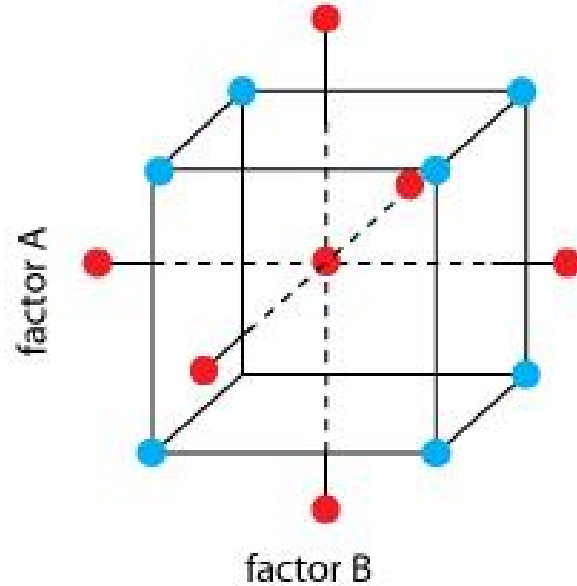


Supporting the Design of Experiments for Synthetic Biology with Clotho 3.0

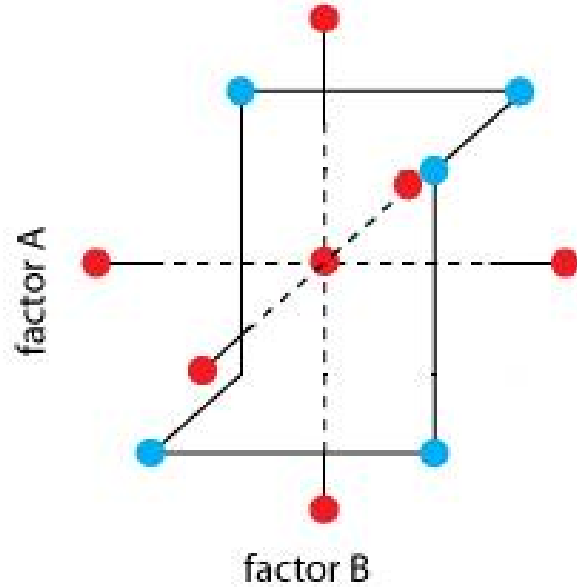


Nicholas Roehner
CIDAR (Densmore Lab)
Boston University

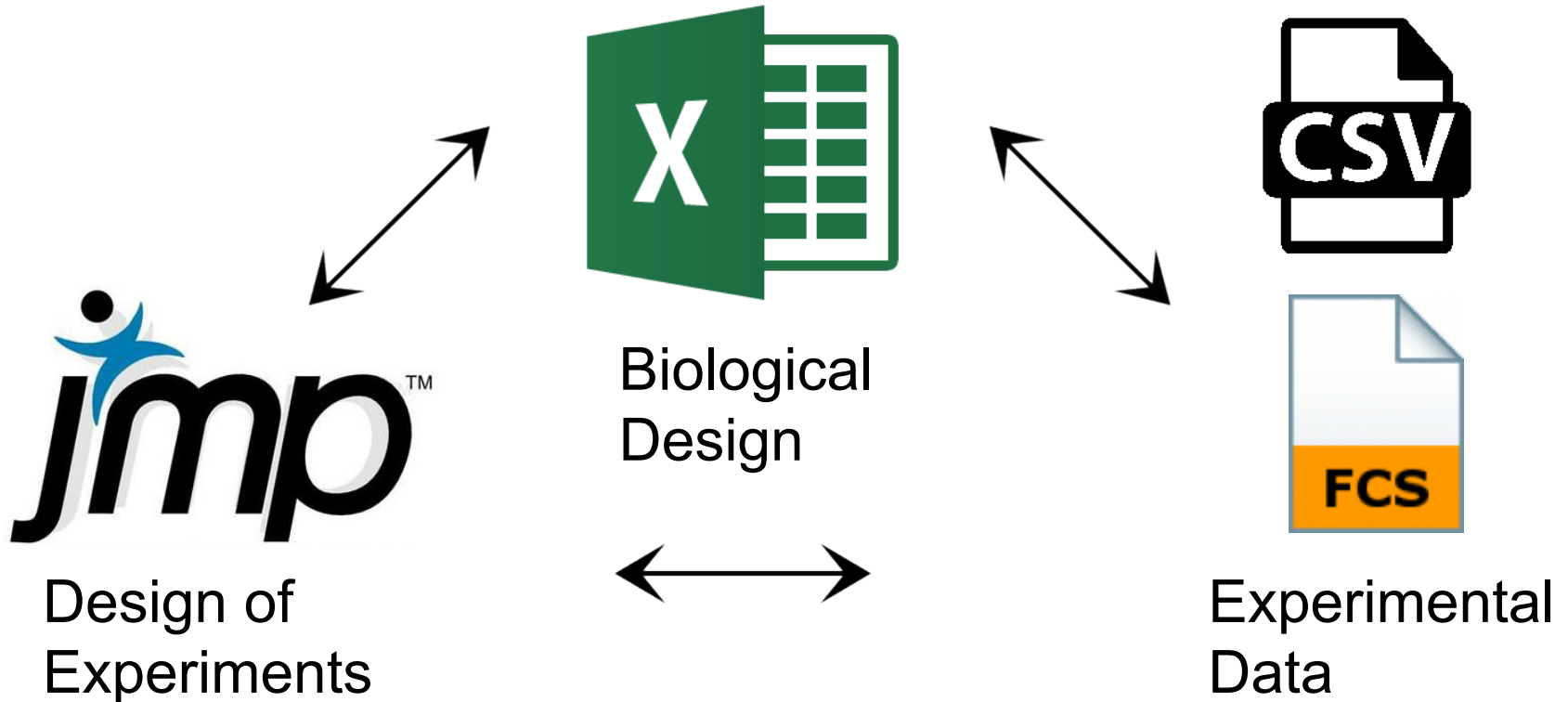
Design of Experiments (DOE)



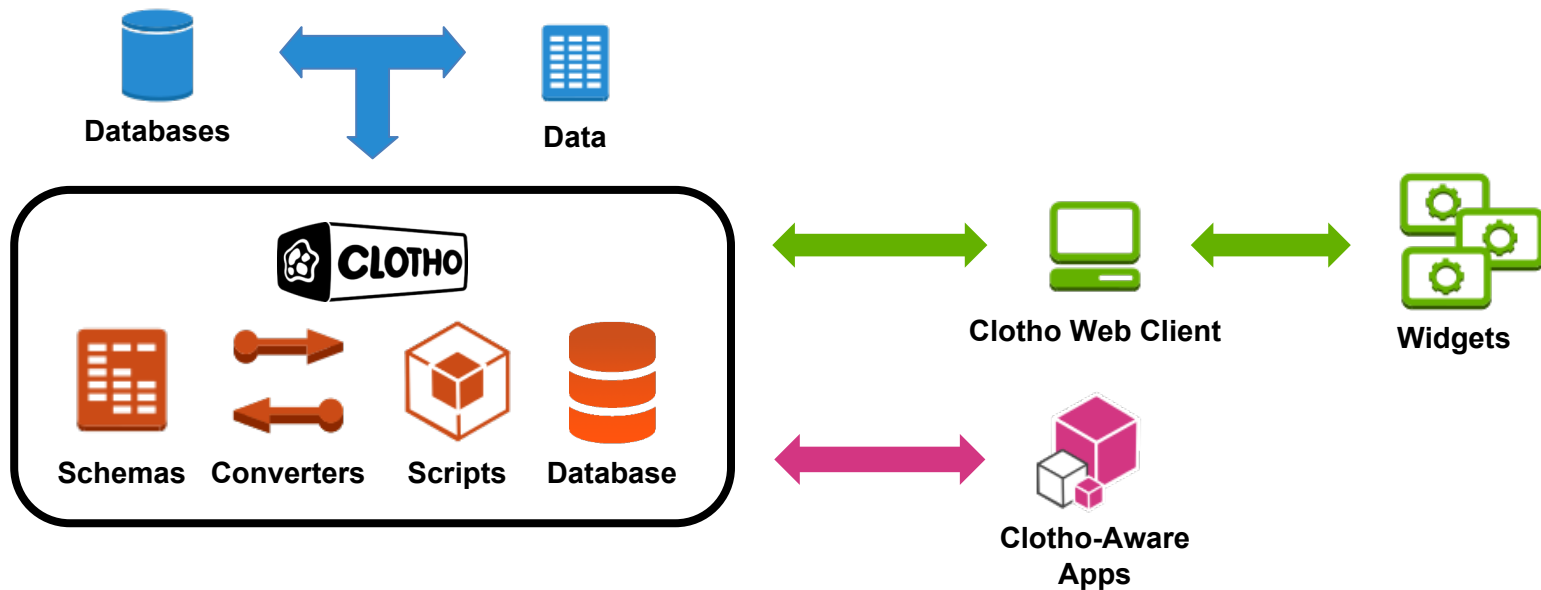
Design of Experiments (DOE)



DOE for Synthetic Biology



Clotho 3.0



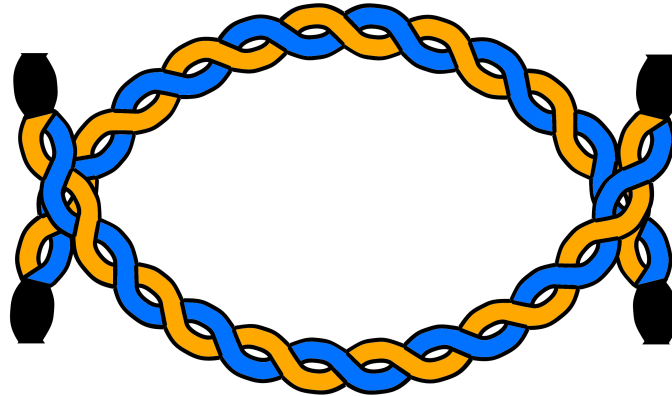
DOE for Synthetic Biology w/ Double Dutch



