The GPS Platform

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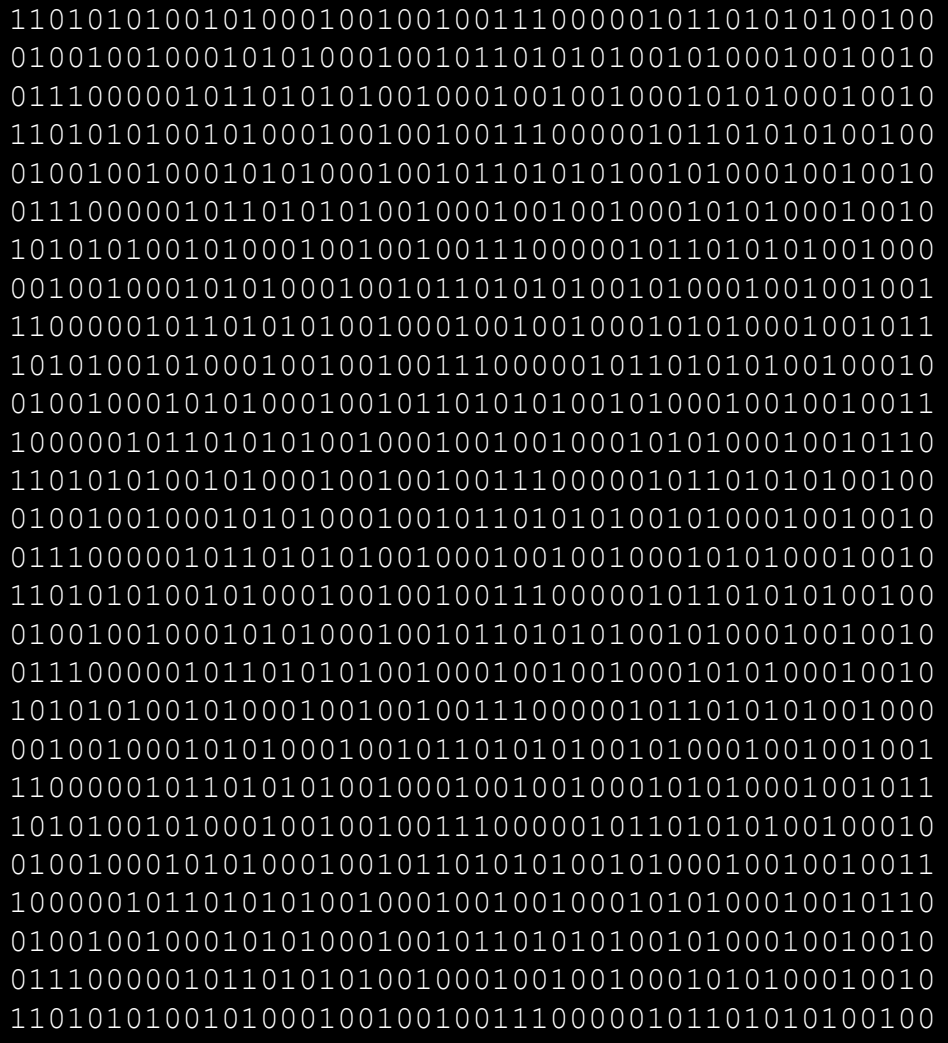
W Data Loop
Biology Hwy



“O, she doth teach the torches to burn bright.”

“Methylate tRNA U54 in pos 5”

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Biology: a string of ACGT

Genes

Proteins

Vectors

Cells

Organisms

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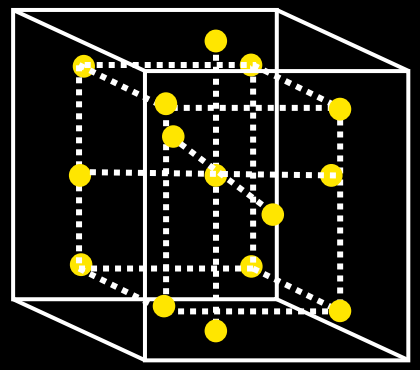
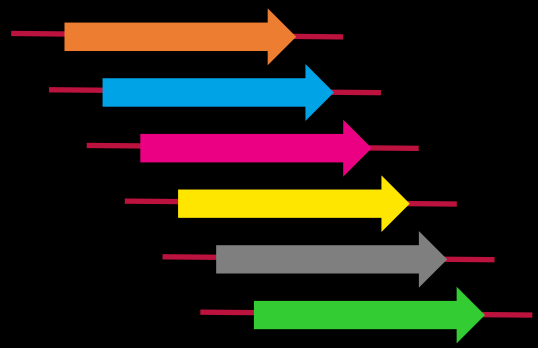
Design of Experiment

