# Planning (Part 2)

Introduction to Automated Science

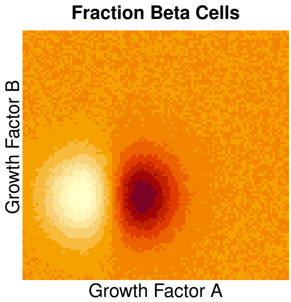
SLAS 2023

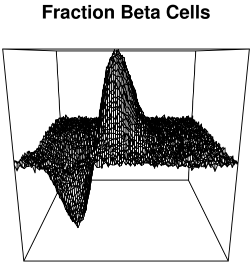
# Example: Optimizing stem cell differentiation

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

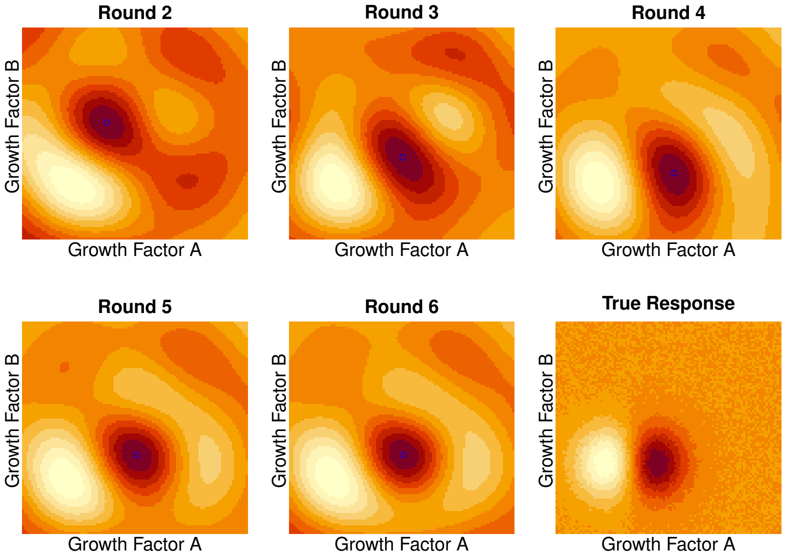
- **Factors**: [Growth Factor A] and [Growth Factor B], both added during differentiation.
- **Response**: Fraction of beta cells after 40 days [0.0–1.0].

For illustration, pretend we know the "true" response surface:



# Sequential experiments and model updates



# Exploitation vs. Exploration

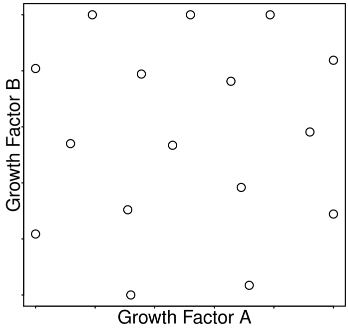
The previous example used pure **exploitation**—using the model's knowledge to find the best predicted response.

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

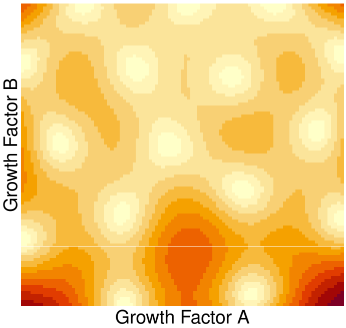
# Model improvement by exploration

Exploration searches the model for inputs that give the most **uncertain** predictions.

