Planning

Introduction to Automated Science

SLAS 2023

Example: Optimizing stem cell differentiation

Our goal is to improve the efficiency of differentiating ESCs into mature, insulin-producing beta cells.

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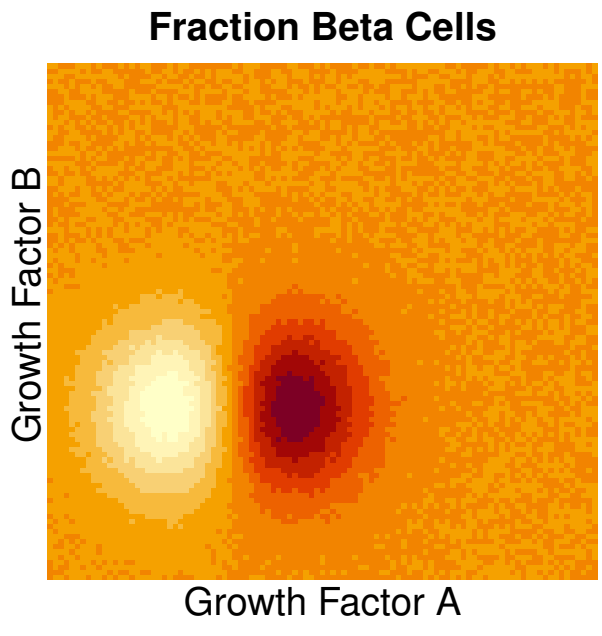
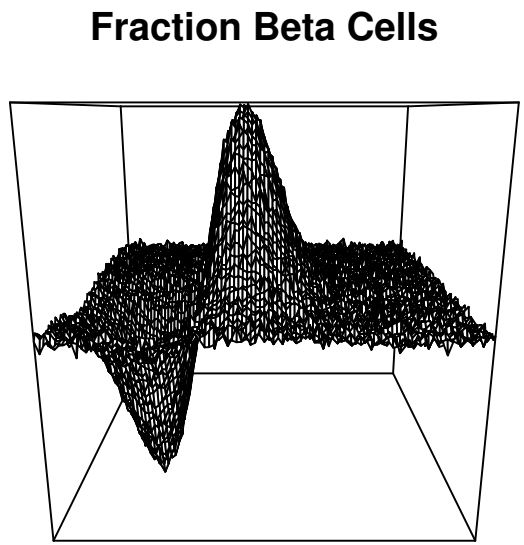
For illustration, pretend we know the “true” response surface:





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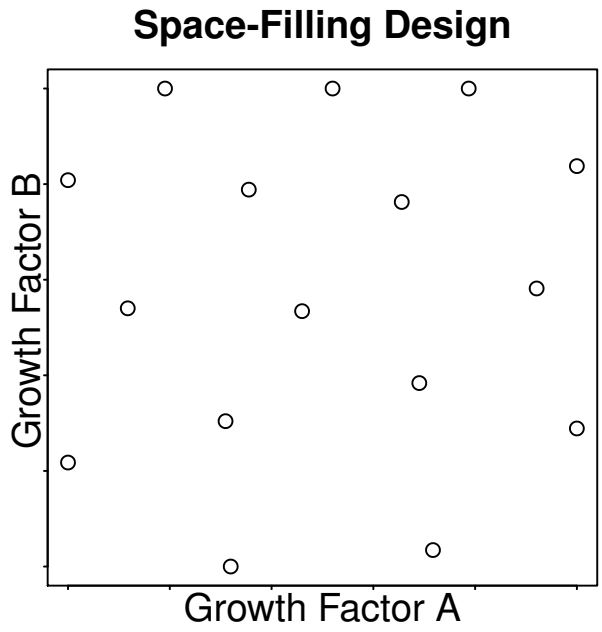

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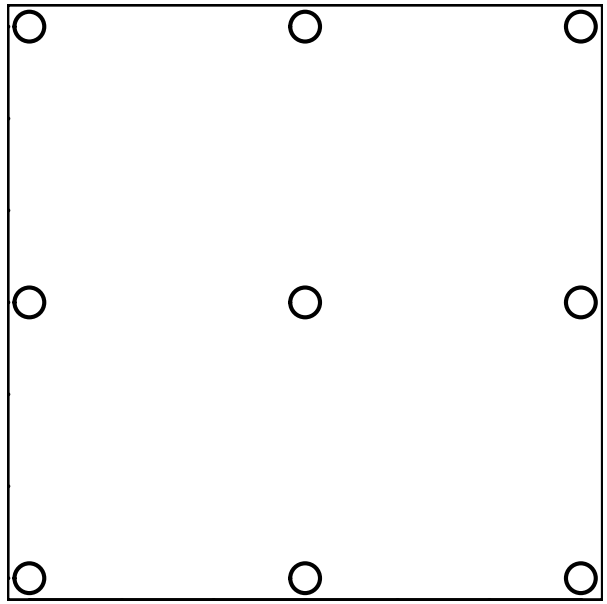
Evenly-spaced designs have two big drawbacks:



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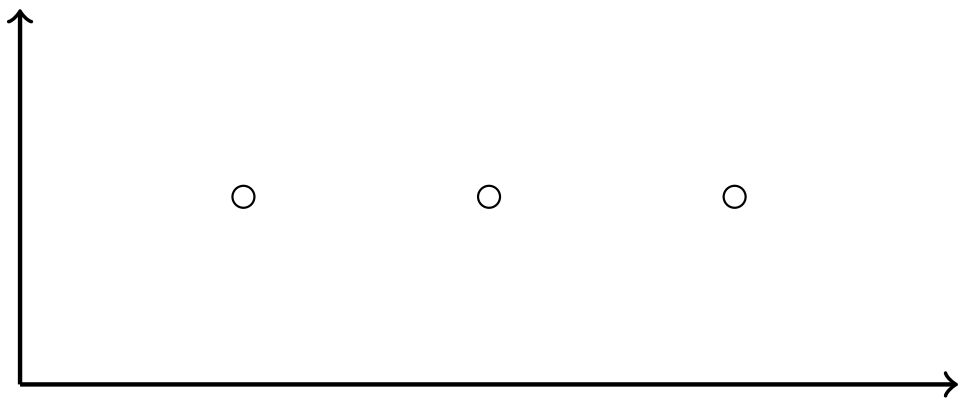