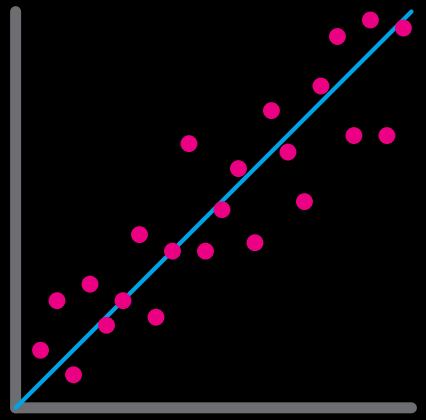


Build



Test

Learn



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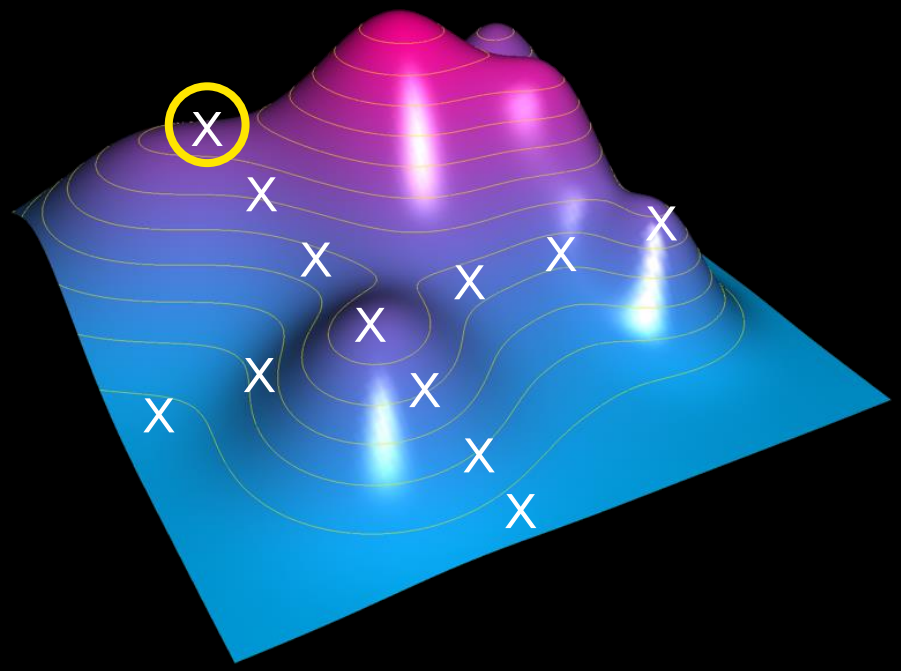
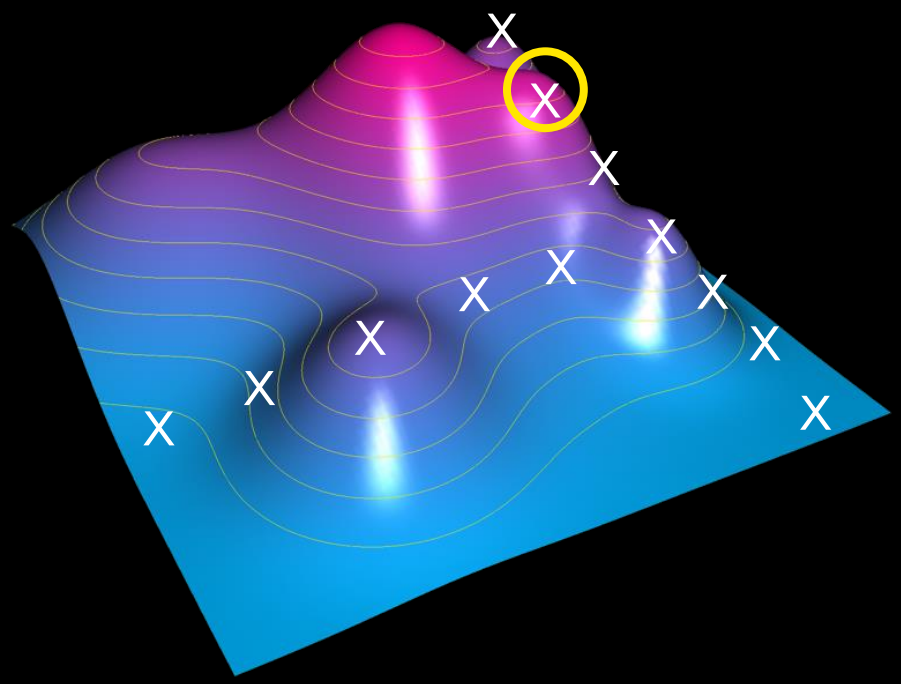
Sequential optimization



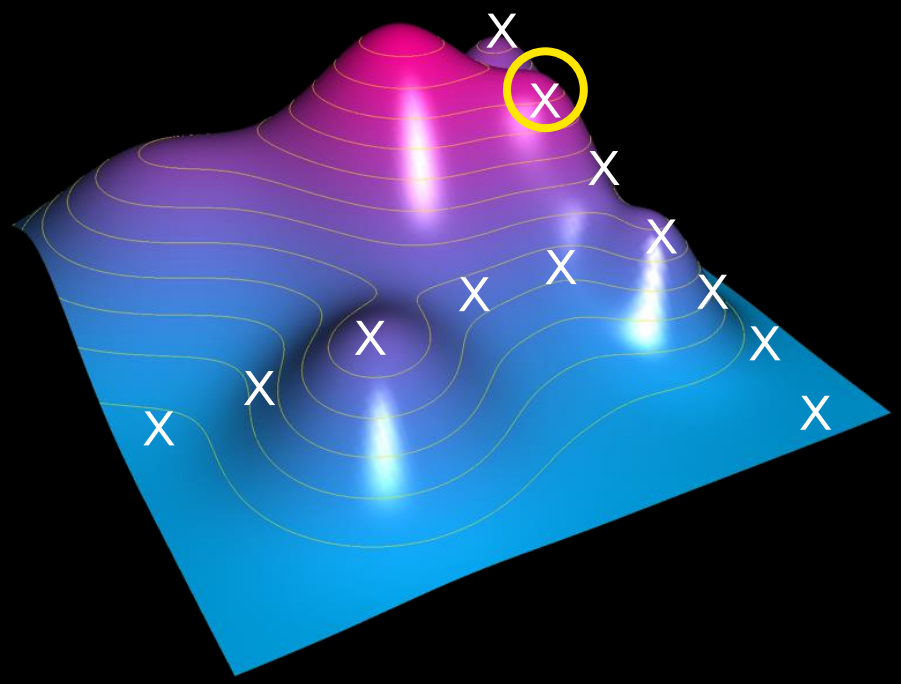
Sequential assays
Optimize for one parameter at a time