Design of
Experiments



Biological
Design

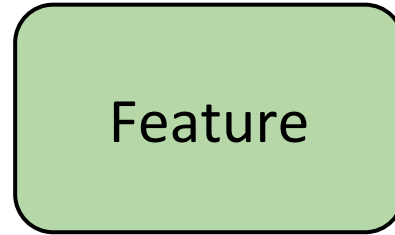


Double Dutch

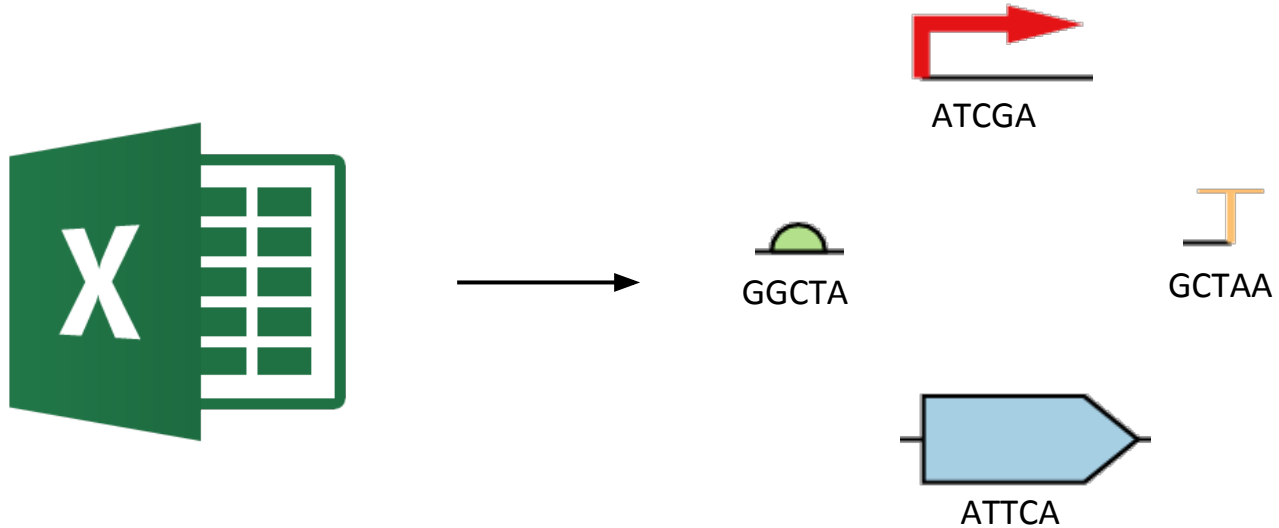
Talk Outline

- Overview of Double Dutch web app
- Double Dutch demo
- Discussion of app extensions

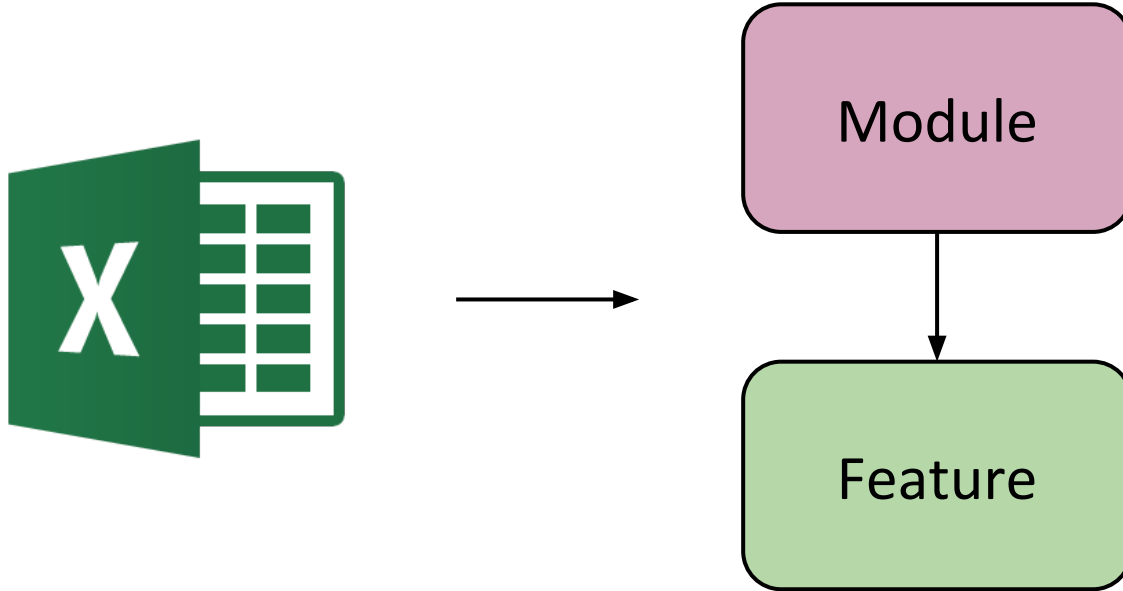
Step 1: Import Features



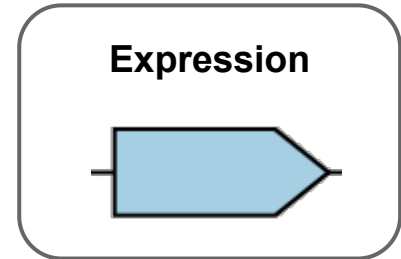
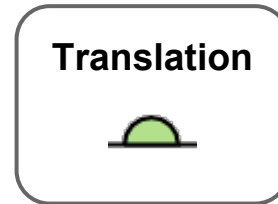
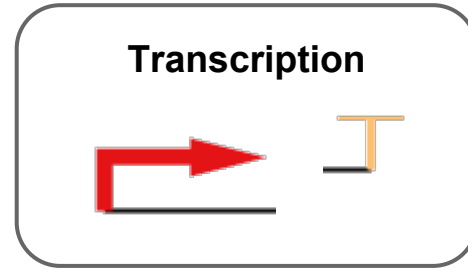
Step 1: Import Features