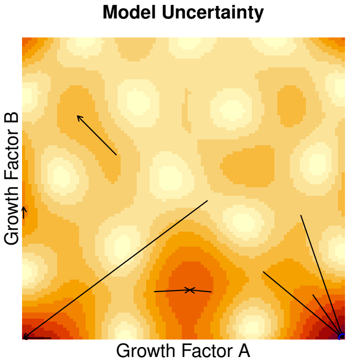
**Space-Filling Design**




**Model Uncertainty**



# Exploring via search by L-BFGS-B



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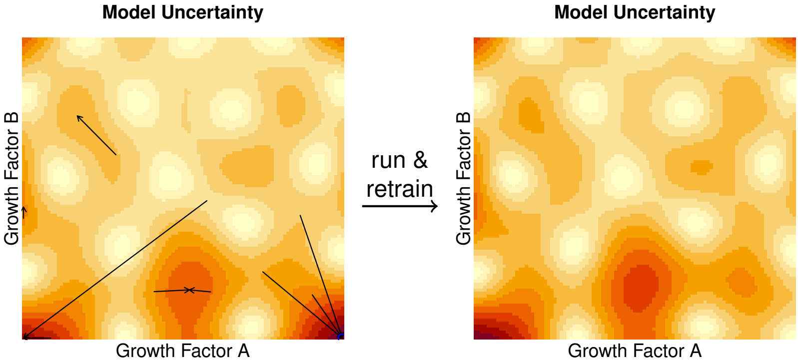
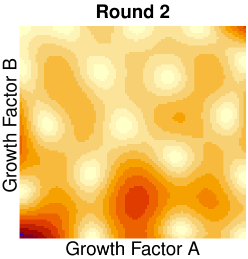


# Exploring: Uncertainty whack-a-mole



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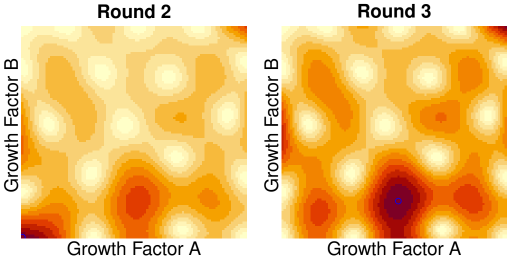

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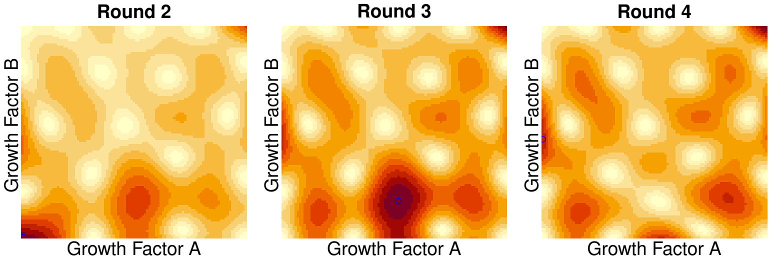

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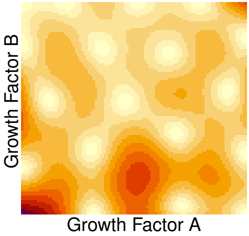
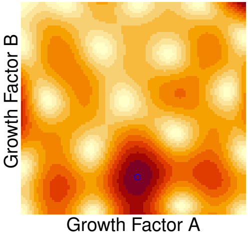
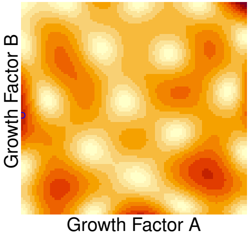
**Round 2**