Sequential optimization

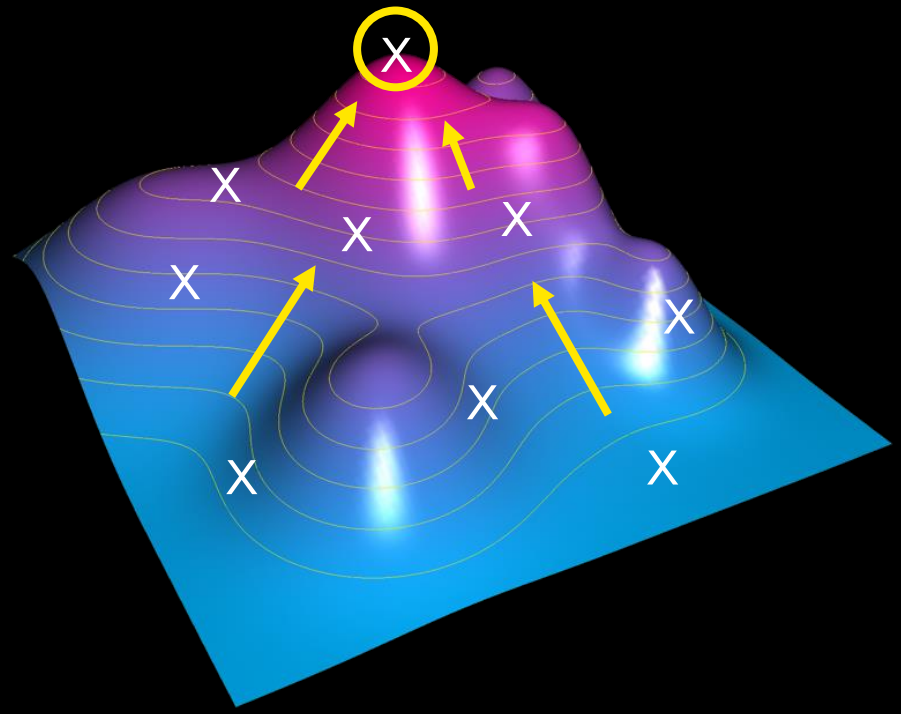


Sequential assays
Optimize for one parameter at a time

Design of Experiments (DoE)

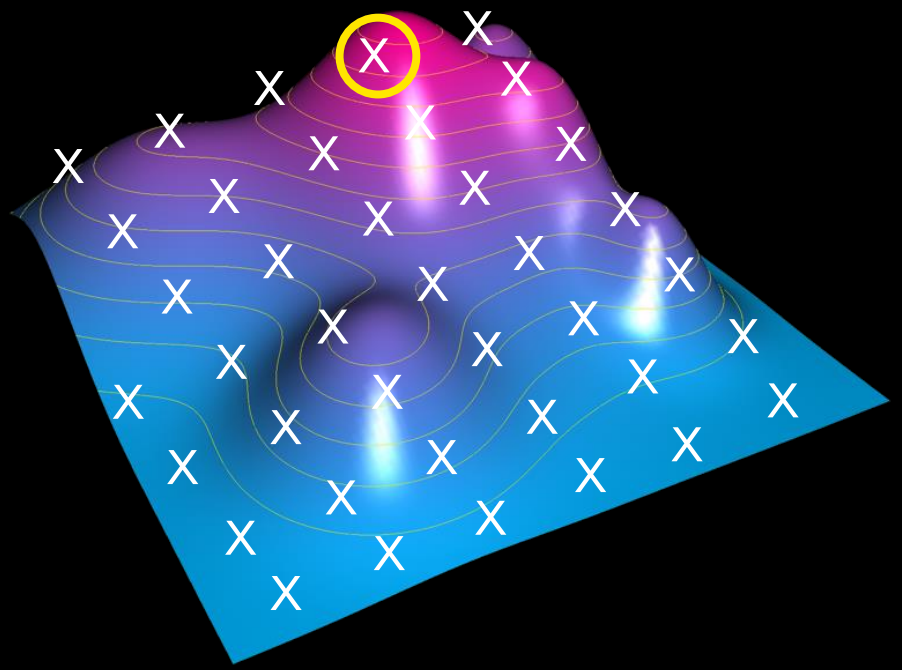


Sequential assays
Optimize for one parameter at a time



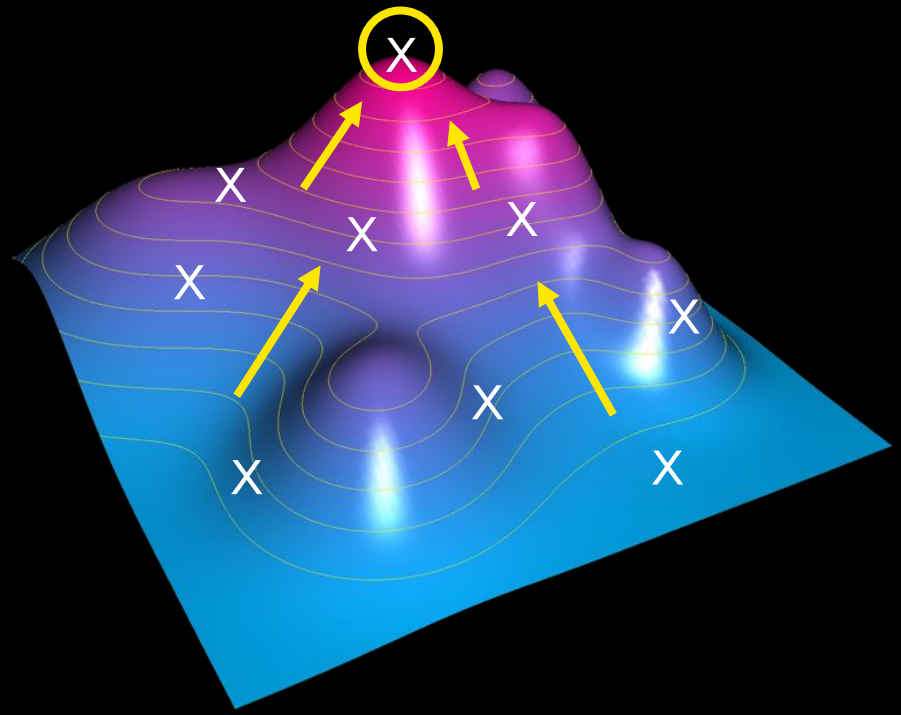
Design Of Experiment
Optimize for two parameters at once