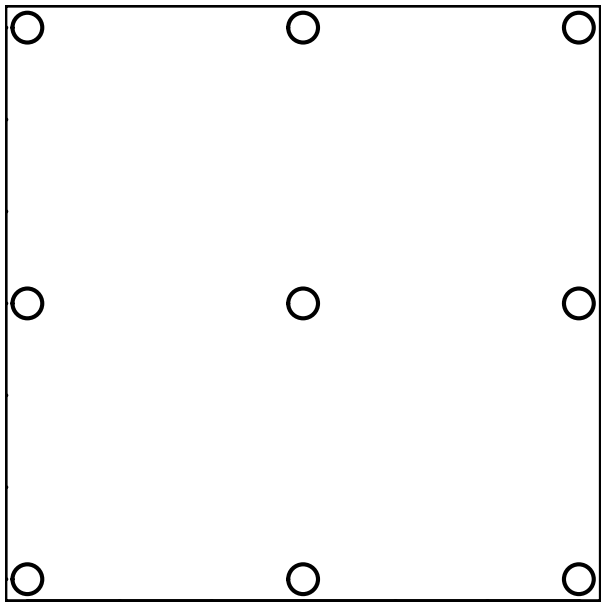

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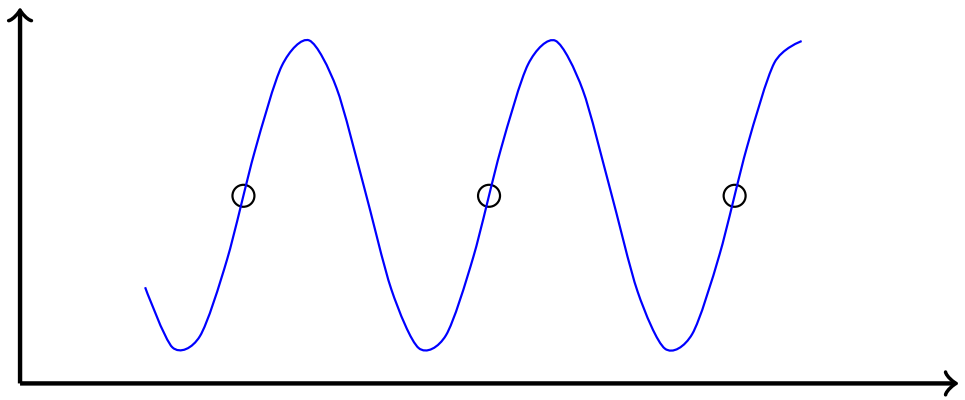

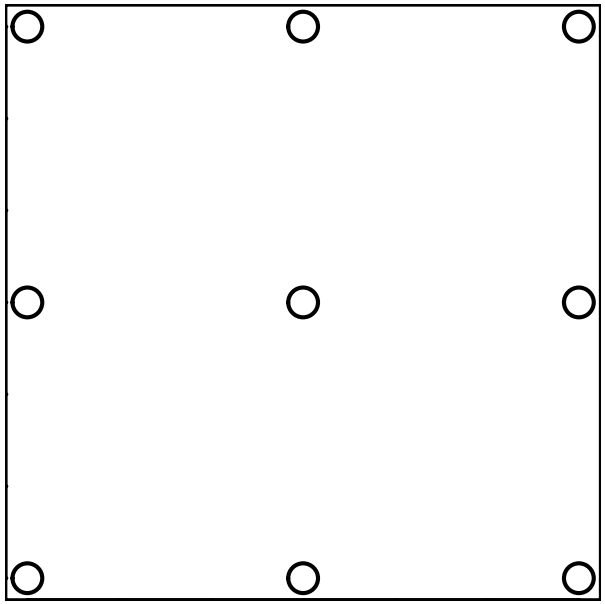

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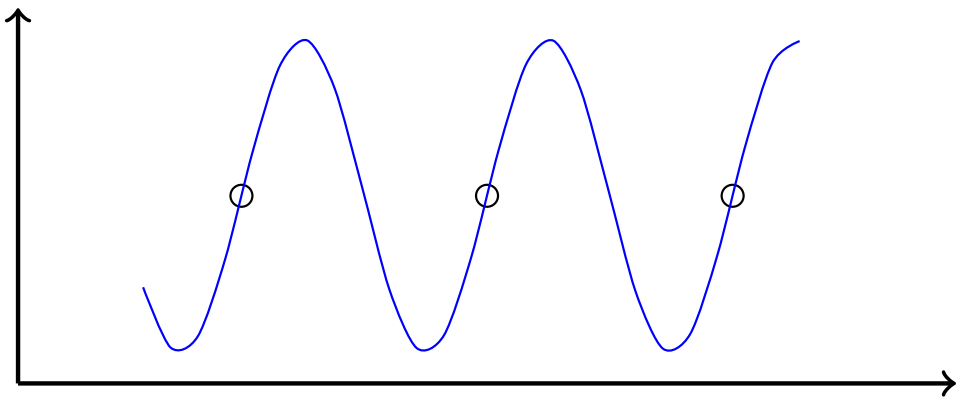
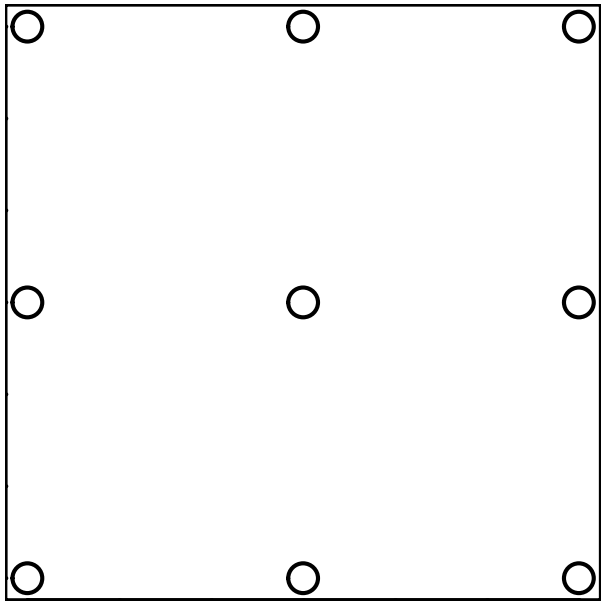
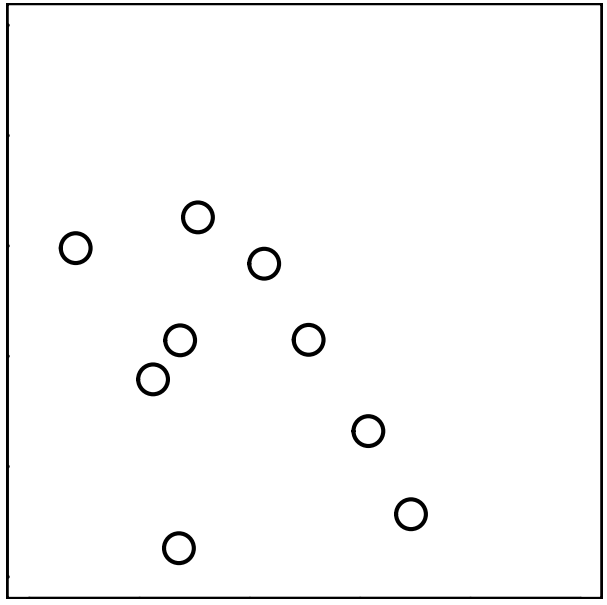




