

Planning (Part 2)

Introduction to Automated Science

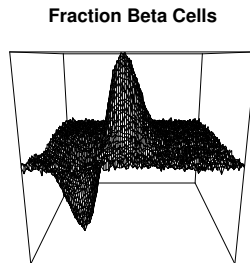
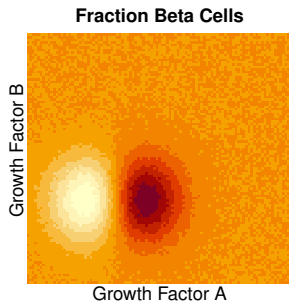
SLAS 2024

Example: Optimizing stem cell differentiation

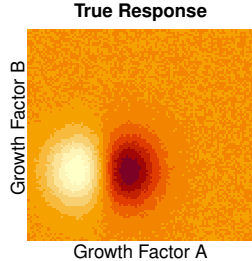
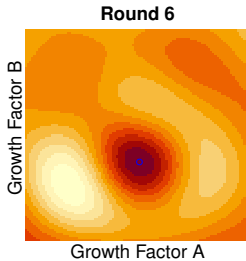
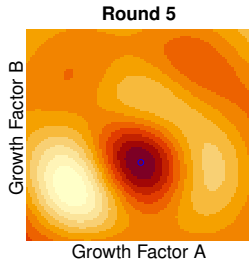
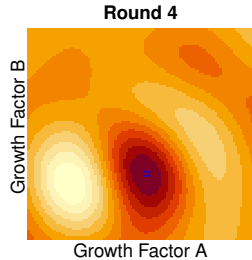
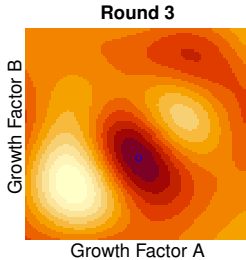
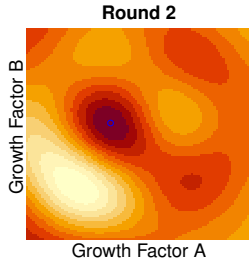
Our goal is to improve the efficiency of differentiating ESCs into mature, insulin-producing beta cells.

- ▶ **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



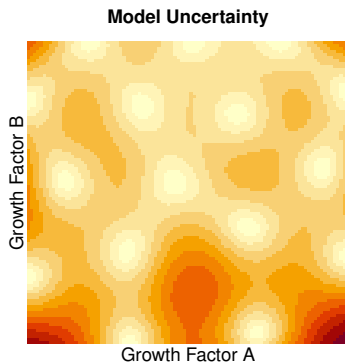
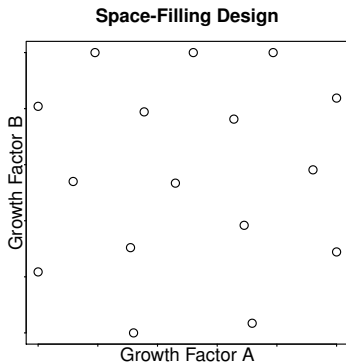
Exploitation vs. Exploration

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

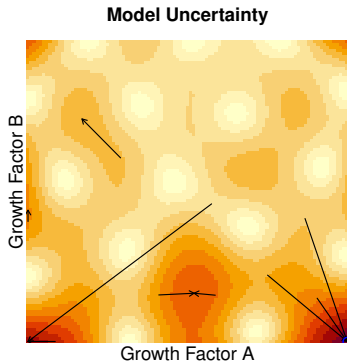
Models can also be improved by **exploration**—placing runs in regions where the model is most uncertain.

Model improvement by exploration

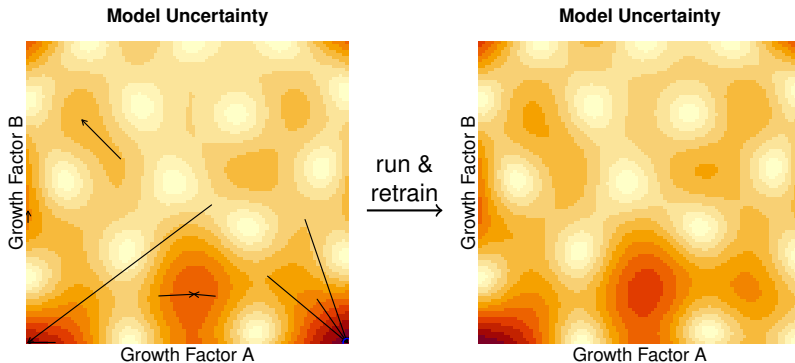
Exploration searches the model for inputs that give the most **uncertain** predictions.