DoE vs Library



A library

Requires high throughput
"low" relevance



Design of Experiment

Can use low throughput
"high" relevant

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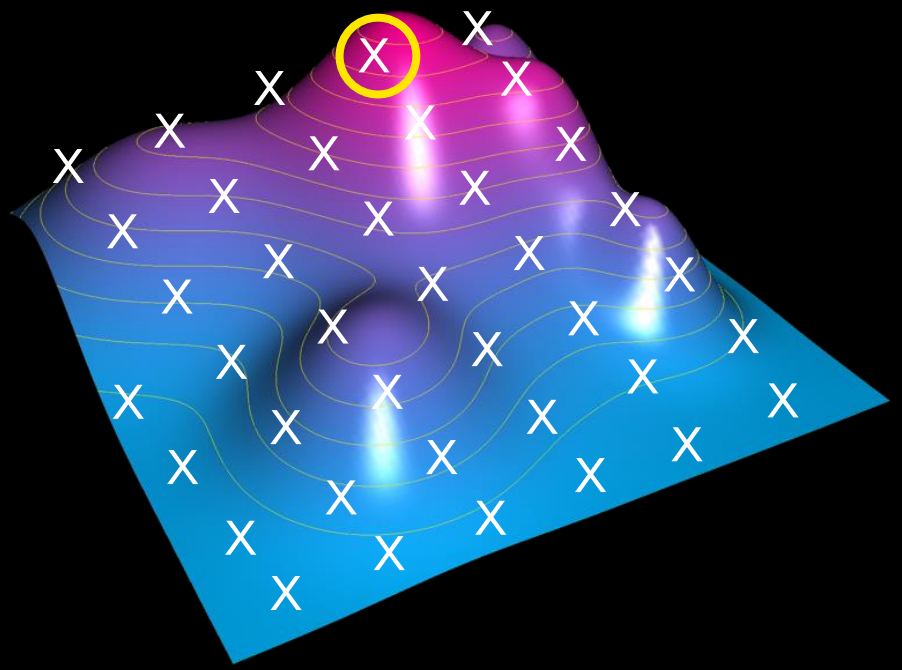
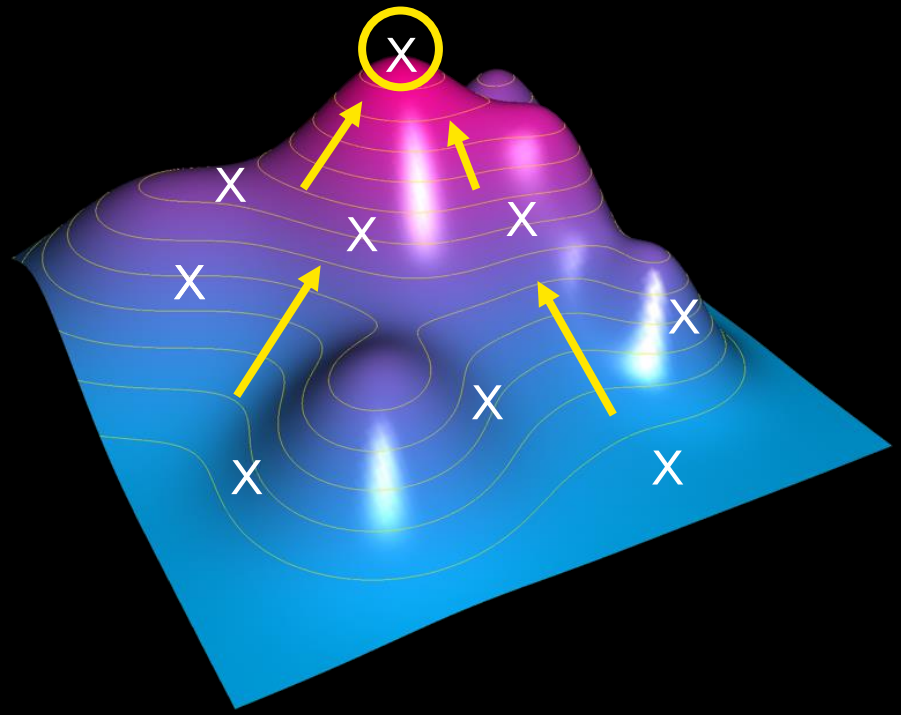
DoE vs Library



A library

Requires high throughput
low relevance **ASSAYS**



Design of Experiment

Can use low throughput
highly relevant **ASSAYS**

What antibody library size is required?

Average yeasts display diversity: 10^{8-9}

Average phage display diversity: 10^{10-11}

Estimated human repertoire: 10^{18-19}

How much of total theoretical diversity
does this cover?

How big of an antibody library is big enough?

Assume CDR length = 10aa = 30aa/variable domain
Assume 20aa choices at each position

$20^{30} = 10^{39}$ (1.7 x 10^{15} moles) possible sequences

Assume 500bp amplicon @ 325kDa each
Assume 1 copy of each sequence option in the library

1.7 x 10^{15} moles x 3.25 x 10^{5} g/mole = 5.25 x 10^{20}g
= 5.25 x 10^{14} metric tons