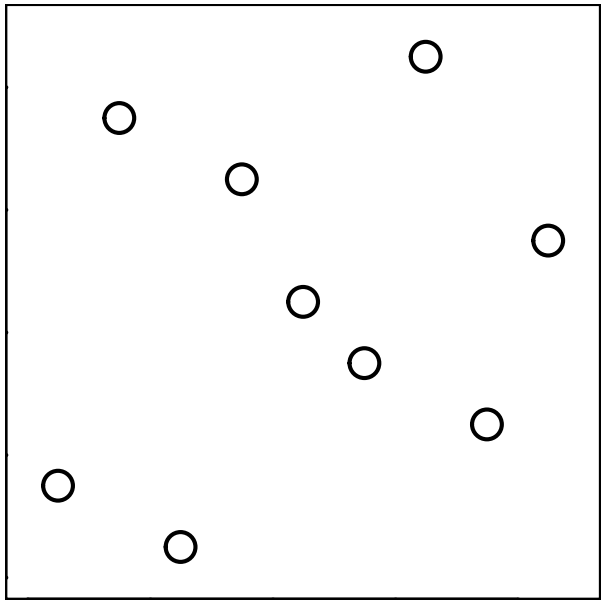
2. Regular designs have poor **projection spacing**. This is a problem because not all factors affect the resonse.

Why not random designs?

Random design are “clumpy”, especially in high dimensions.



Latin Hypercube Designs



A Latin Hypercube Design (LHD) is a semi-random design that guarantees uniform projection.

- Each dimension is divided into n intervals.
- Points are placed randomly, but only one point is allowed in each interval along each dimension.
- Points can be placed in the center or a random position in each "square".
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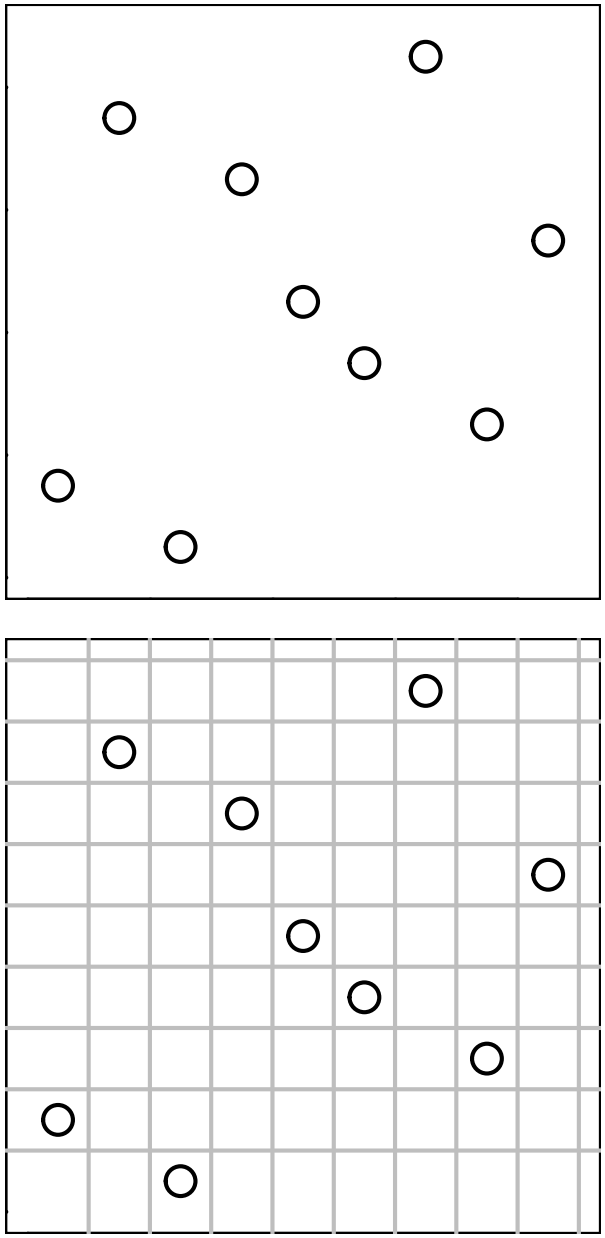
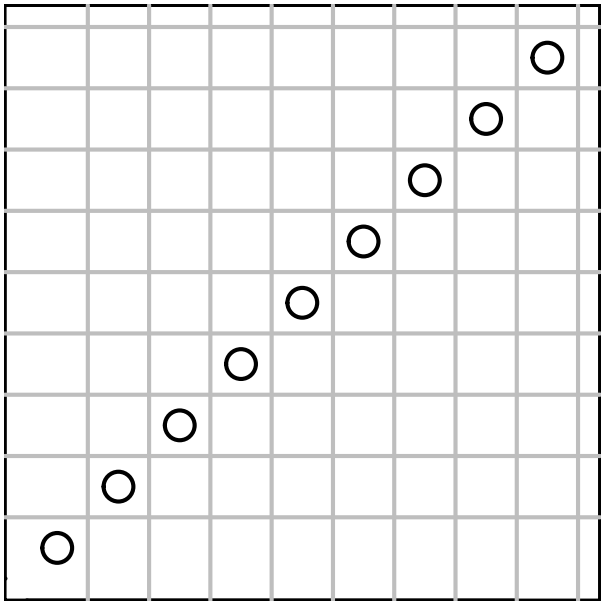


Beware of randomness (again)



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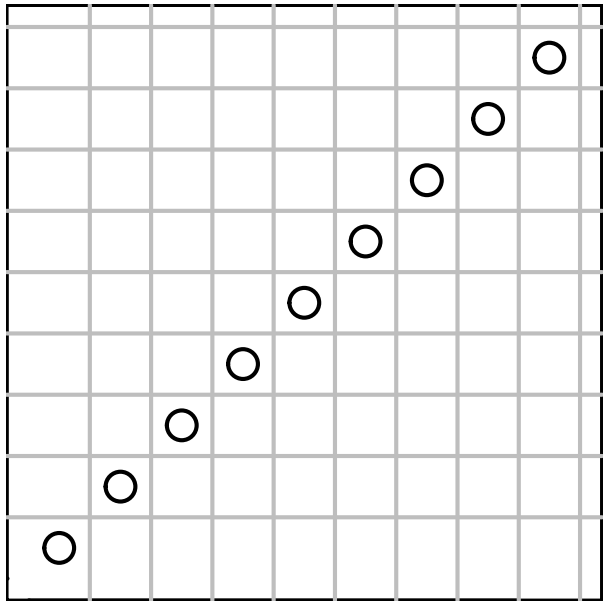

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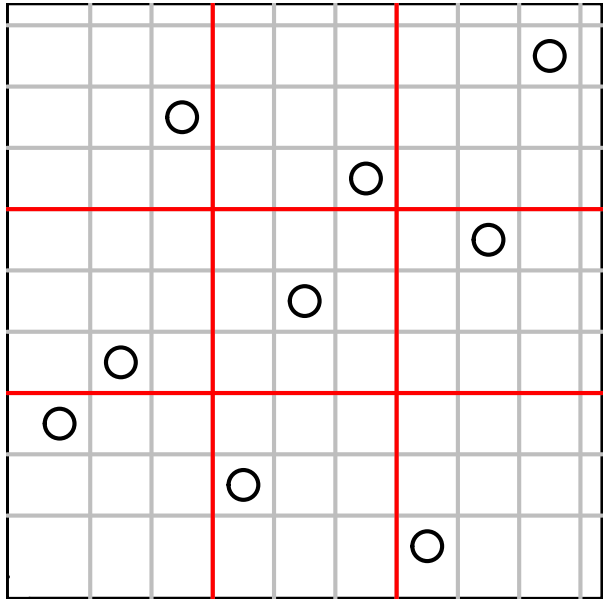

One alternative is an Orthogonal Array LHD.