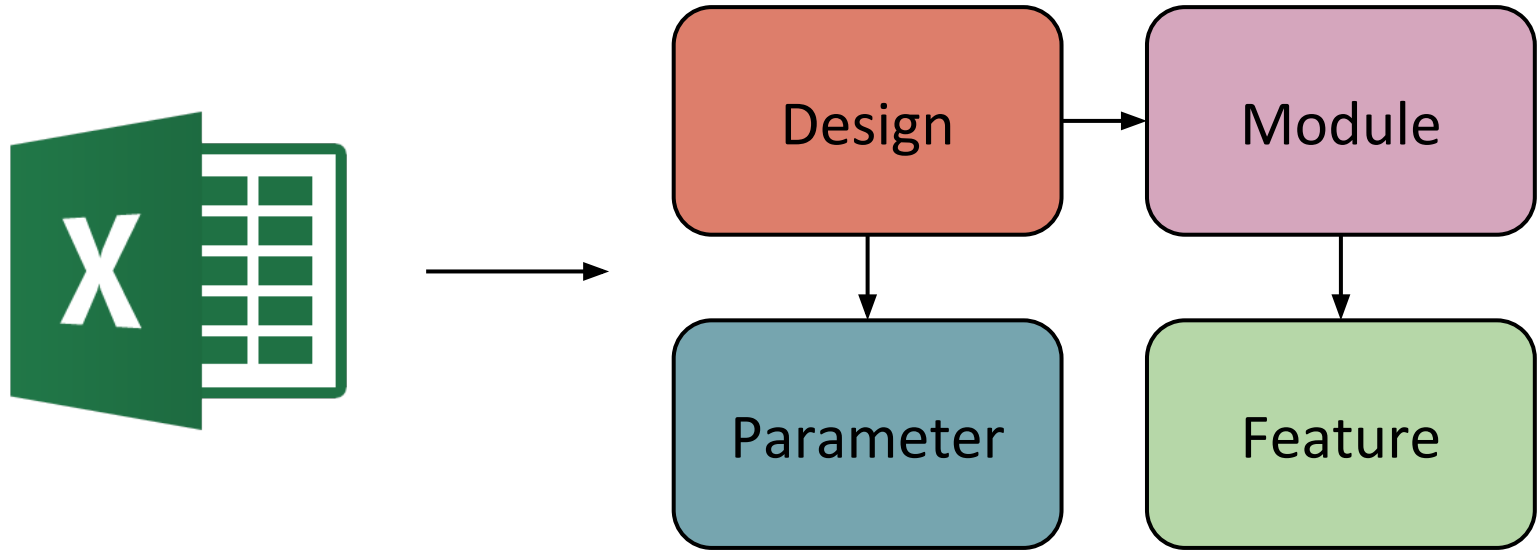
Step 2: Infer Modules



Step 2: Infer Modules



Step 3: Parameterize Modules



Step 3: Parameterize Module



10356 REU

Transcription



Translation



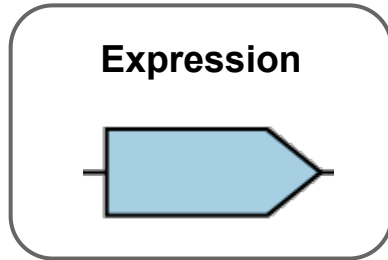
2.89 REU

Expression



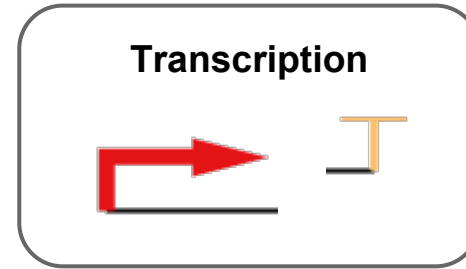
Step 4: Categorize as Factors or Levels

Available Factors

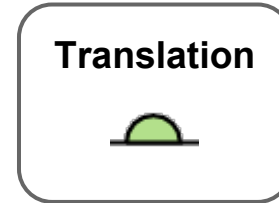


Available Levels

10356 REU

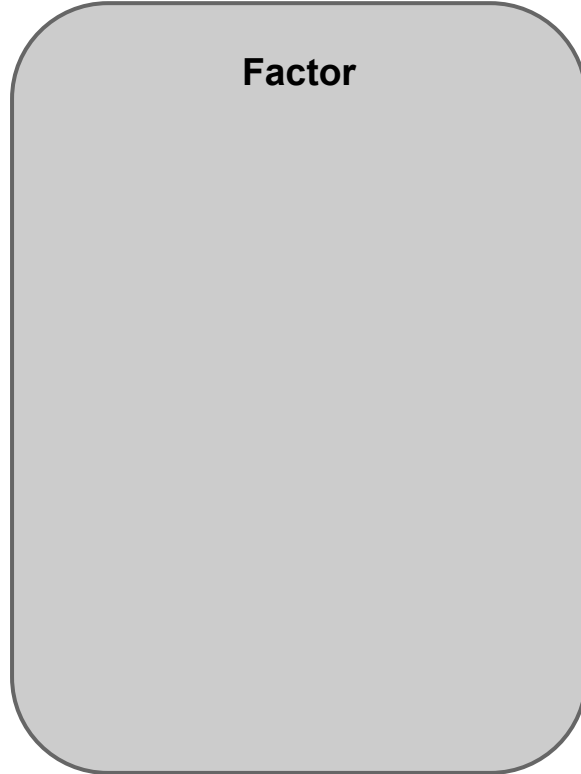


Translation

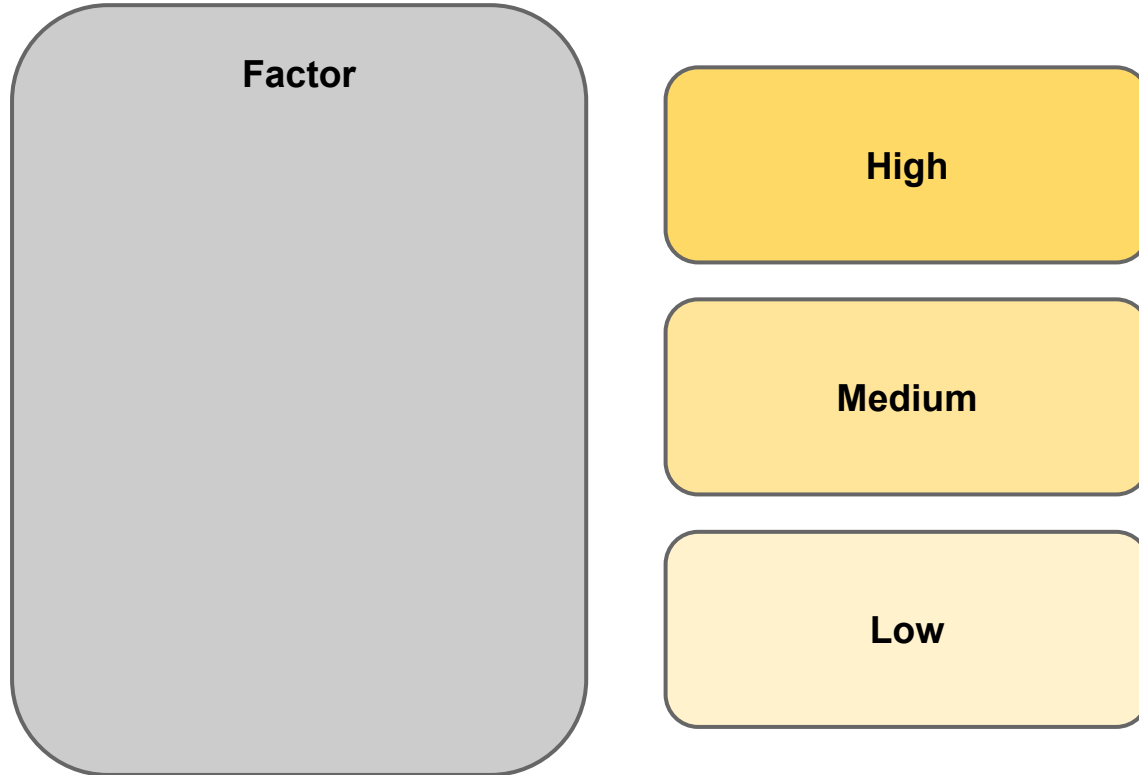


2.89 REU

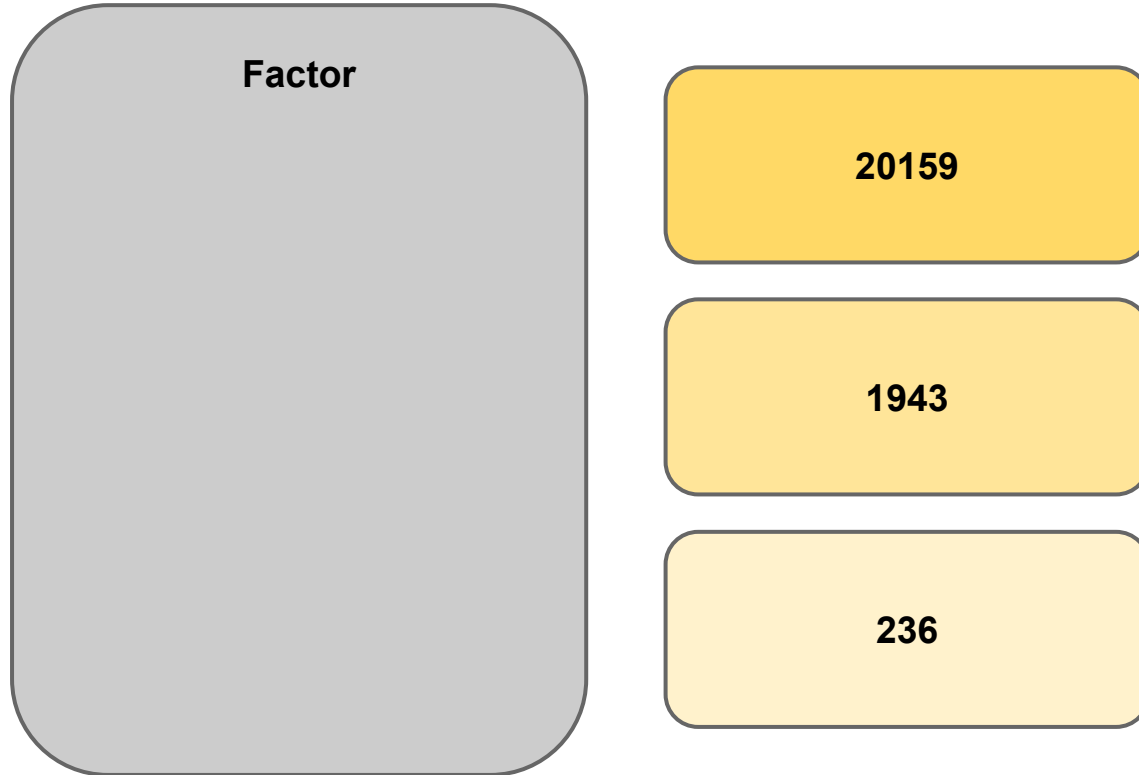
Step 5: Assign Levels to Factors



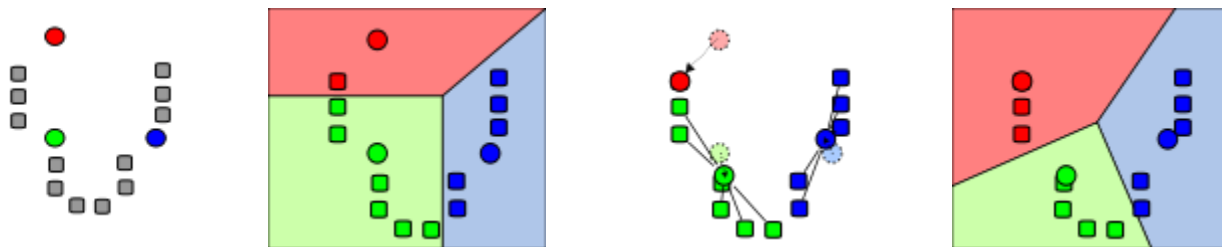
Step 5a: Choose # of Levels per Factor



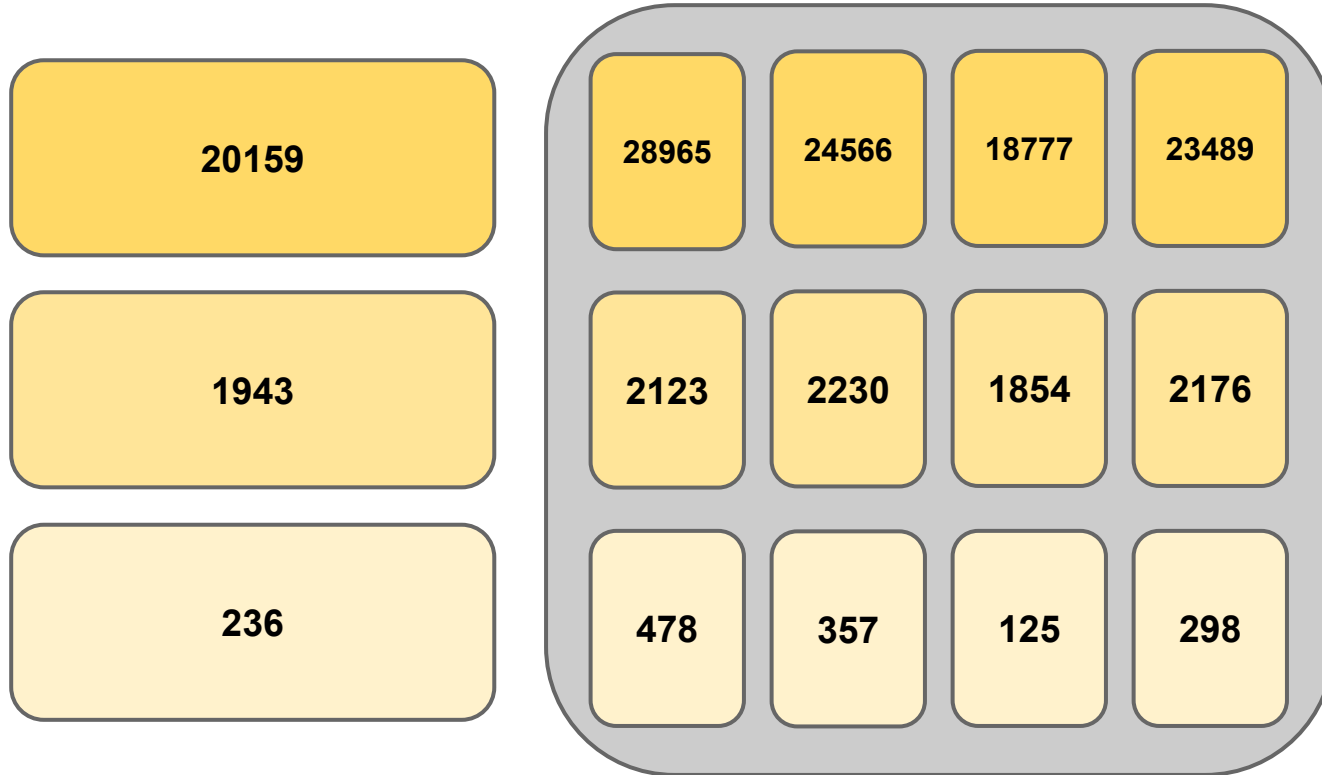
Step 5b: Quantify Target Levels



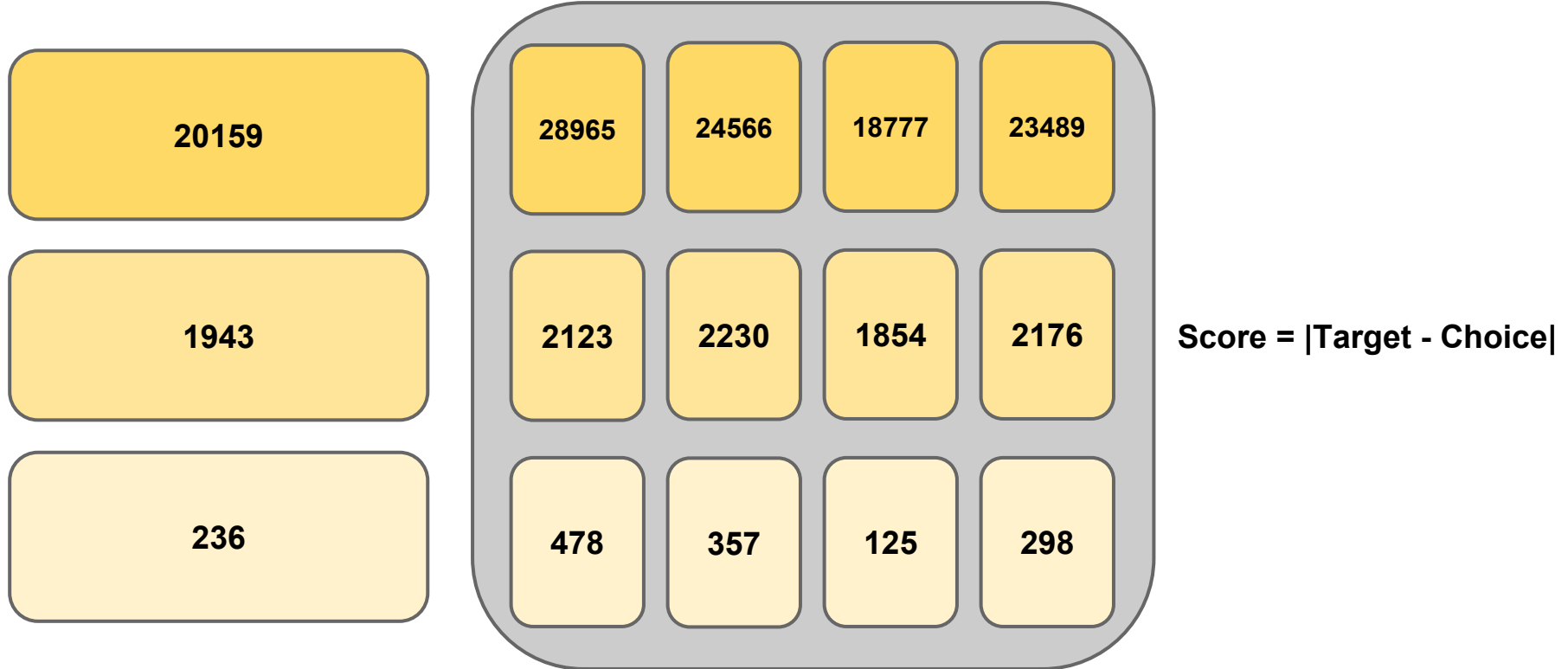
K-Means Clustering



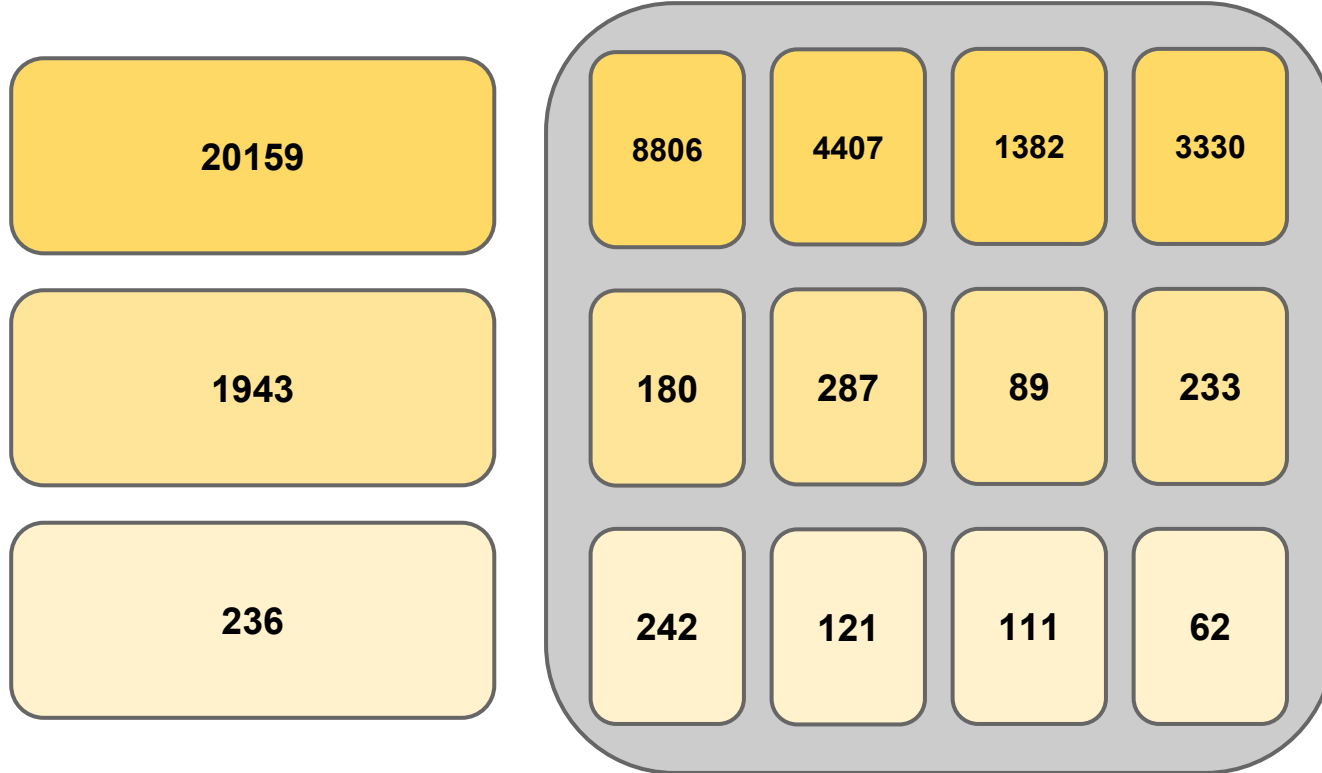
Step 5c: Partition Level Choices



Step 5d: Score Level Choices

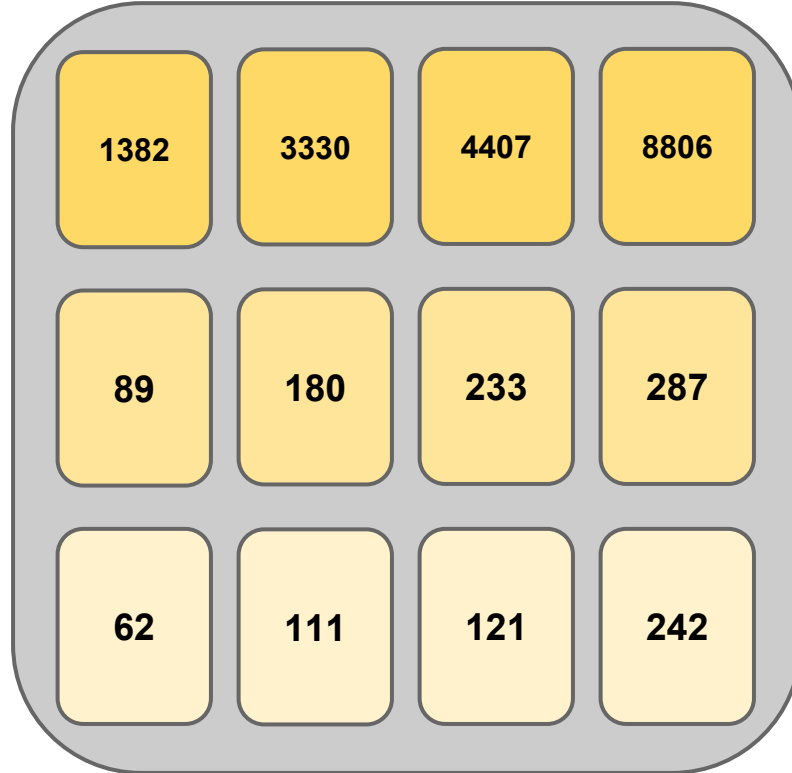


Step 5d: Score Level Choices



$$\text{Score} = |\text{Target} - \text{Choice}|$$

Step 5e: Sort Level Choices



A 3x4 grid of level choices, each represented by a rounded square button. The buttons are arranged in three rows and four columns. The top row has the highest values (1382, 3330, 4407, 8806) and the darkest yellow color. The middle row has intermediate values (89, 180, 233, 287) and a medium yellow color. The bottom row has the lowest values (62, 111, 121, 242) and the lightest yellow color. The entire grid is enclosed in a gray rounded rectangle.

1382	3330	4407	8806
89	180	233	287
62	111	121	242

Step 5f: Greedy Search

1382	3330	4407	8806
89	180	233	287
62	111	121	242

1382	3330	4407	8806
89	180	233	287
62	111	121	242

Step 5f: Greedy Search

1382	3330	4407	8806
89	180	233	287
62	111	121	242

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Step 5f: Greedy Search

1382	3330	4407	8806
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Step 5f: Greedy Search

