Applying Rare Event Simulation Methods to ICU Data

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Rare Event Simulation

Rare event simulation methods are advanced statistical algorithms used to sample from regions in a space which basic simulation methods struggle to reach.

Given some space $\Omega \subset \mathbb{R}^d$, a rare subset F (known as the failure region) can be defined as the region where some real valued function (known as the performance function) exceeds some threshold. If Ω is endowed with a probability density function f, then the size of the region can be defined as

$$\mathbb{P}(F) = \int_{\Omega} \mathbb{1}_F(\boldsymbol{x}) f(\boldsymbol{x}) d\boldsymbol{x}.$$

This quantity is known as the probability of failure and the integral can be calculated by sampling from the failure region and then using the Law of Large Numbers. Since F is rare, it is difficult to sample from, and so advanced techniques are required.

Subset Simulation [1] is a rare event simulation method that uses Markov chains to perform a localised version of sampling. The idea of the algorithm is to sample from the neighbourhood of the samples with the highest performance. The algorithm creates a sequence of regions

$$F_1 \supset F_2 \supset ... \supset F_m \supset F,$$

which are progressively better approximations of the failure region. Using Bayes Theorem the probability of failure can be modelled as a product of larger and easier to calculate probabilities

$$\mathbb{P}(F) = \mathbb{P}(F_1)\mathbb{P}(F_2|F_1)...\mathbb{P}(F_m|F_{m-1})\mathbb{P}(F|F_m).$$

By choosing an appropriate performance function, Subset Simulation can be used sample from rare regions in wide range of contexts.

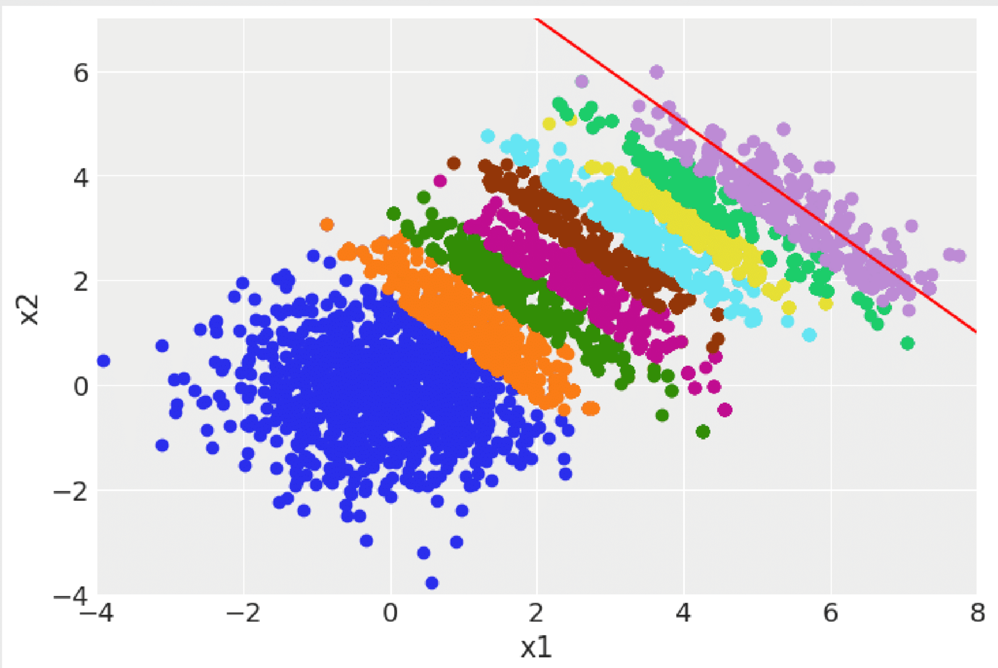

Figure 1. 2-dimensional Subset Simulation example. Uses $g(x_1, x_2) = x_1 + x_2$ for the performance function, 9 for the threshold and a standard bivariate Normal distribution as the probability density function. Red line indicates the failure region. Different colours indicate different intermediate regions.

