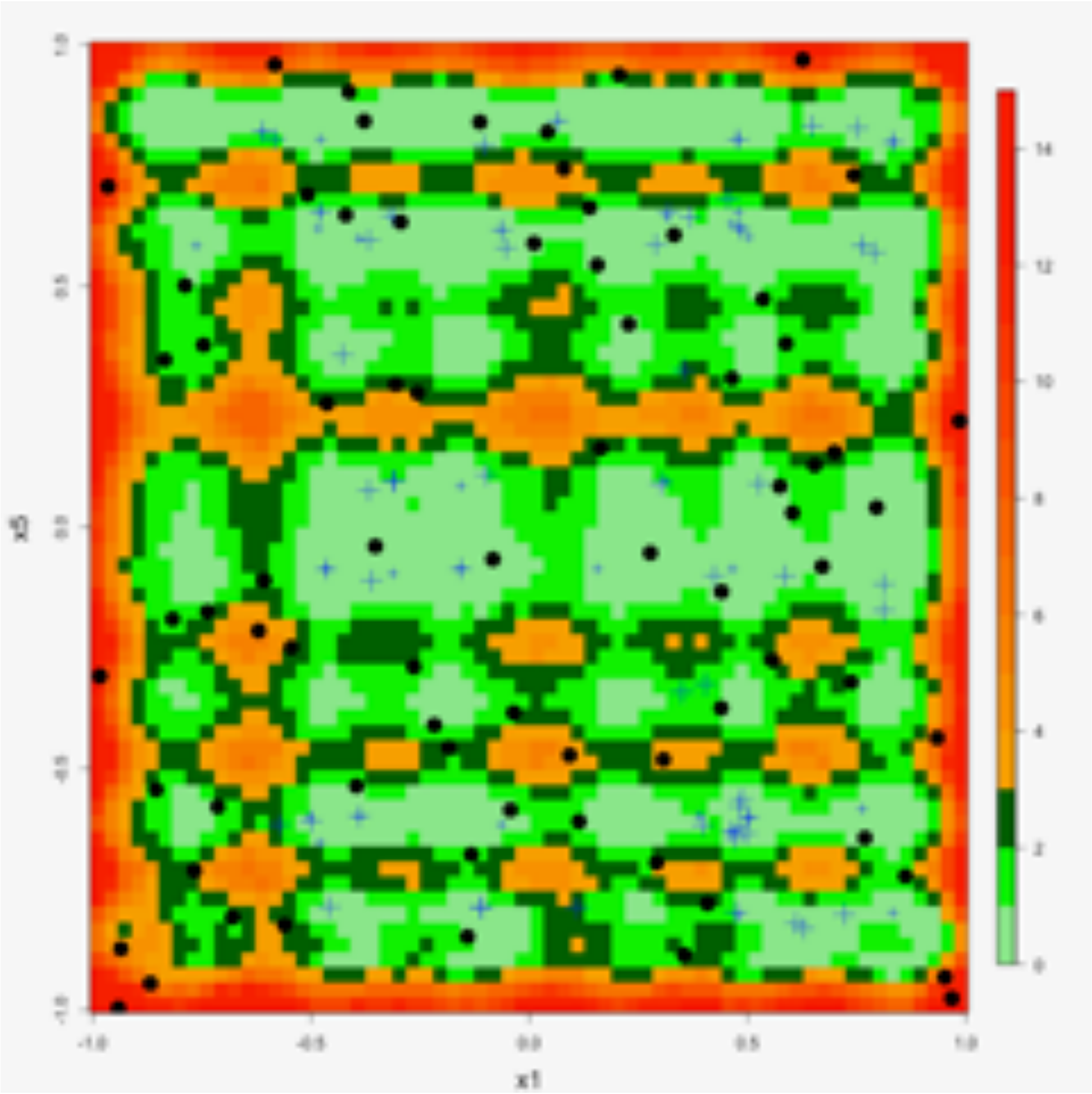


Wave 2: 6% of the parameter space remains



Wave 3: 5% of the parameter space remains





x5
x1

History Matching

- Geometry of NROY
- Design for wave 2 +
- Geometric not probabilistic
- Bayes Linear
- Fast - pre-calibration
- Interaction between computer and real world experiments