1382	3330	4407	8806
89	180	233	287
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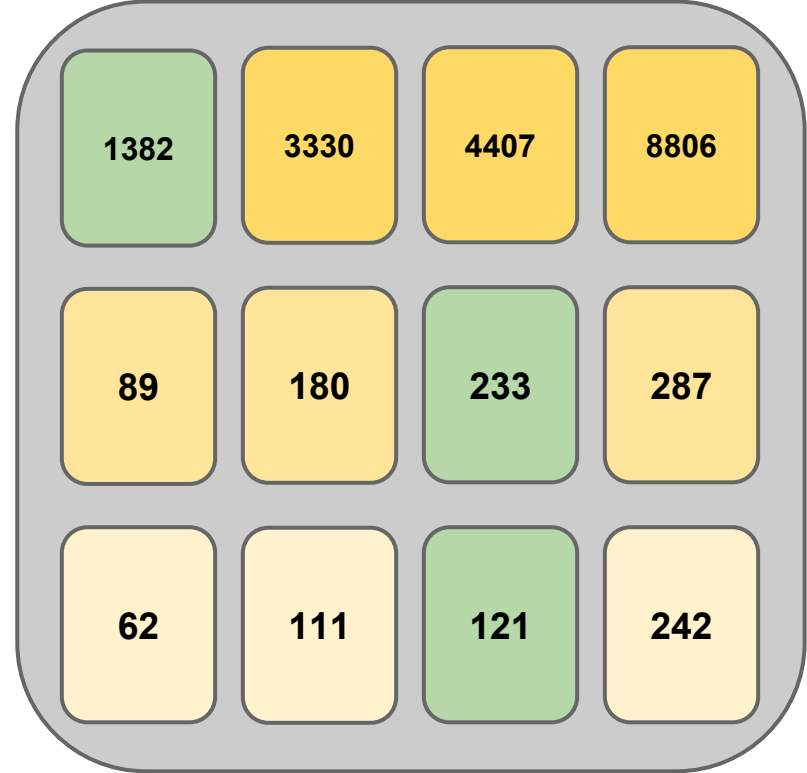
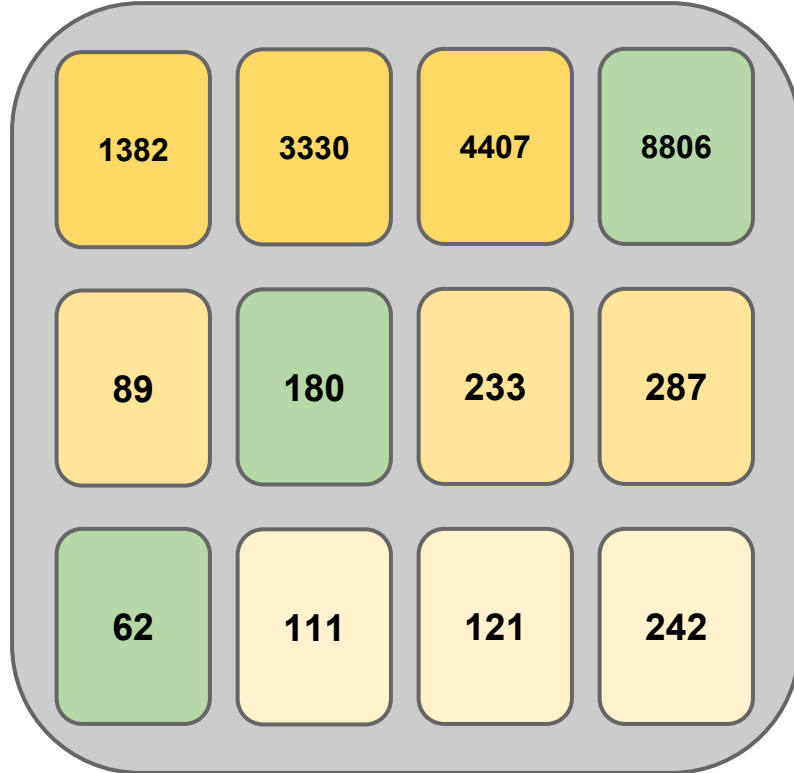
1382	3330	4407	8806
89	180	233	287
62	111	121	242

Step 5f: Greedy Search

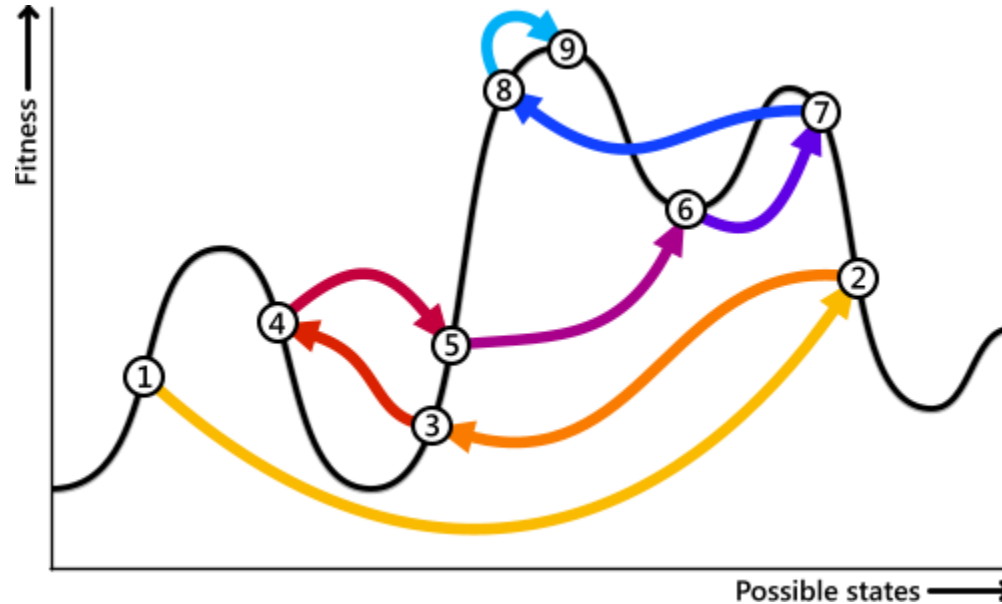
1382	3330	4407	8806
89	180	233	287
62	111	121	242

1382	3330	4407	8806
89	180	233	287
62	111	121	242

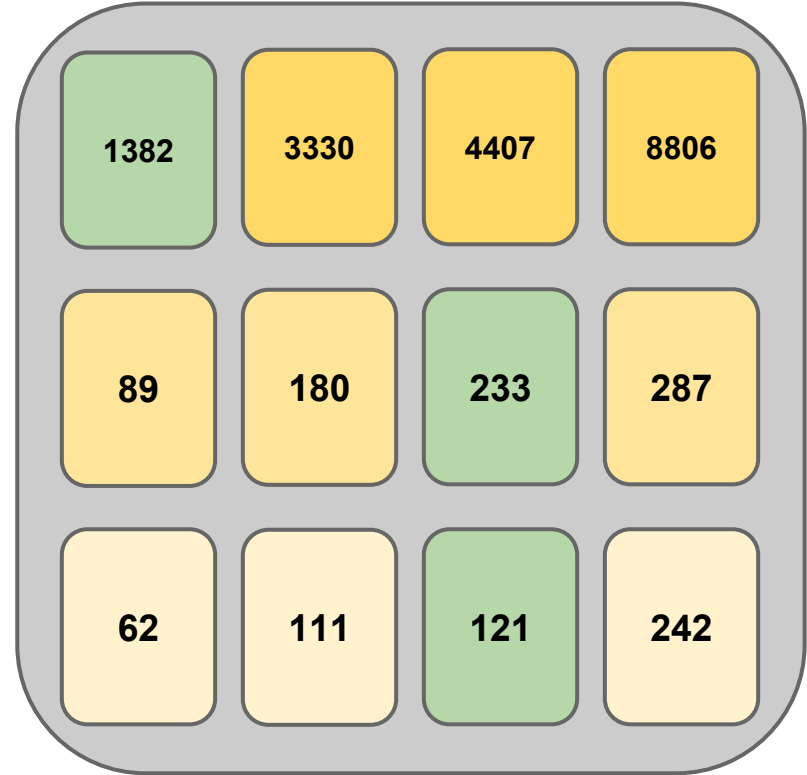
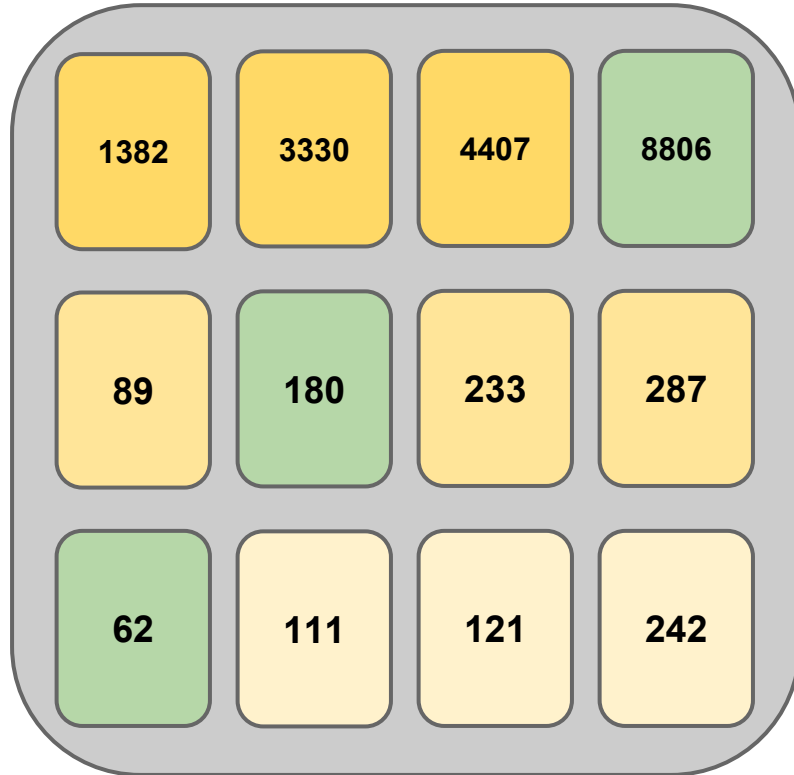
Step 5f: Greedy Search



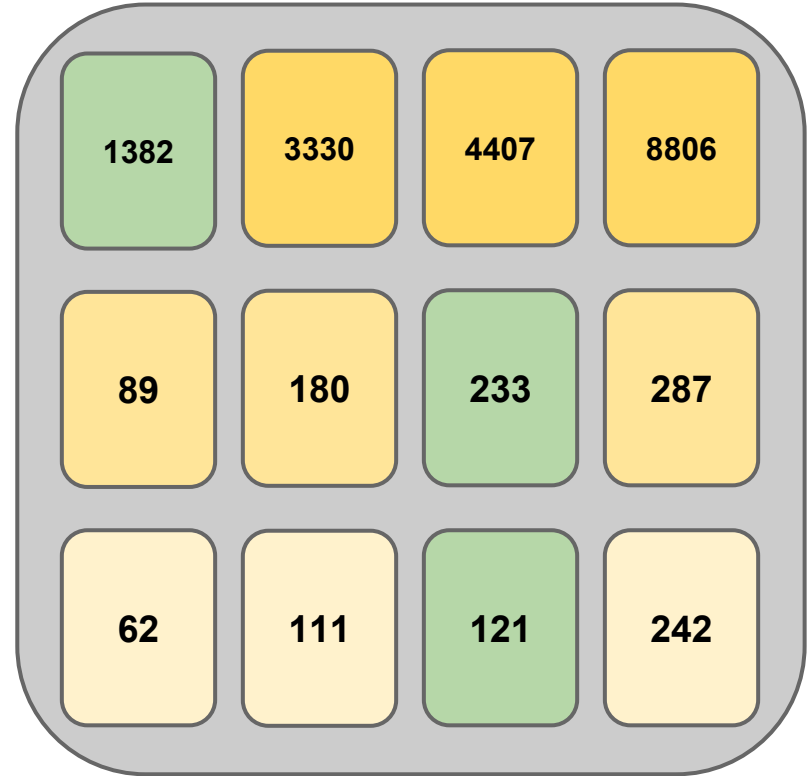
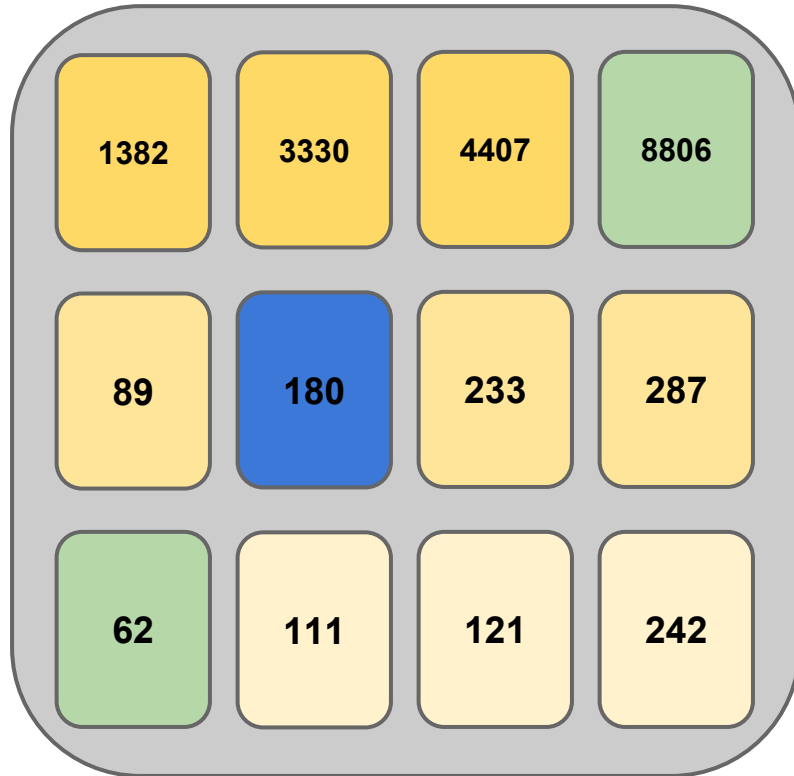
Local Optimum and Simulated Annealing