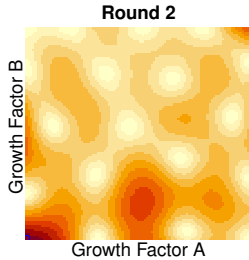
Exploring via search by L-BFGS-B



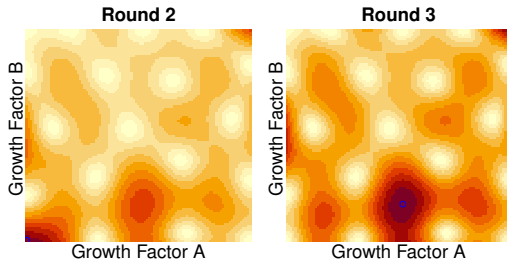
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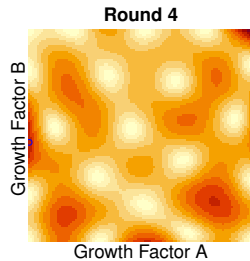
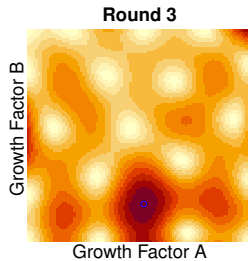
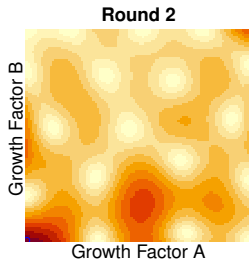
Exploring: Uncertainty whack-a-mole



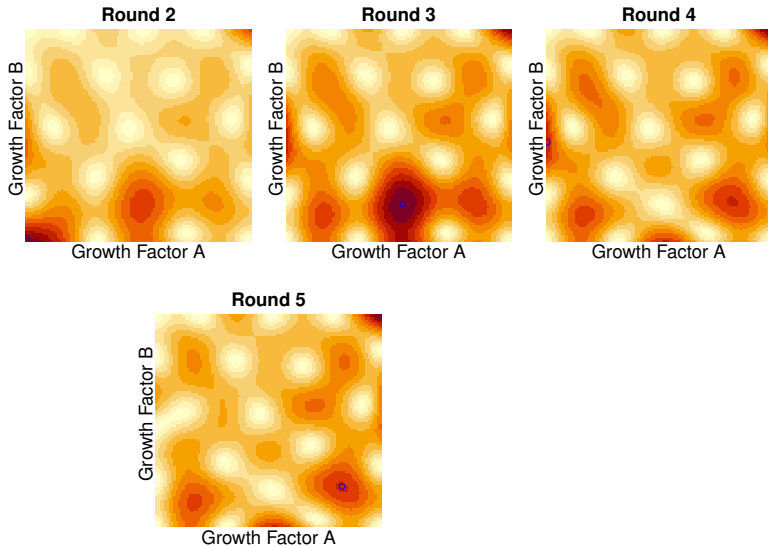
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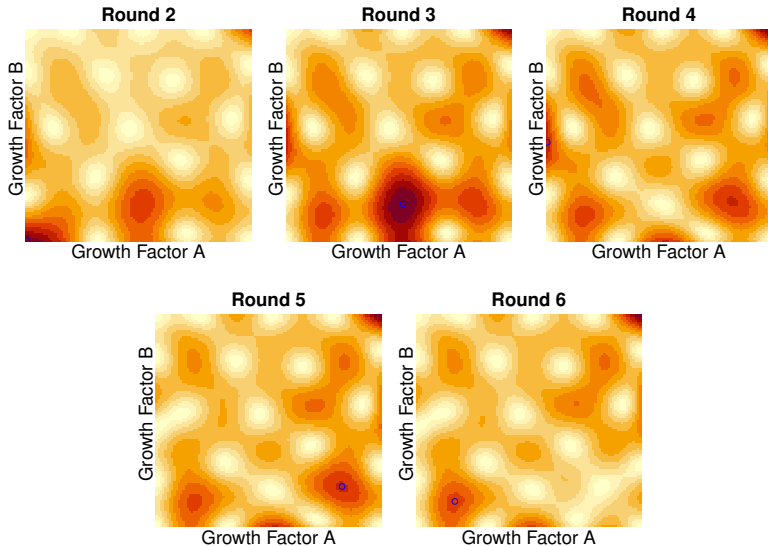
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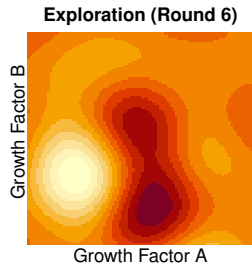
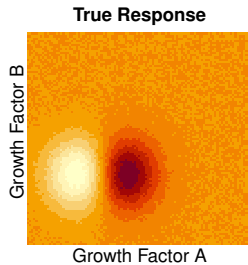
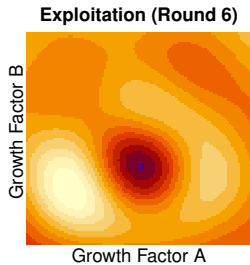
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Comparing exploitation and exploration