Another option: Maximin Designs

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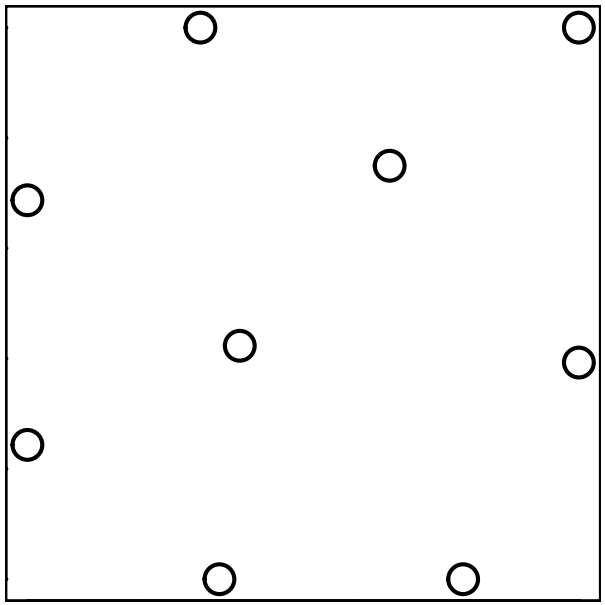
The *maximin* design matrix with n samples, called X_n is

$$\arg\max_{X_n} \min\{d(x, x'), \forall x \neq x'\}$$

Augmenting maximin designs

We can add more points to an existing design by spacing them apart from previous points.

Original Design



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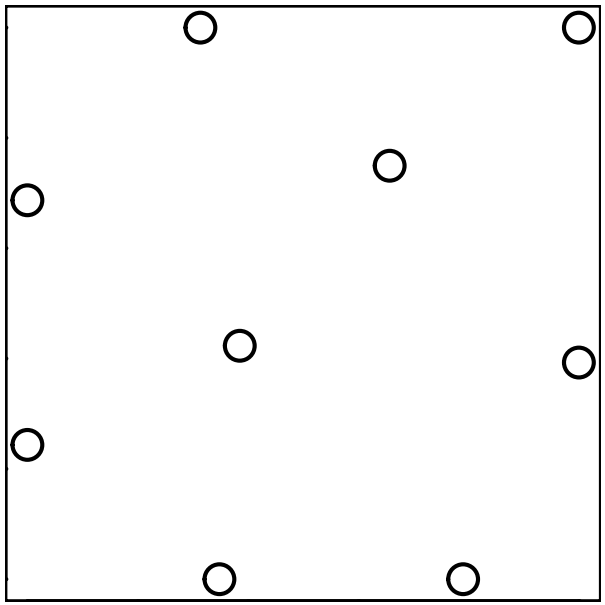

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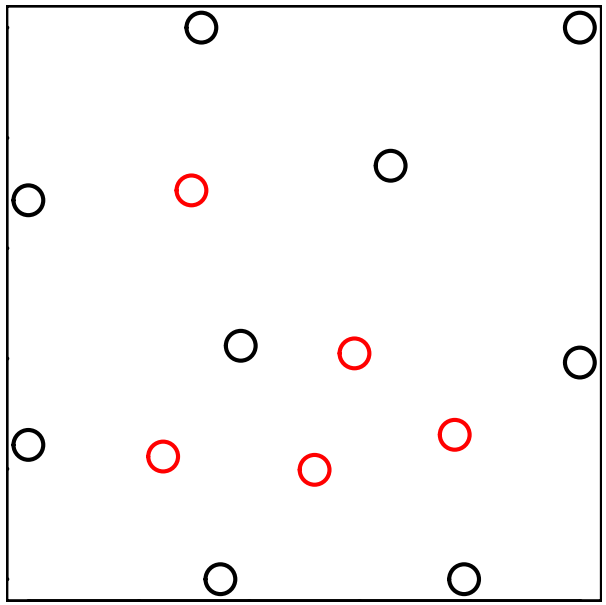

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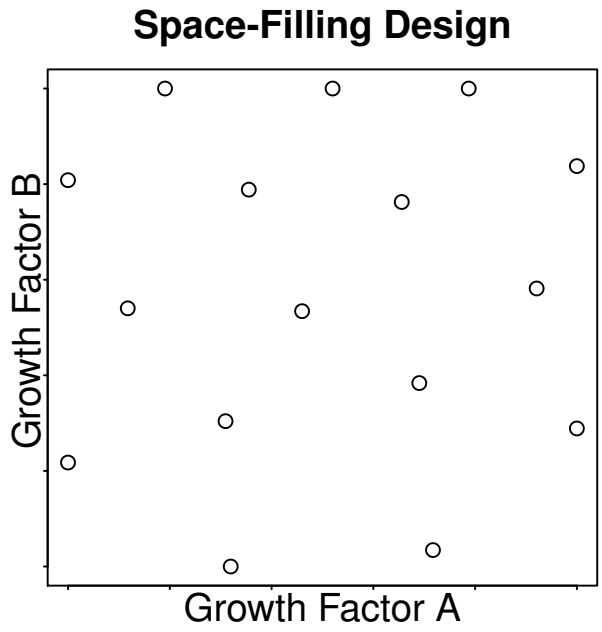
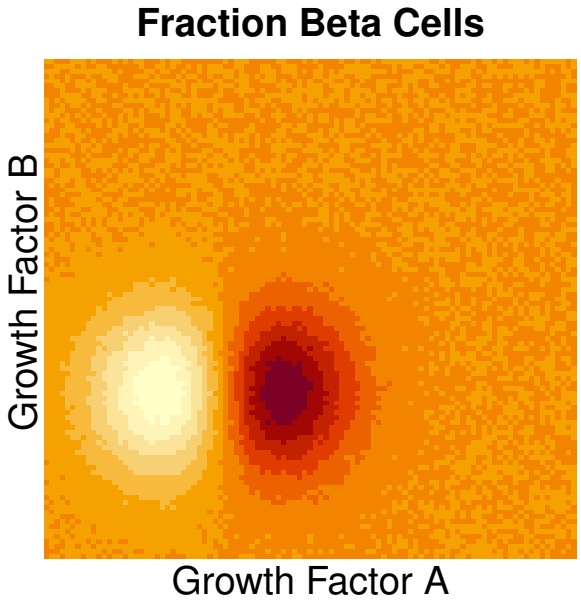
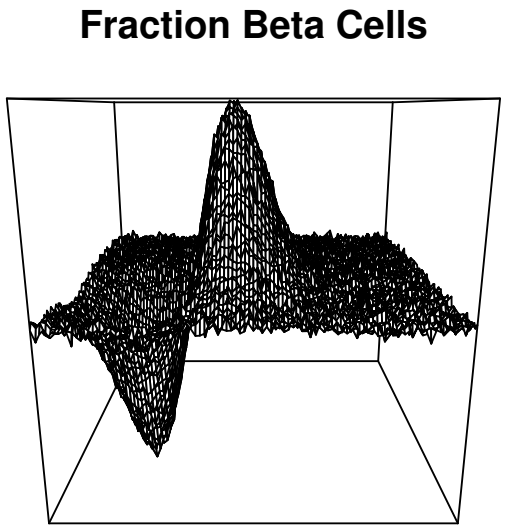