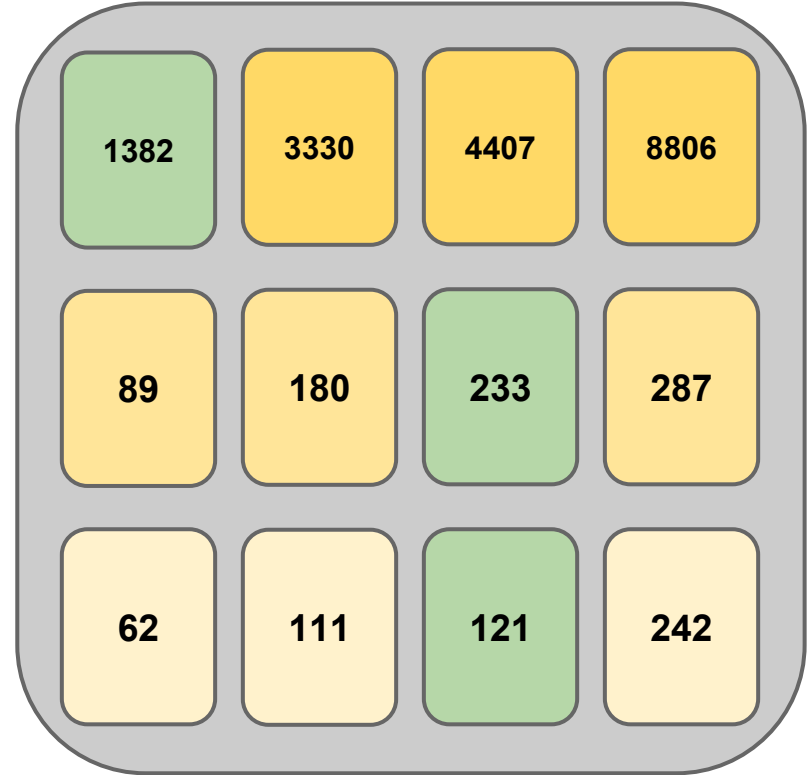
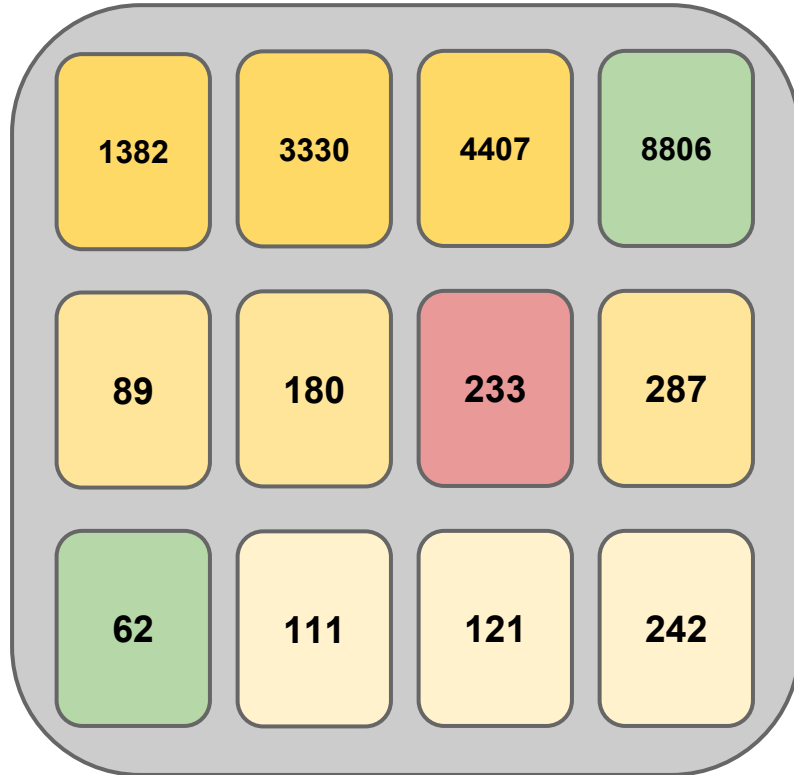
Step 5g: Simulated Annealing



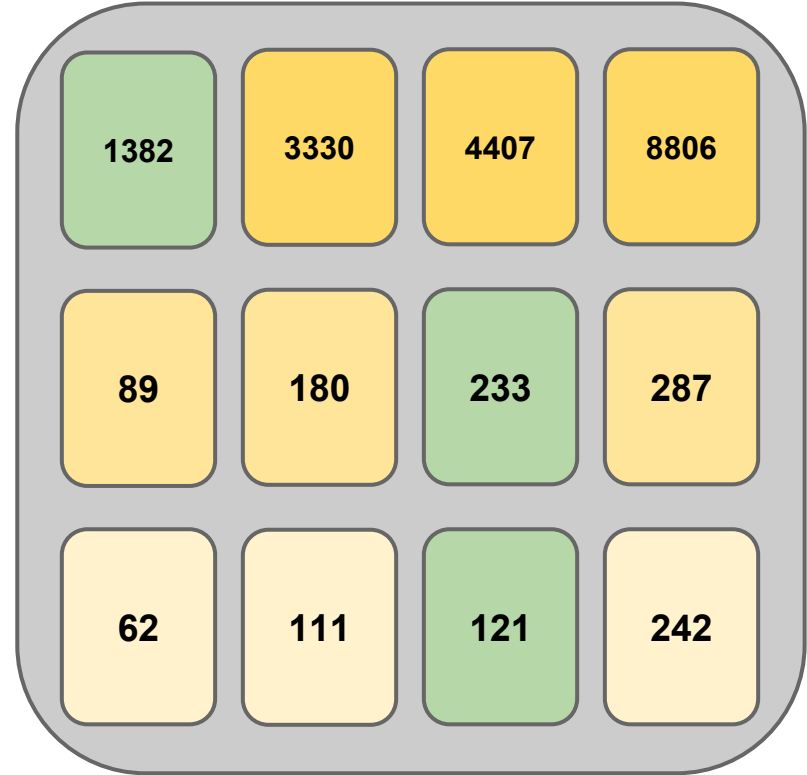
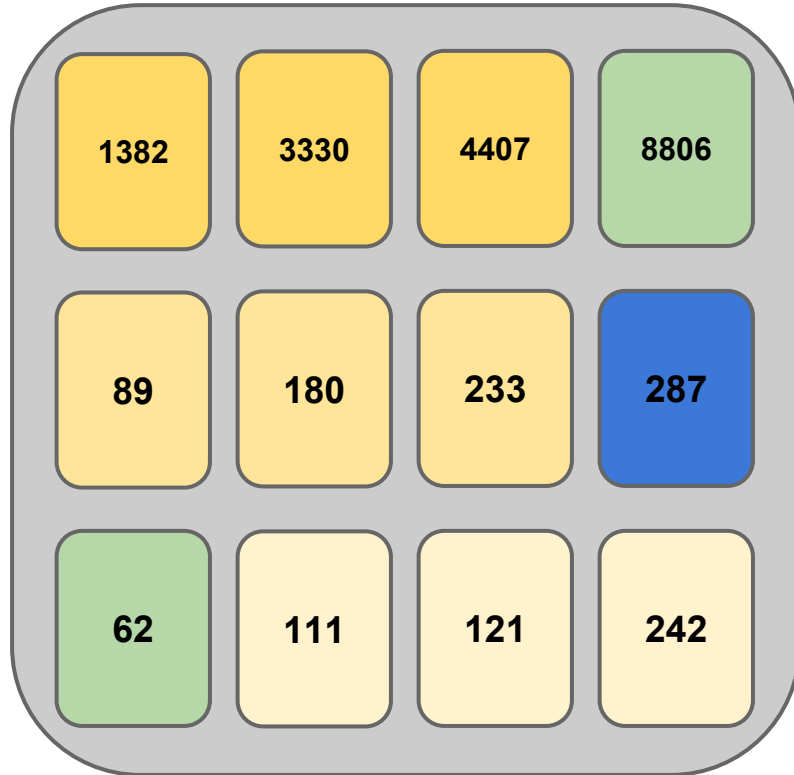
Step 5g: Simulated Annealing