History Matching an Alveoli Model

History Matching is a statistical method used to (pre-)calibrate models with data. The idea of History Matching is to label sets of input parameter settings, $\boldsymbol{x}$, as implausible by comparing the output of the model, f, to observed data y. The comparison uses a measure of implausibility

$$I(\boldsymbol{x}) = \frac{|E[f(\boldsymbol{x})] - y|}{\sqrt{Var(f(\boldsymbol{x}))}}.$$

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If I is taken as the performance function, Subset Simulation can be used to sample from the rare region of non implausible parameters [3].

At CHIMERA the modelling team is working on a model of the alveoli within the lungs. This model requires three input parameters for each alveolar unit and so the input space can be very high dimensional.

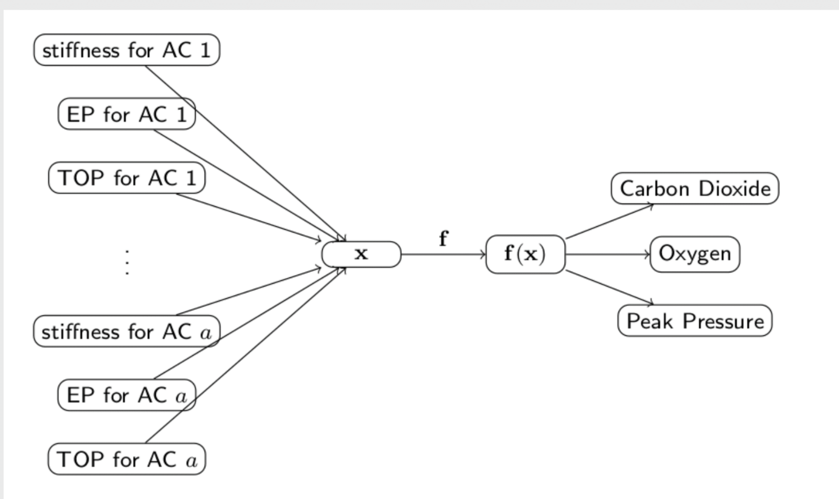


Figure 2. Schematic of alveoli model. EP - Extrinsic Pressure, TOP - Threshold opening pressure, a - Number of alveoli units.

At CHIMERA History Matching is being used to calibrate the alveoli model against medical data in order to reduce the size of the input space.

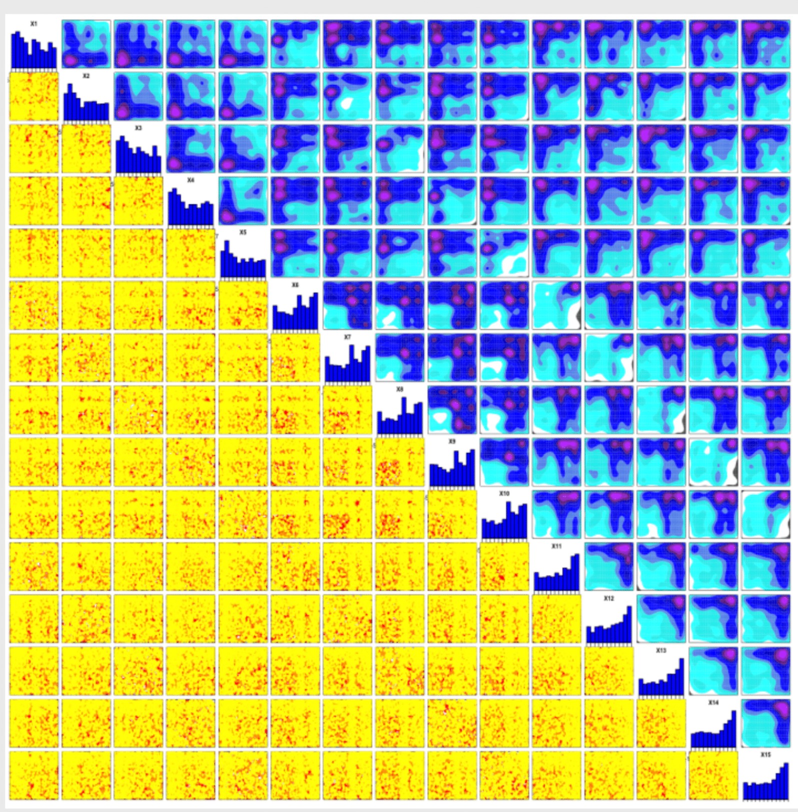


Figure 3. The implausible space found with History matching on a 5 alveoli/15 dimensional model.