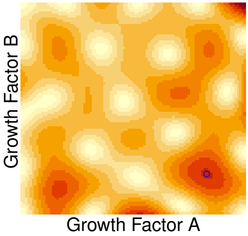

**Round 3**




**Round 4**




**Round 5**



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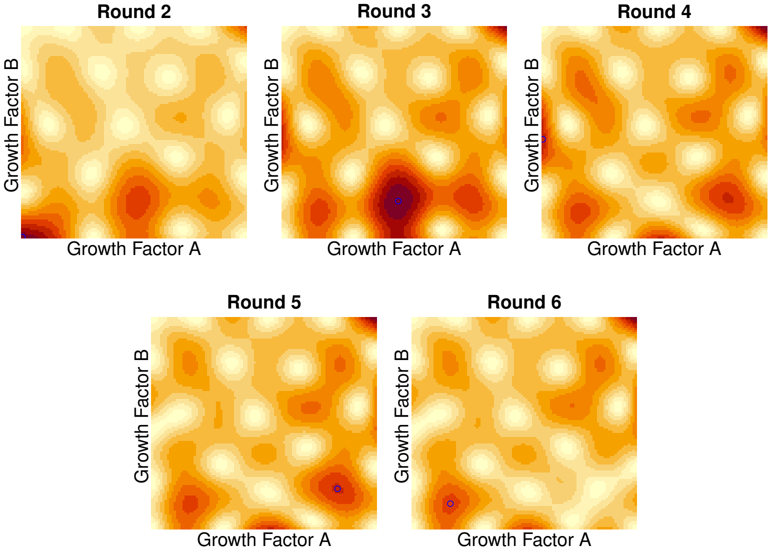
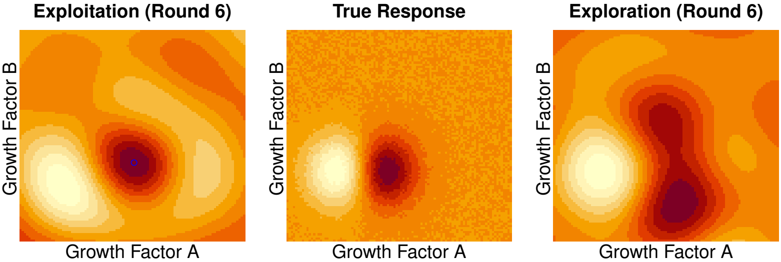


# Comparing exploitation and exploration



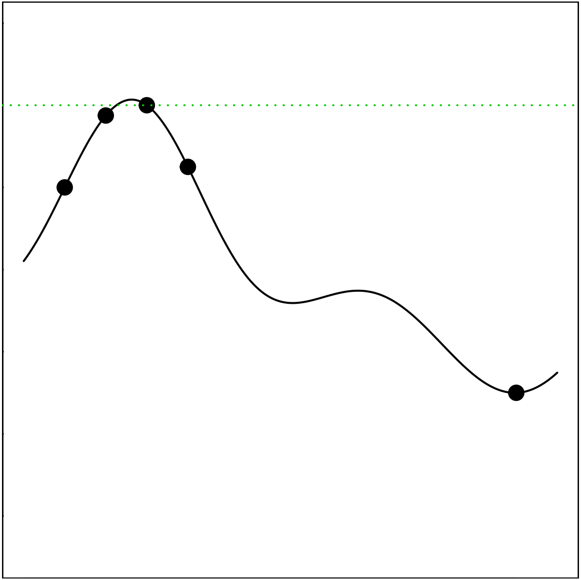
# Should we exploit or explore?

**Both.** Good algorithms balance discovery and refinement.

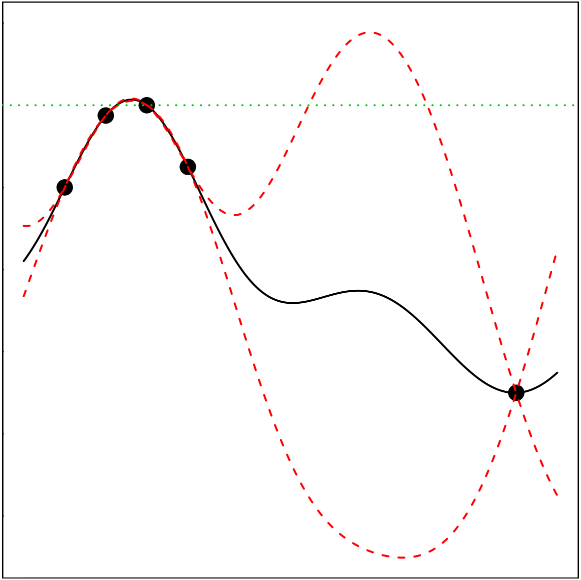
The *best* balance is an open problem. Some solutions:

- Always dedicate some (small) fraction of your runs to exploring.
- Explore early, exploit later.
- Alternate between batches of exploration and exploitation.
- Use a *hybrid metric* like Expected Improvement.