Comparing our model after running the initial design

True Response





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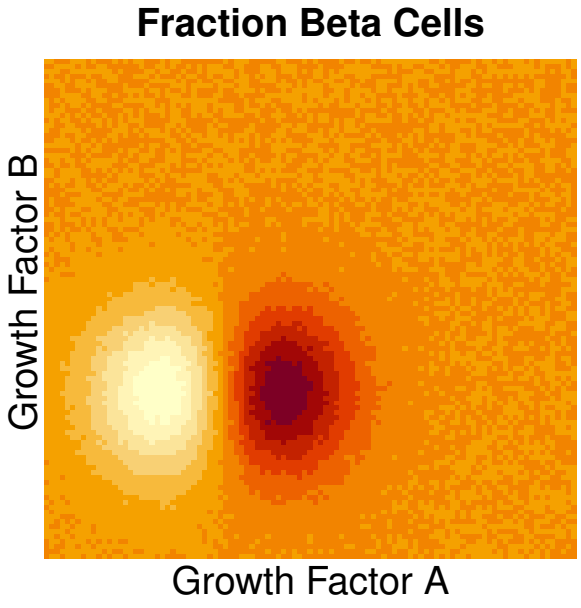
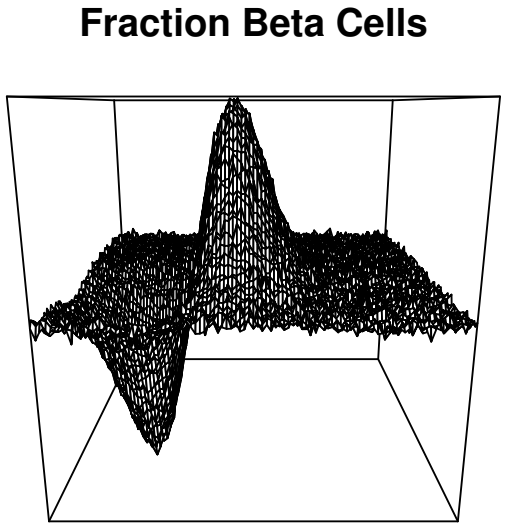
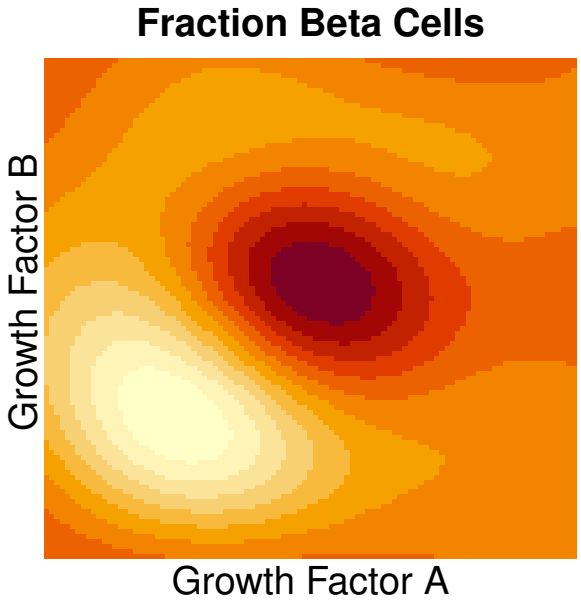
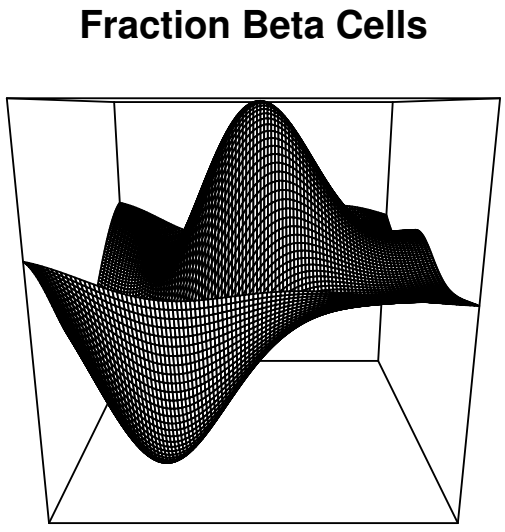




Initial Model Prediction





Searching for the next run

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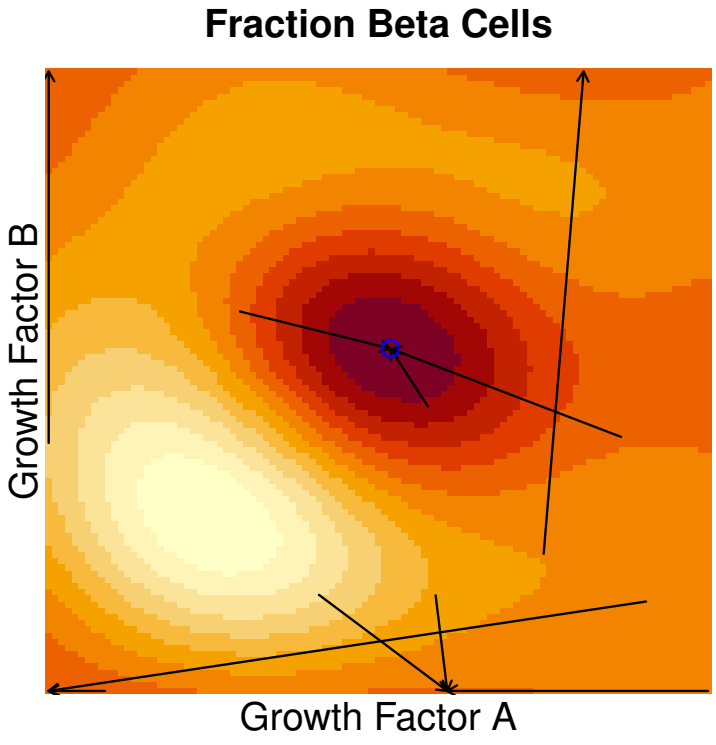
To find the *global optimum*, we restart the optimizer many times at random points.