Bayesian Hierarchical Model of Heart Rate and Temperature

A model's parameters can be updated using Bayesian inference. This involves using Bayes Theorem to combine a prior belief about the parameters and a likelihood function, where the likelihood function gives a likelihood score to each set of parameters given the data observed. The result is a posterior distribution for the parameters.

If the prior is used as the distribution of the parameters and a perturbed likelihood function is taken as the performance function, the posterior distribution can be considered a failure region and so Subset Simulation can be used to obtain samples [4].

At CHIMERA this technique is being used to sample from the posterior of a Bayesian hierarchical model that describes the relationship between heart rate and temperature of ICU patients. A Bayesian hierarchical model allows data from different patients to affect the overall distribution in a controlled manner.

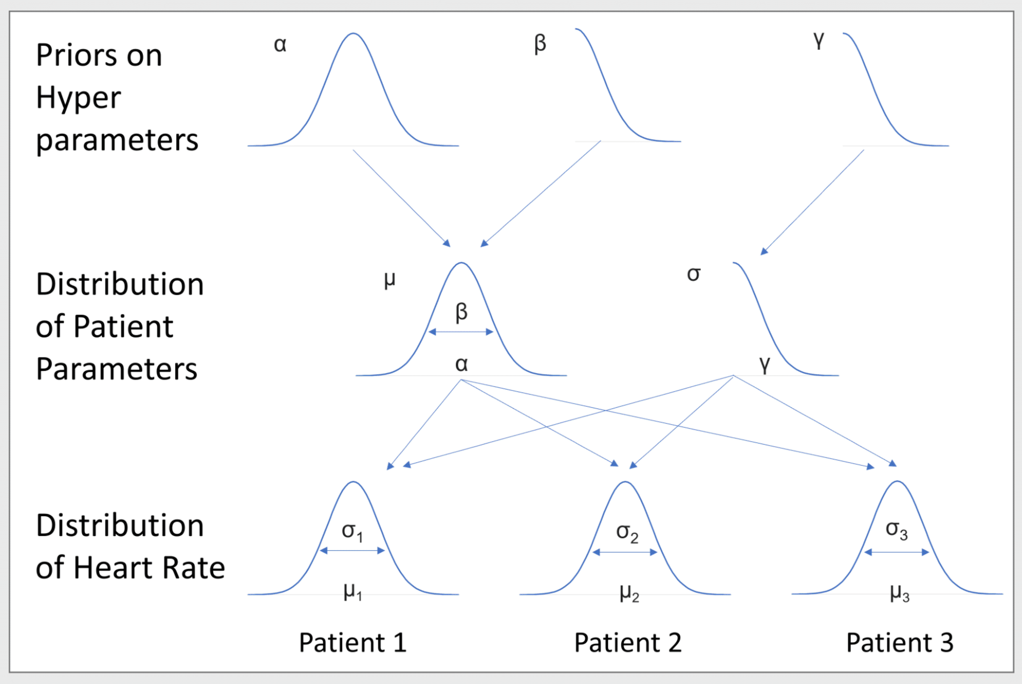


Figure 4. A schematic of the Bayesian hierarchical model of temperature and heart rate. Each patient's data influences the overall distribution of parameters. Priors of the hyper-parameters allow for the input of clinical experts.

For a given temperature and age range a distribution of heart rates is created. This distribution is easier to analyse than the empirical data, especially for unusual temperatures and ages where there might not be so much data. The output of this model could potentially be useful to clinicians who wish to know how unusual a patients heart rate is for their current temperature.