Assume an ultra large crude carrier (ULCC) has max DWT
~525,000 metric tons

5.25 x 10^{14} MT / 5.25 x 10^{5} MT/ULCC = 10^{9} ULCC's

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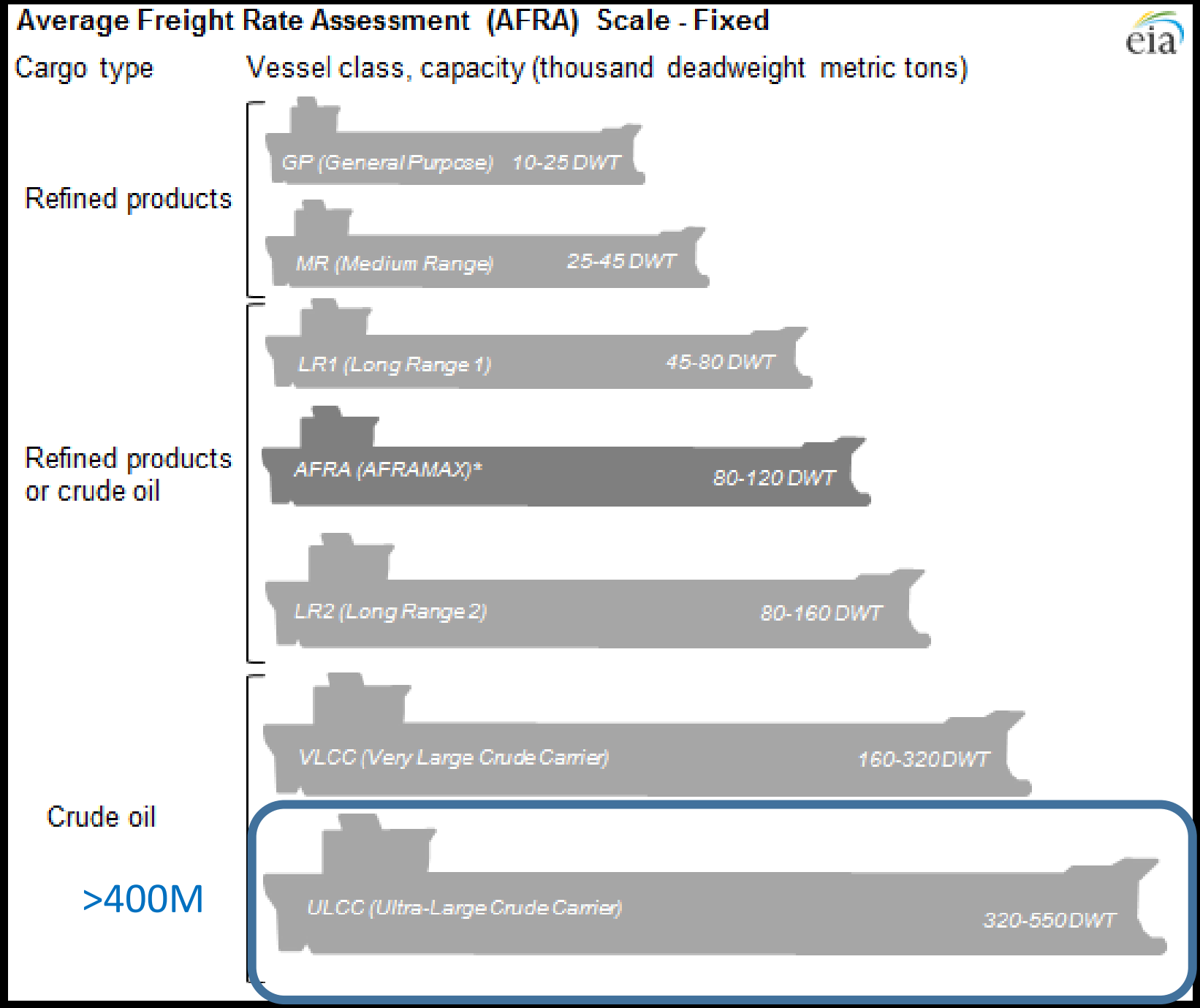

Average Freight Rate Assessment (AFRA) Scale - Fixed
eia
Cargo type
Vessel class, capacity (thousand deadweight metric tons)
Refined products
GP (General Purpose) 10-25 DWT
MR (Medium Range) 25-45 DWT
Refined products or crude oil
LR1 (Long Range 1) 45-80 DWT
AFRA (AFRAMAX)* 80-120 DWT
LR2 (Long Range 2) 80-160 DWT
Crude oil
VLCC (Very Large Crude Carrier) 160-320 DWT
ULCC (Ultra-Large Crude Carrier) 320-550 DWT
>400M


ФВП
HELLESPONT ALHAMBRA
MAJURO

People use less information than they think to make up their minds

Nadav Klein[a,1] and Ed O'Brien[b,1]

[a]Harris School of Public Policy, University of Chicago, Chicago, IL 60637; and [b]Booth School of Business, University of Chicago, Chicago, IL 60637

Edited by Susan T. Fiske, Princeton University, Princeton, NJ, and approved November 2, 2018 (received for review March 27, 2018)

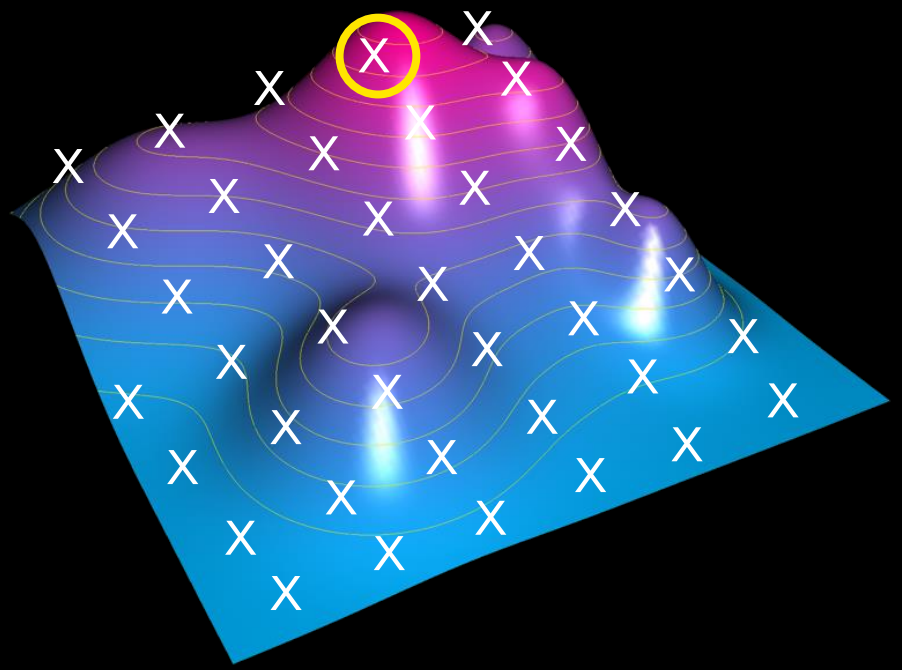
A world where information is abundant promises unprecedented opportunities for information exchange. Seven studies suggest these opportunities work better in theory than in practice: People fail to anticipate how quickly minds change, believing that they and others will evaluate more evidence before making up their minds than they and others actually do. From evaluating peers, marriage prospects, and political candidates to evaluating novel foods, goods, and services, people consume far less information than expected before deeming things good or bad. Accordingly, people acquire and share too much information in impression-formation contexts: People overvalue long-term trials, overpay for decision aids, and overwork to impress others, neglecting the speed at which conclusions will form. In today's information age, people may intuitively believe that exchanging ever-more information will foster better-informed opinions and perspectives—but much of this information may be lost on minds long made up.