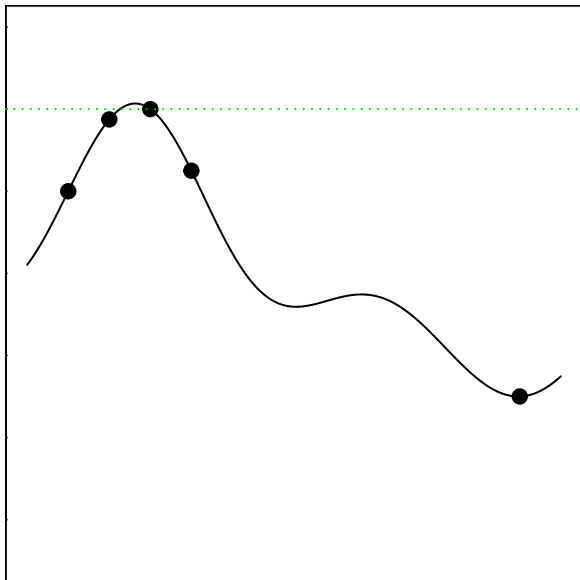
Should we exploit or explore?

Both. Good algorithms balance discovery and refinement.

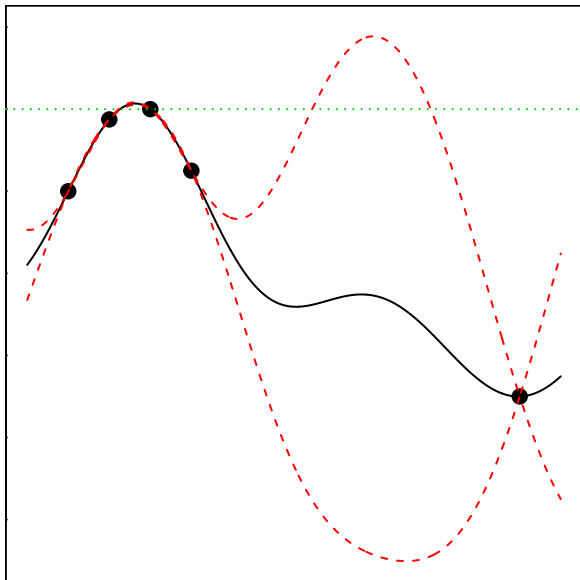
The *best* balance is an open problem. Some solutions:

- ▶ 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

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

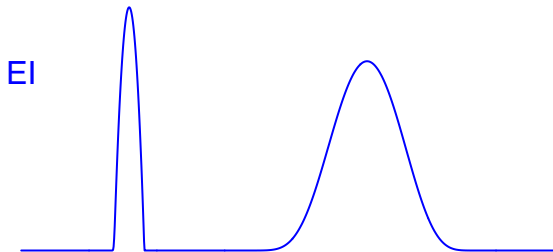
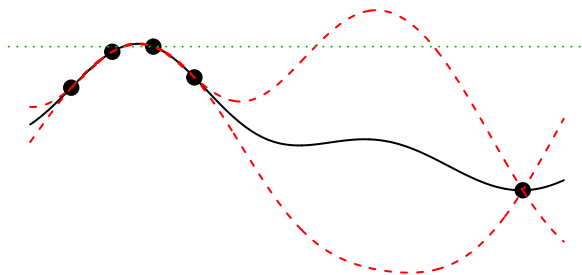
The *improvement* in the objective at a new input x is

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

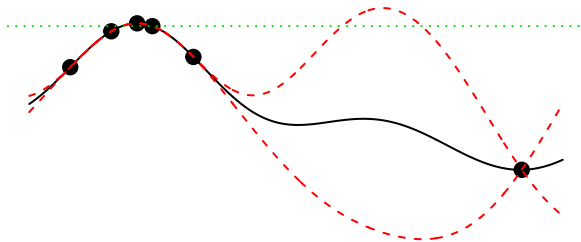
where the maximization “floors” the improvement at zero.