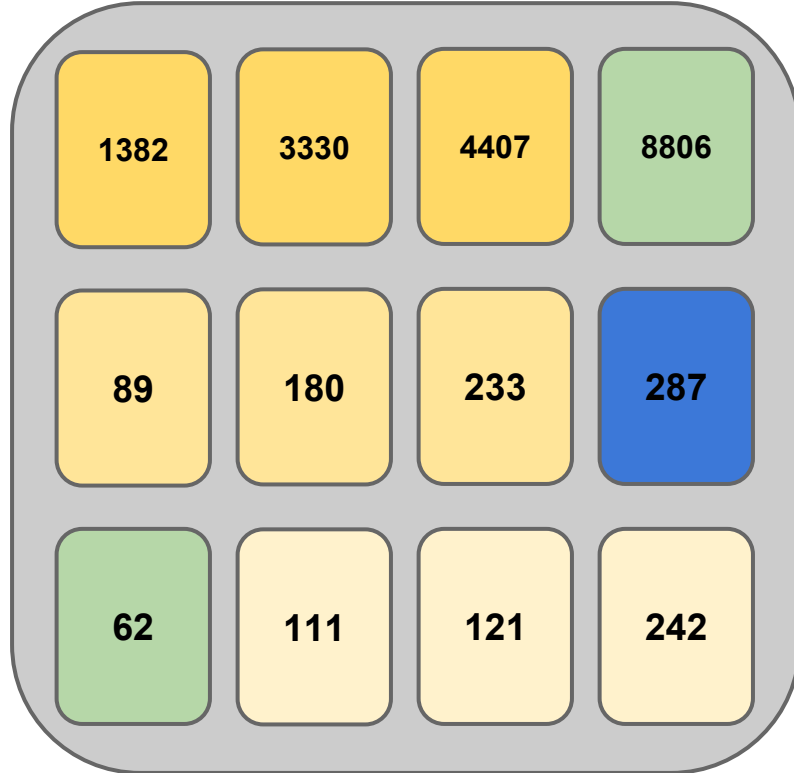
Step 5g: Simulated Annealing



Step 5g: Simulated Annealing

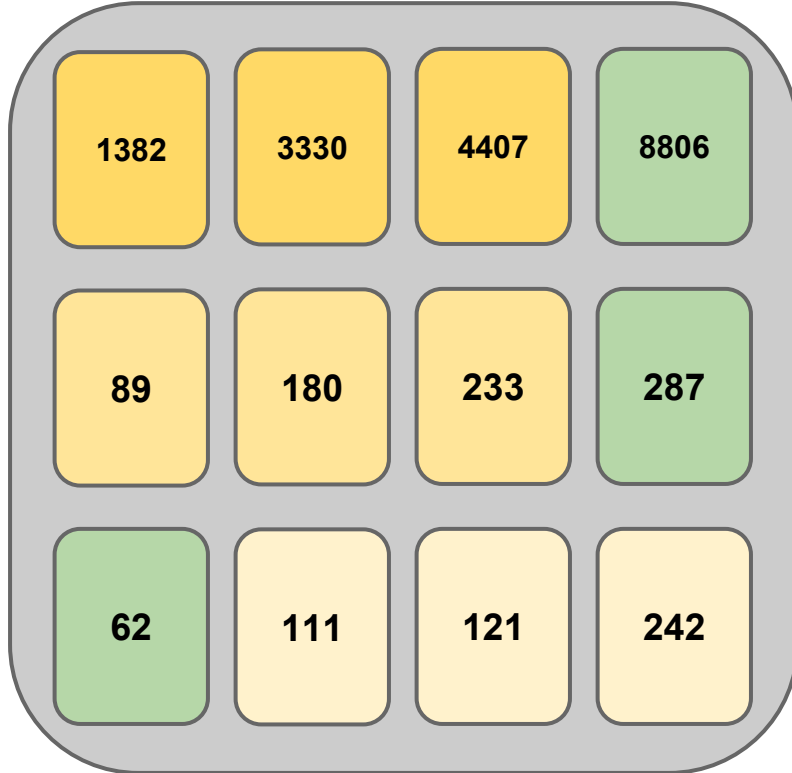


Step 5g: Simulated Annealing



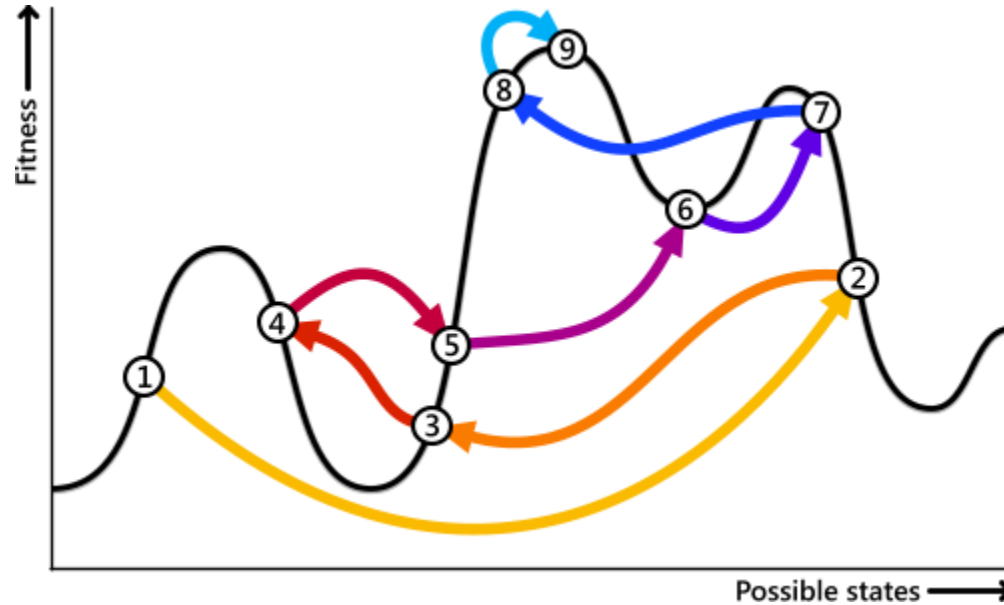
$$P(\text{accept}) = e^{[(\text{oldScore} - \text{newScore})/\text{Temp}]}$$

Step 5g: Simulated Annealing

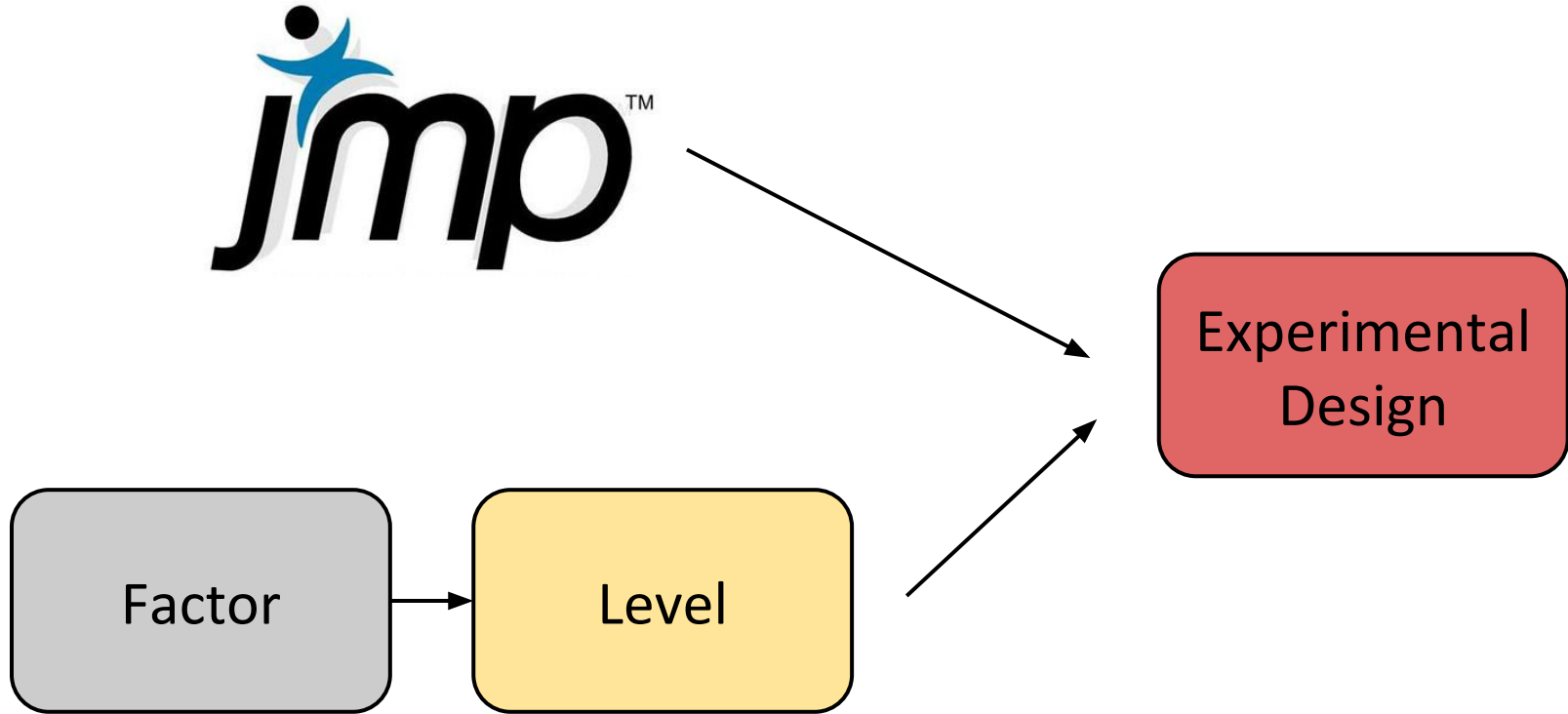


$$P(\text{accept}) = e^{[(\text{oldScore} - \text{newScore})/\text{Temp}]}$$

Simulated Annealing



Step 6: Generate Experimental Design



Step 6: Generate Experimental Design

4th Order	A	B	C	D	E	F
1	0	1	1	1	-1	-1
2	0	1	0	0	0	0
3	1	1	1	1	-1	1
4	0	0	0	-1	1	0
5	-1	1	0	0	0	0
6	-1	-1	-1	1	1	0
7	0	-1	0	-1	0	0
8	1	1	-1	-1	1	-1
9	0	0	-1	0	1	-1
10	1	0	0	0	0	-1