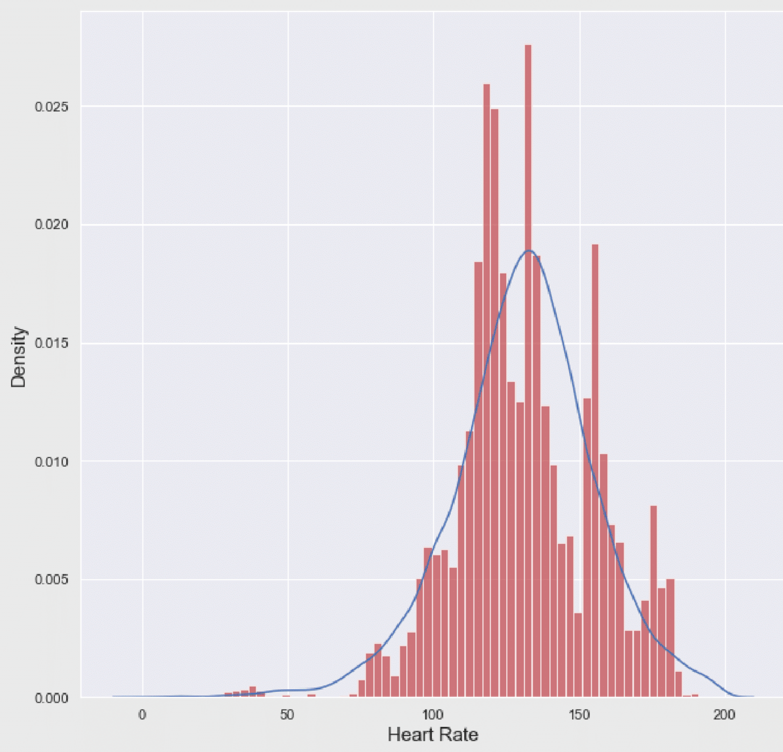


Figure 5. Heart rate distribution for patients who are 0-0.25 years old and have temperature 34.7 °C. The red bars show empirical data and the blue line is a kernel density estimate of the output of the model.

Improving Subset Simulation

Subset Simulation will always exploit the current highest performing regions. This can lead to other regions that have strong potential being under explored. In the worst the cases this results in no samples being produced in failure region.