critical piece of predicted versus actual tipping points. Critically, we emphasize that nearly all studies follow a "preexperience" paradigm, such that all participants, including predictors, first experience the stimulus once in full before rating it (beyond just reading a description). Thus, predictors are fully informed about "what" to imagine, with any subsequent mispredictions reflecting "how much" they thought they would need to experience before making up their minds. Studies 1 to 4 document this discrepancy across many judgments, from the (unforeseen) speed at which people form preferences to the (unforeseen) speed at which people judge others. Studies 5 to 7 highlight its problematic consequences: Gaining and providing access to information are not nearly as valuable as people think.

Results

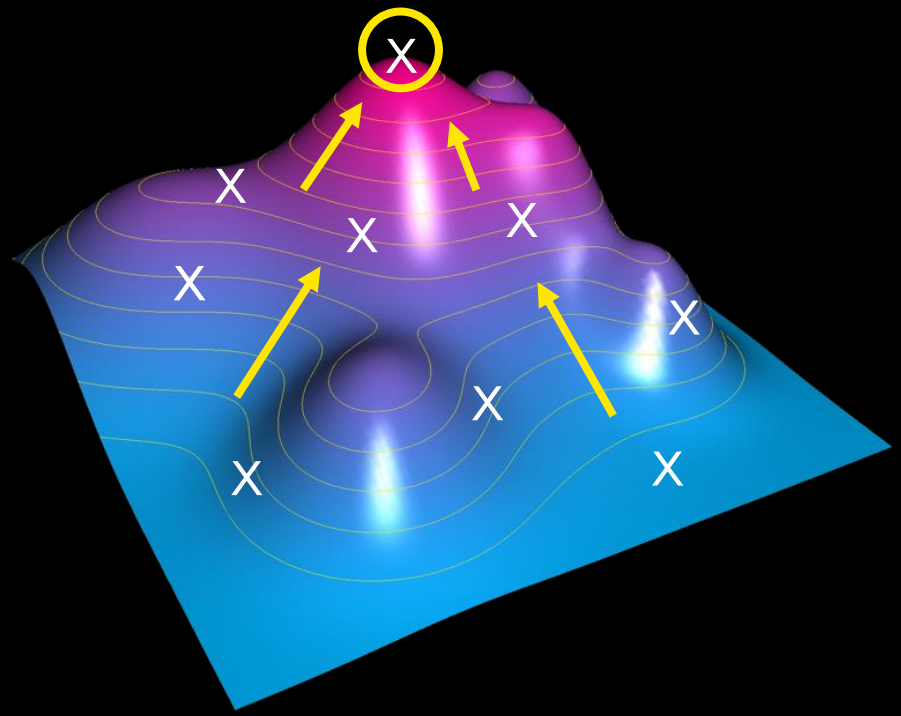
Study 1. In study 1, participants viewed different paintings featuring the same novel style of art, with no variation between the

Design of Experiments (DoE)



A library

Requires high throughput
low relevance **ASSAYS**

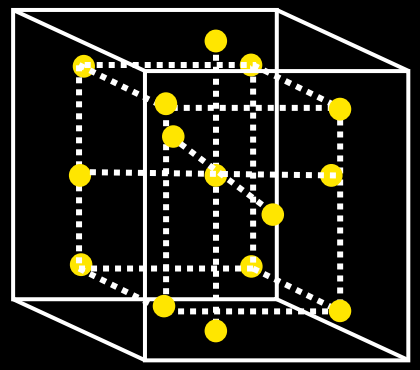


Design Of Experiment

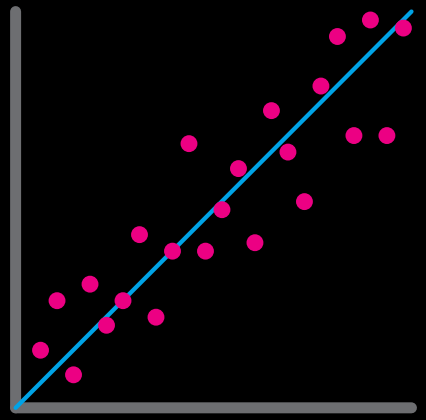
Can use low throughput
highly relevant **ASSAYS**