Searching for a global optimum by L-BFGS-B



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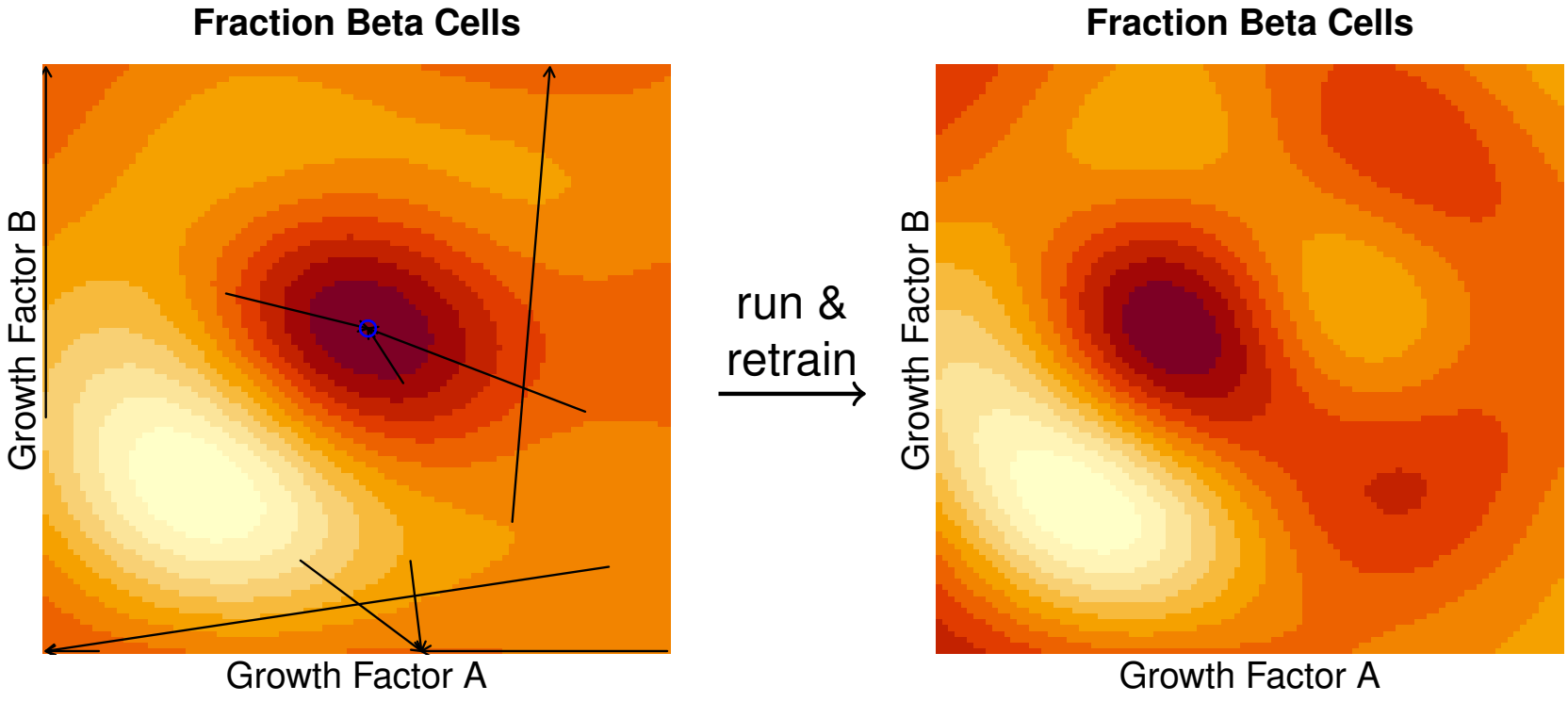
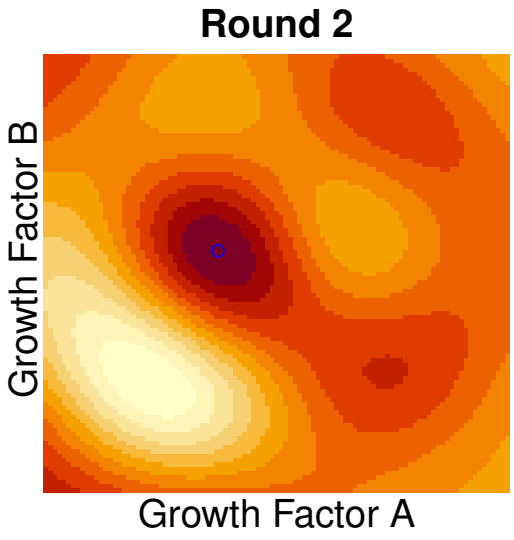


The true optimum was not where the model predicted. Retraining the model moved the model's estimate of the optimum for the next round.

Sequential experiments and model updates



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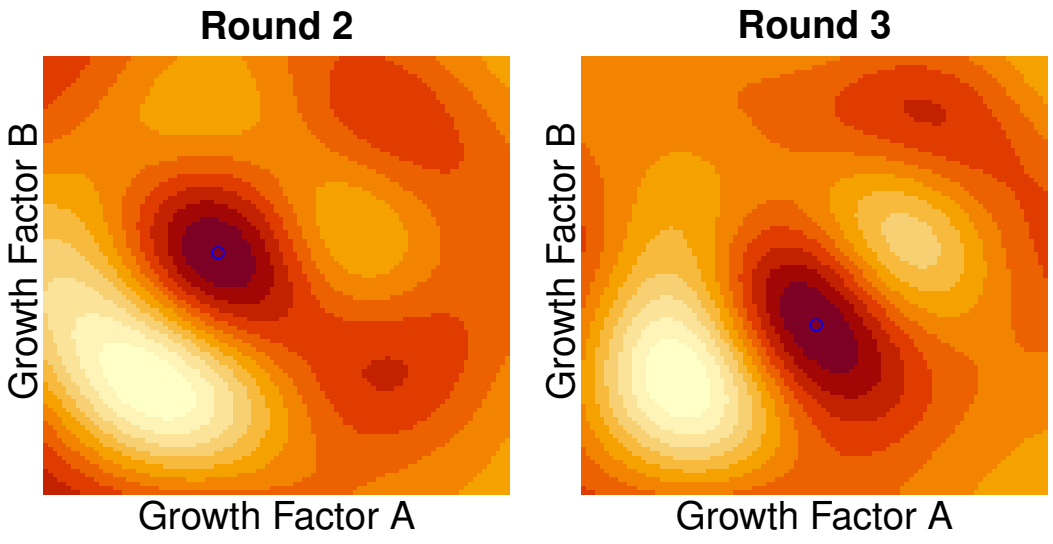