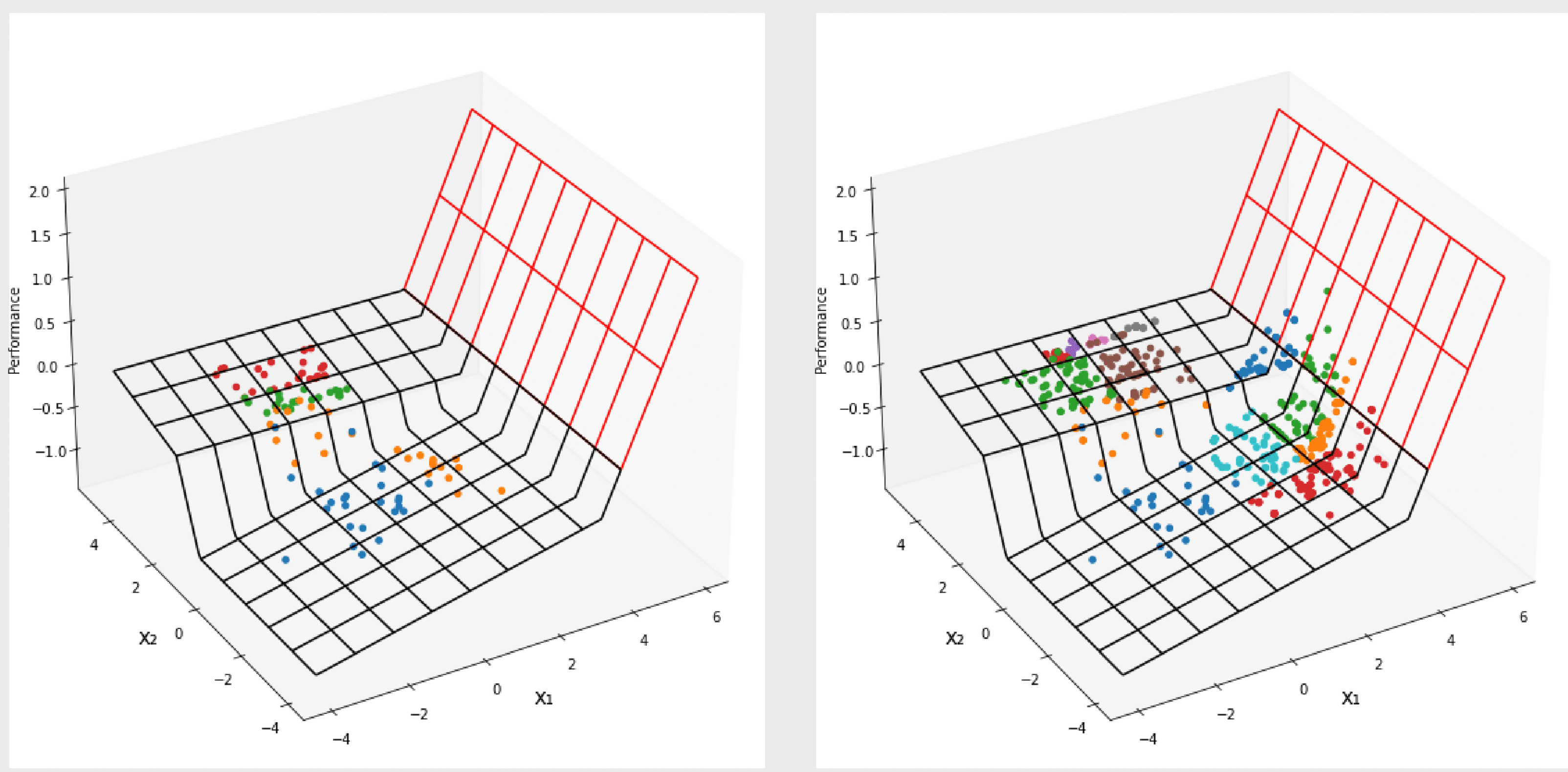
An improvement currently being developed at CHIMERA involves dynamically partitioning the space and then sampling in the neighbourhood of the best performing samples in each partition. This approach promotes more exploration at the cost of more evaluations of the performance function.

A simple example can be constructed to show the need for such and improvement. Take the performance function as $g(x) = -\min(g_1(x), g_2(x))$ where

$$g_1(x) = \begin{cases} 4 - x_1 & x_1 > 3.5 \\ 0.85 - 0.1x_1 & x_1 \leq 3.5 \end{cases}$$

$$g_2(x) = \begin{cases} 0.5 - 0.1x_2 & x_2 > 2 \\ 2.3 - x_2 & x_2 \leq 2. \end{cases}$$

In this case Subset Simulation can be lead astray by the initially steep gradient in the wrong direction [2]. Exploring the space more carefully leads to the failure region being populated.



(a) Standard Subset Simulation. Colours show different intermediate regions. (b) Improved Subset Simulation. Colours show different partitions.

Figure 6. Subset Simulation run using g as performance function. The red area of mesh is the failure region which the standard Subset Simulation does not find.

References

[1] Siu-Kui Au and James L. Beck. "Estimation of small failure probabilities in high dimensions by subset simulation". In: *Probabilistic Engineering Mechanics* 16 ().
[2] Karl Breitung. "The geometry of limit state function graphs and subset simulation: Counterexamples". In: *Reliability Engineering & System Safety* 182 (), pp. 98–106.
[3] Zitong Gong et al. "History Matching with Subset Simulation". In: (). DOI: 10.1615/Int.J.UncertaintyQuantification.2021033543.
[4] Daniel Straub and Iason Papaioannou. "Bayesian Updating with Structural Reliability Methods". In: *Journal of Engineering Mechanics* 141 ().