Step 6: Generate Experimental Design

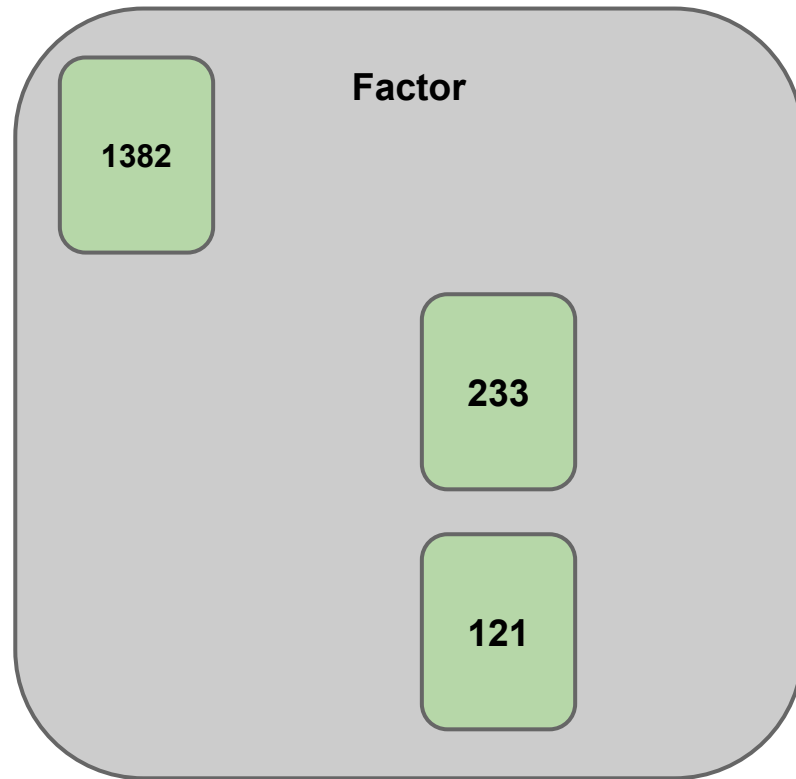
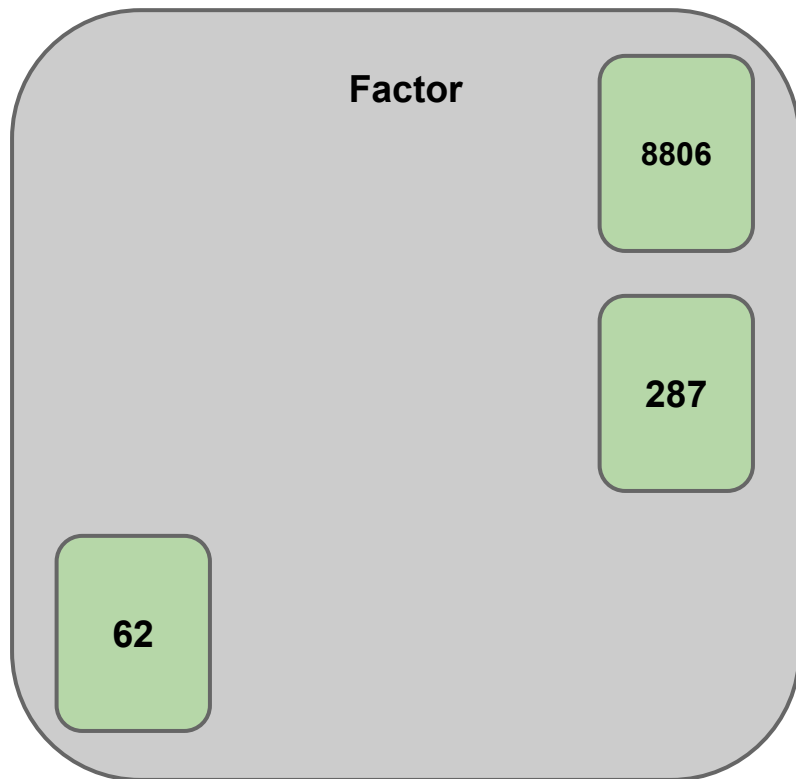
	1
	0
	-1

20159

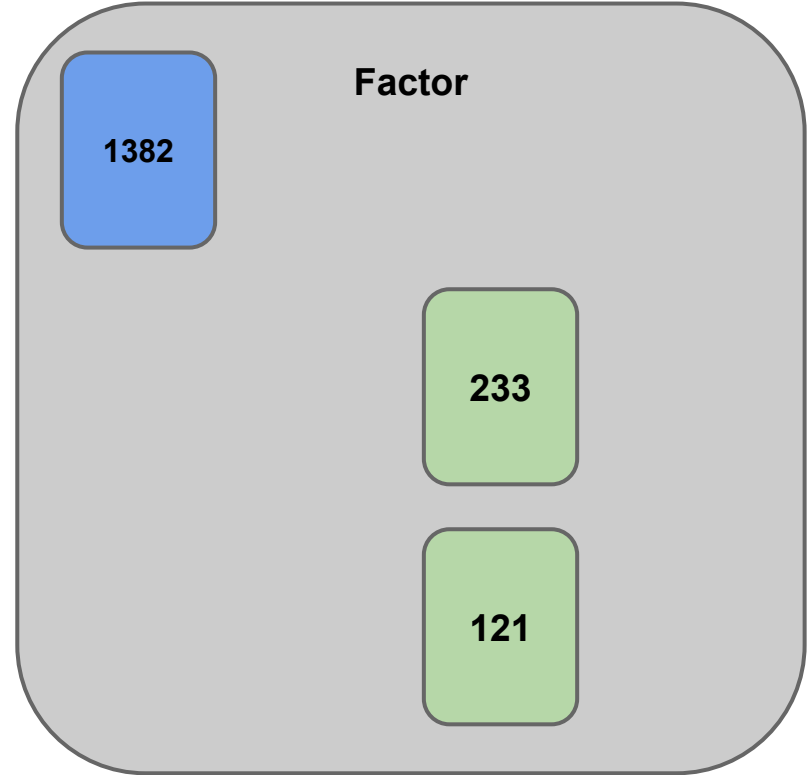
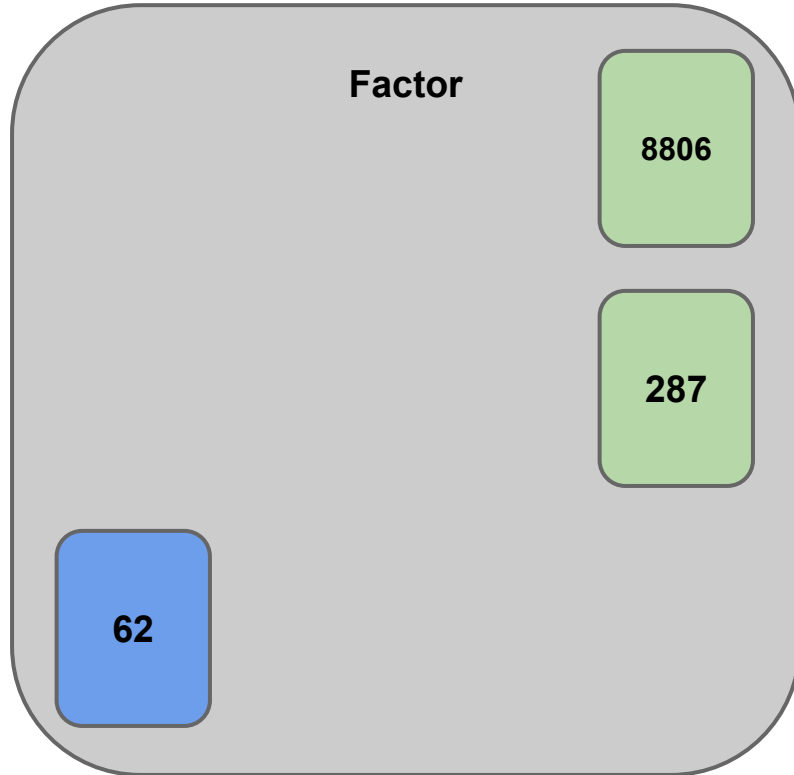
1943

236

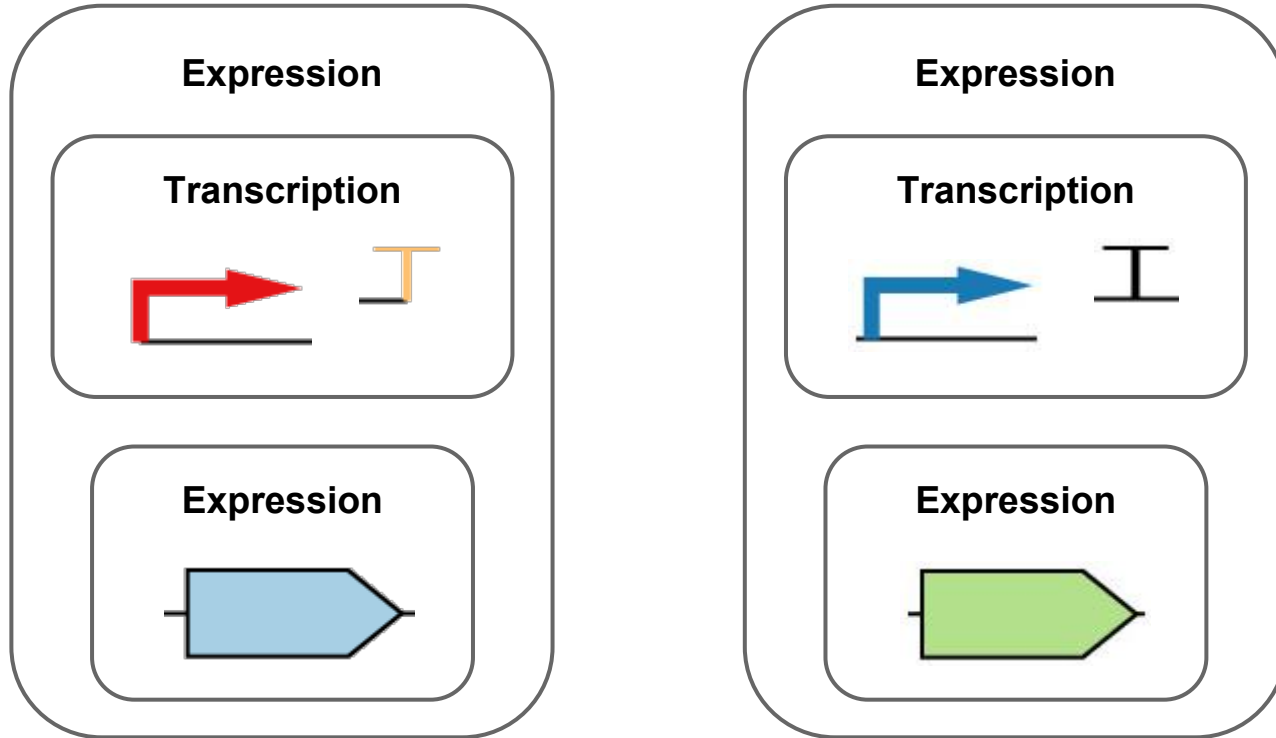
Step 6: Generate Experimental Design



Step 6: Generate Experimental Design



Step 7: Generate Biological Designs



Planned Extensions

- Validate composition of modules associated with factors and levels in experimental designs.
- Fit empirical models to experimental data.
- Incorporate Pigeon for design visualization.
- Export designs in additional file formats (Euegene, SBOL, JSON).
- Generate picklists for automated assembly.

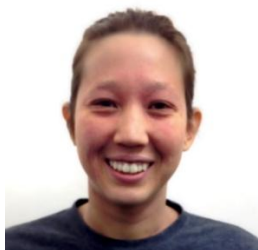
Clotho Team



**Douglas
Densmore**



**J. Christopher
Anderson**



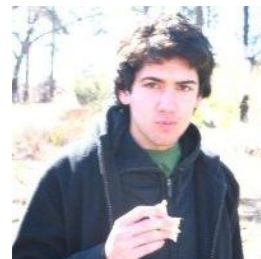
**Stephanie
Paige**



**Prashant
Vaidyanathan**



**Bill
Cao**



**Maxwell
Bates**