PATUM

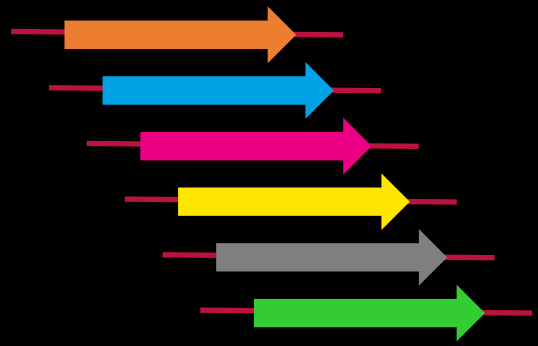
Design of Experiment



Learn



GPS platform



Build

Test

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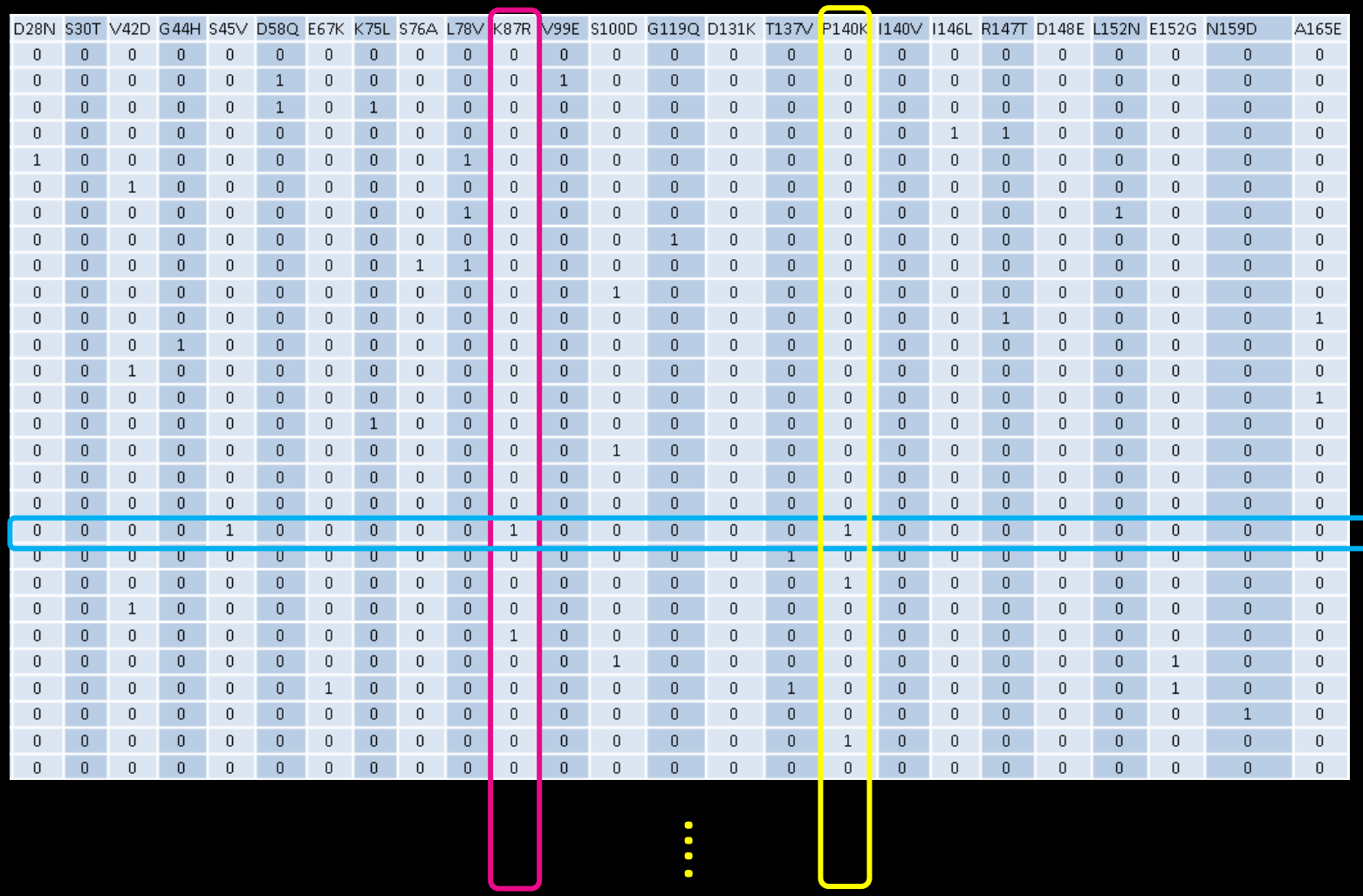
DoE: variable matrix

AA substitutions (Variables)

Protein Variants



D28N	S30T	V42D	G44H	S45V	D58Q	E67K	K75L	S76A	L78V	K87R	V99E	S100D	G119Q	D131K	T137V	P140K	I140V	I146L	R147T	D148E	L152N	E152G	N159D	A165E
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
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0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

- Target affinity
- Cross reactivity
- Functionality
  - blocking
  - activating
  - cell based
  - other
- Solubility
- Expression titer
- Thermostability
- Immunogenicity
- Patentability

... etc ...