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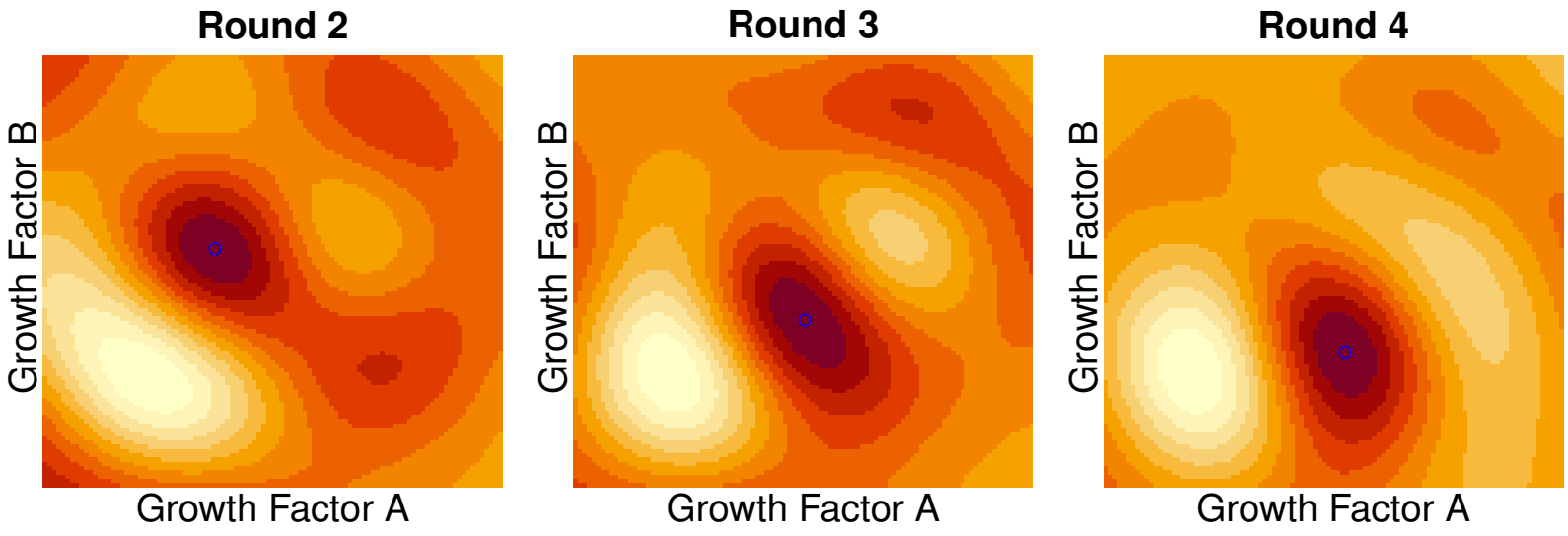

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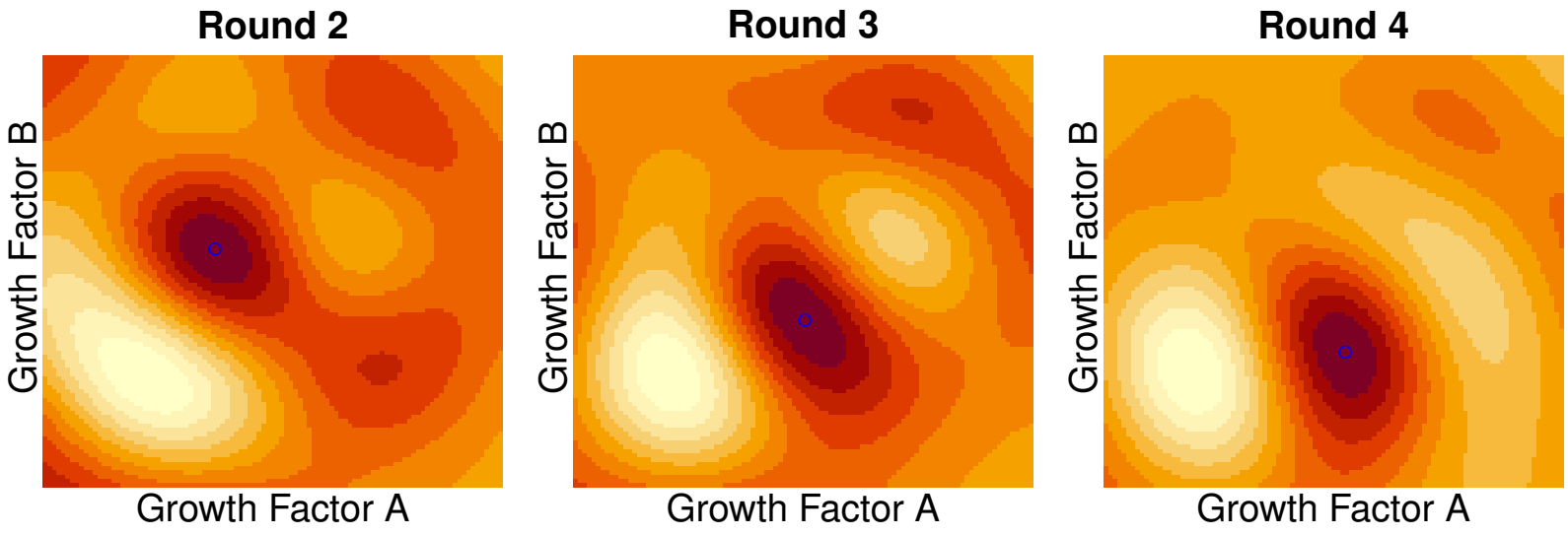