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

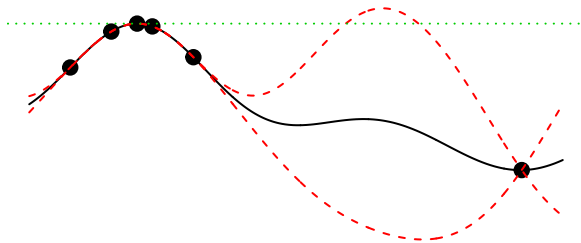
Visualizing Expected Improvement



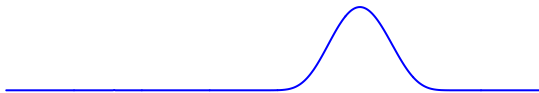
Picking the next sample



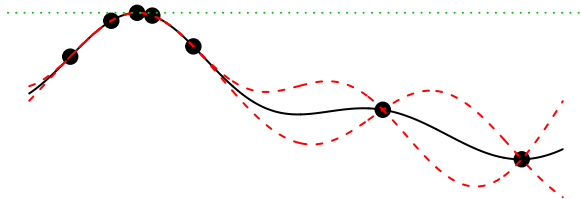
Recalculating Expected Improvement for Round 2



EI



After the second update: no expectation of improvement



EI



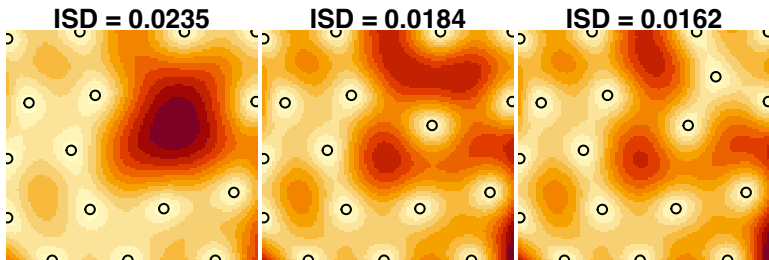
Do sequential designs always work?

- ▶ Sequential design methods are **last sample optimal**.
- ▶ After $N - 1$ runs, sequential design finds the optimal location for the last run.

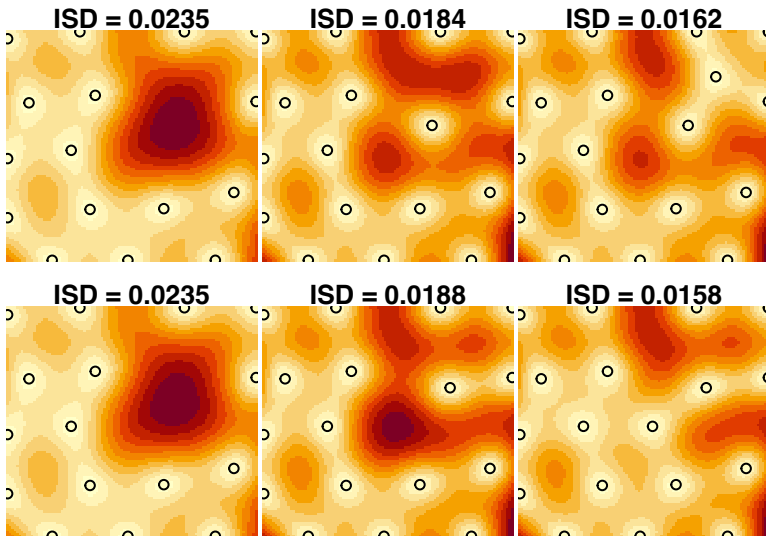
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- ▶ After $N - 1$ runs, sequential design finds the optimal location for the last run.
- ▶ However, sequential design is *greedy*. If $N - 2$ of N runs are finished, two rounds of sequential design may not be optimal.

Limited lookahead in active learning



Limited lookahead in active learning



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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- ▶ **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.