# A 1-D example (Gramacy 2020) for Expected Improvement



# What happens when we consider uncertainty?



# Optimizing for improving the response

A key insight in Bayesian optimization was the switch to *expected improvement* (Schonlau 1997).

As usual, assume we've measured $n$ responses $y_n$ at locations $X_n$. Define

$$y_{\max} = \max\{y_1, \ldots, y_n\}.$$

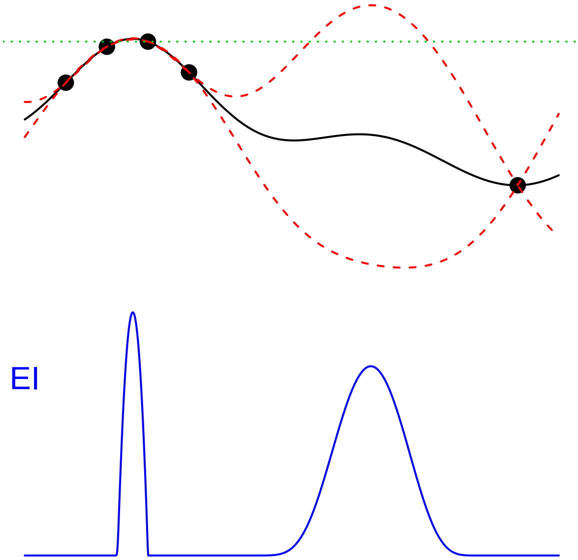
The *improvement* in the objective at a new input $x$ is

$$I(x) = \max\{0, y(x) - y_{\max}\}$$

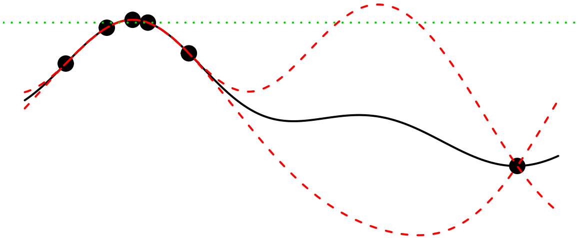
where the maximization "floors" the improvement at zero.

The *expected improvement* $\mathrm{EI}(x) = \mathbb{E}\{I(x)\}$ quantifies how much we expect the best objective value to increase after measuring at point $x$.