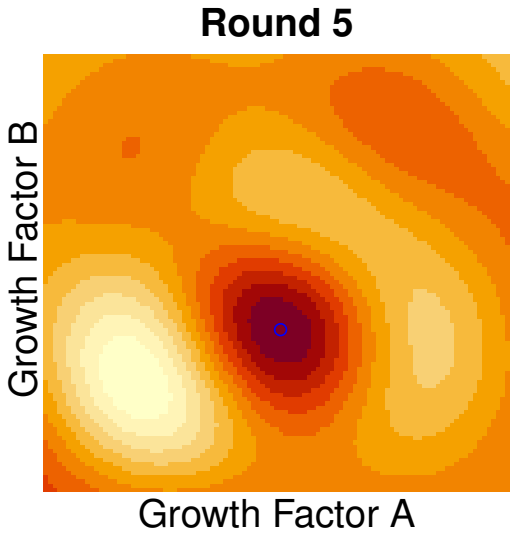

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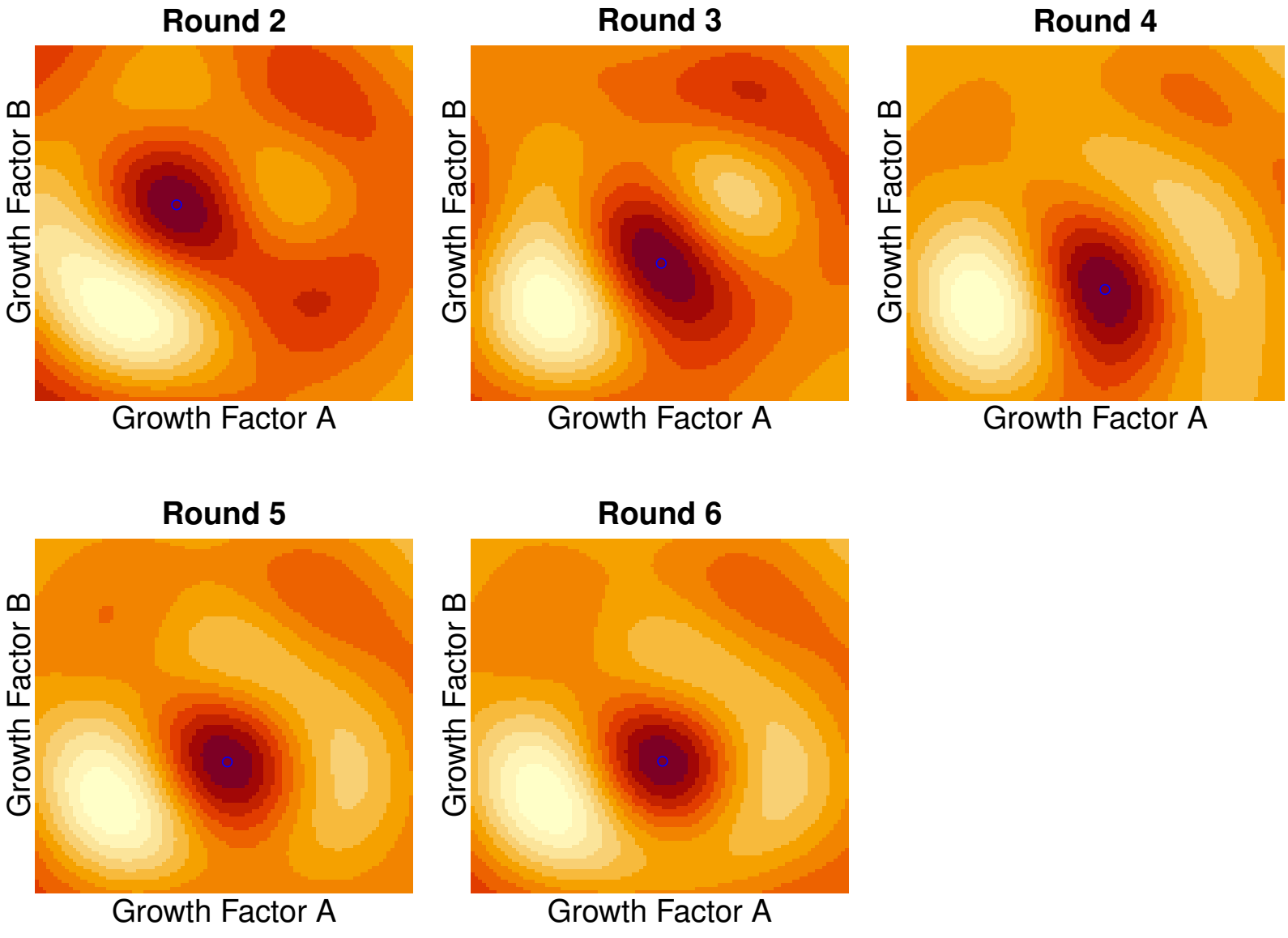

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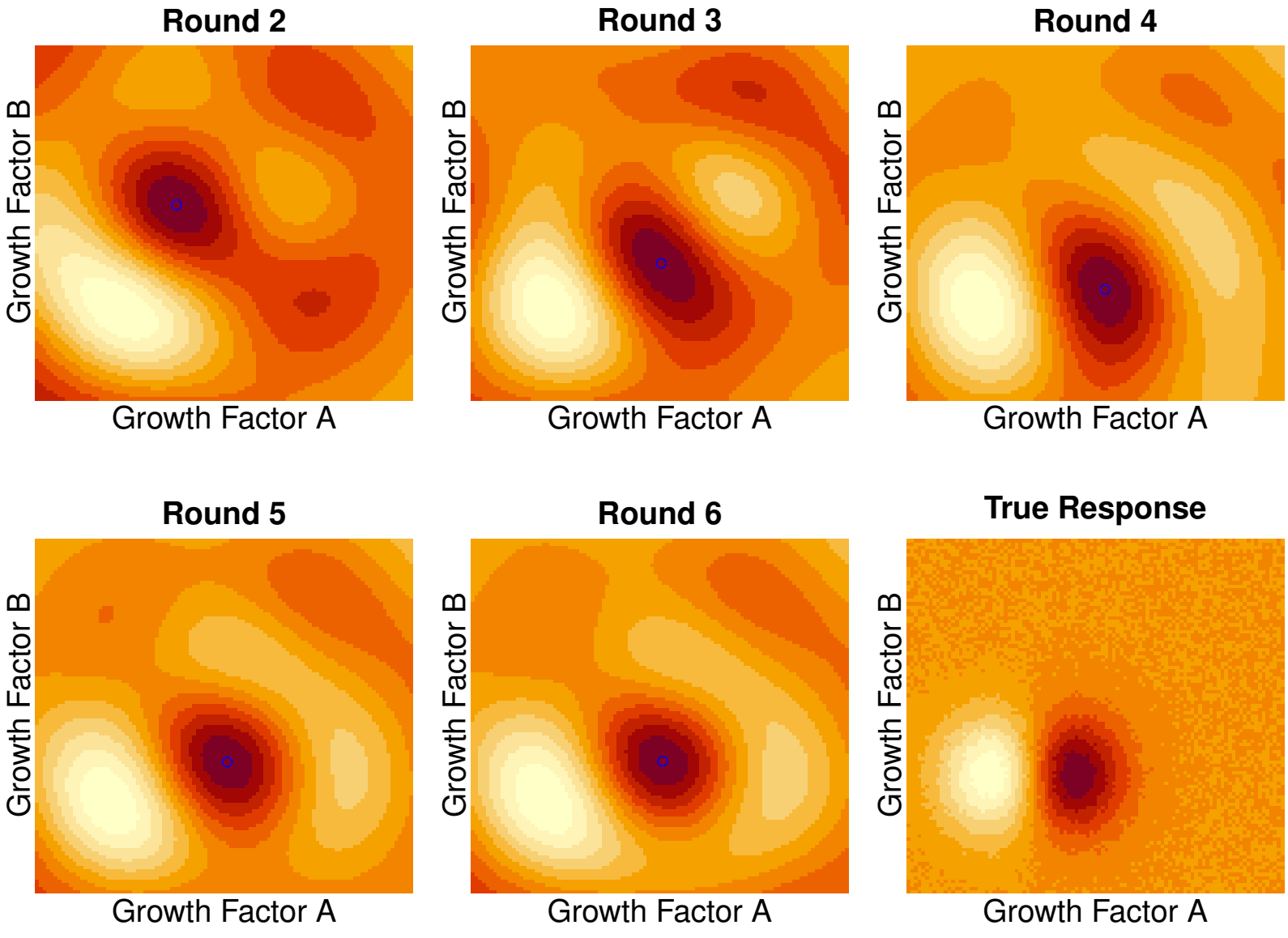

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However, our nonlinear search used **3,235 model predictions** to select these 22 runs.

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Models can also be improved by **exploration**—placing runs in regions where the model is most uncertain.

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- True global optimization requires **exploitation** and **exploration**.