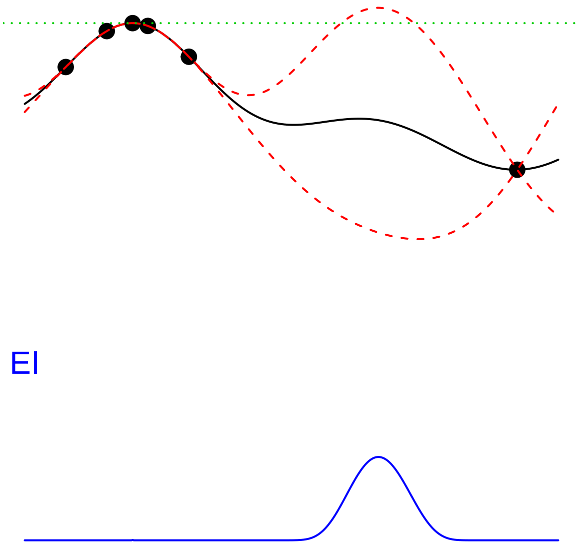
# Visualizing Expected Improvement



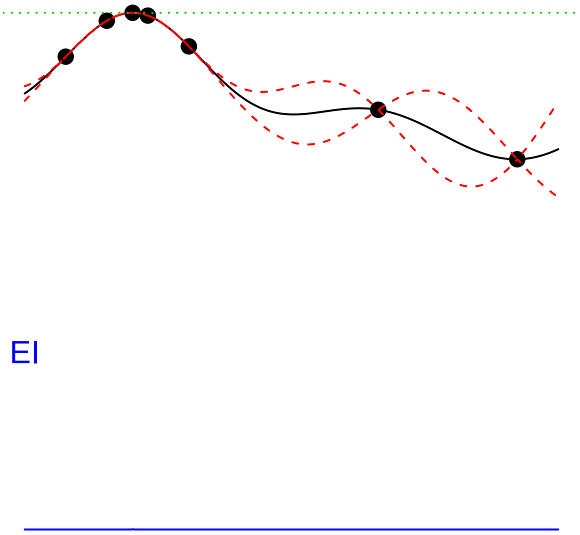
# Picking the next sample



# Recalculating Expected Improvement for Round 2



After the second update: no expectation of improvement



# Do sequential designs always work?

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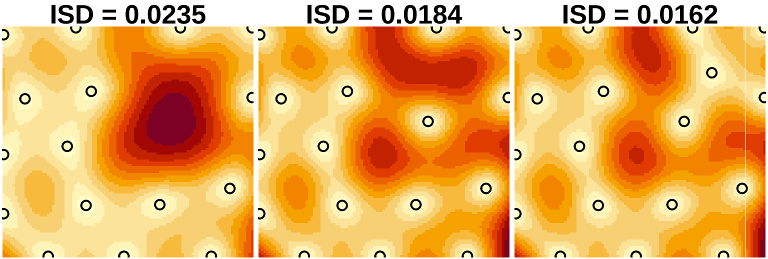
- After $N-1$ runs, sequential design finds the optimal location for the last run.
- However, sequential design is *greedy*. If $N-2$ of $N$ runs are finished, two rounds of sequential design may not be optimal.

# Limited lookahead in active learning



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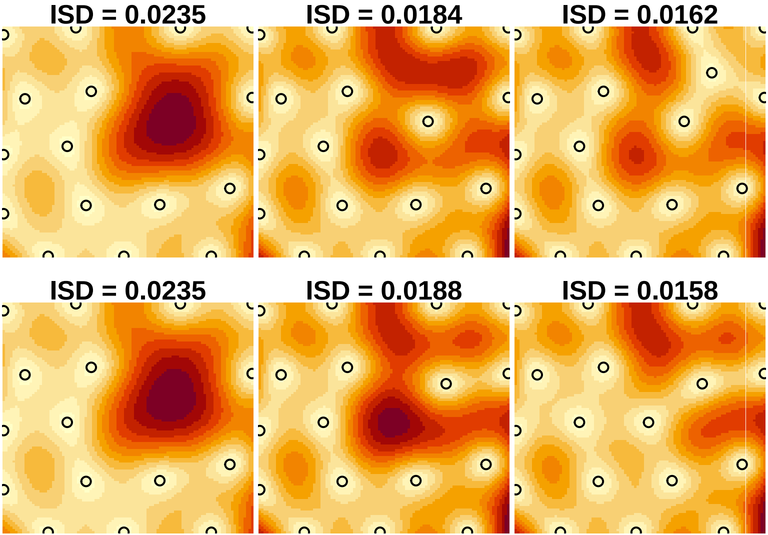

# What’s wrong with being greedy?

Imagine we have two runs left. There are two strategies:

1. Select both points with our current information. This ignores the new information available in the second-to-last point.
2. Select the first point using current information and select the second point using the updated model. The first point ignores the existence of the second point.

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The "best" solution is often a compromise between two extremes. Given a budget of $N$ runs and an initial design, we could

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For example, Let $N = 36$ and $n = 16$, so we have 20 runs to go. We could

1. Place runs in 5 batches of 4 points, **or**
2. Place 4 batches of 4 points, followed by 4 one-at-a-time updates.

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- However, exploration is still required to ensure the model predicts well over all possible treatments.
- **Characterization** explores by searching for uncertain regions of the model. The uncertain regions are in need of more data.
- Sometimes we limit characterization to treatments with responses in a range of interest.
- Balancing exploration and exploitation is an open challenge.