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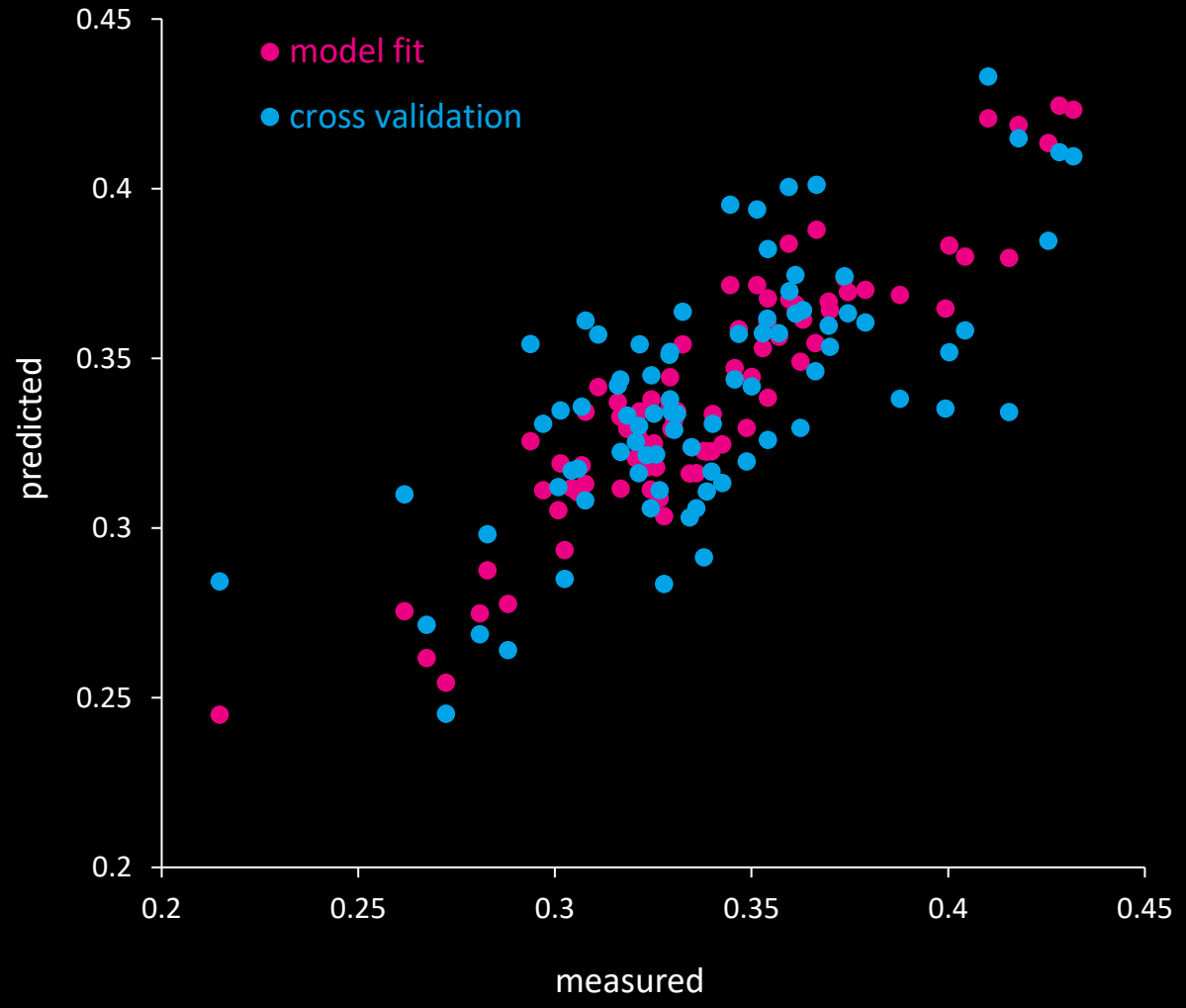
Machine learning models



- Consensus Models from several algorithms
- Models for every measured attribute
- Models on fitness functions
- Cross-validated leaving 15% out
- ~96 variants per round

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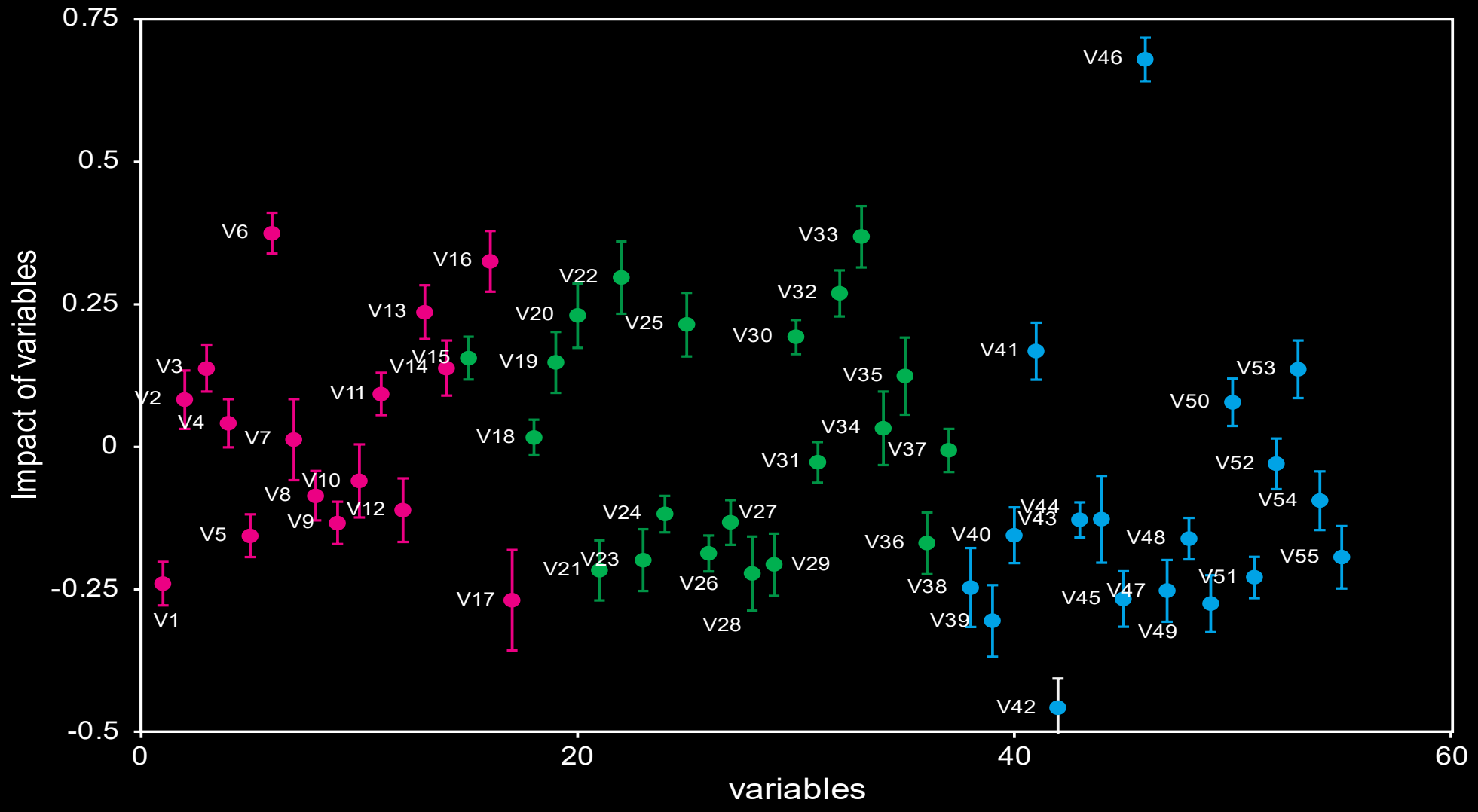
Mapping variable impact



Quantifies impact of substitutions

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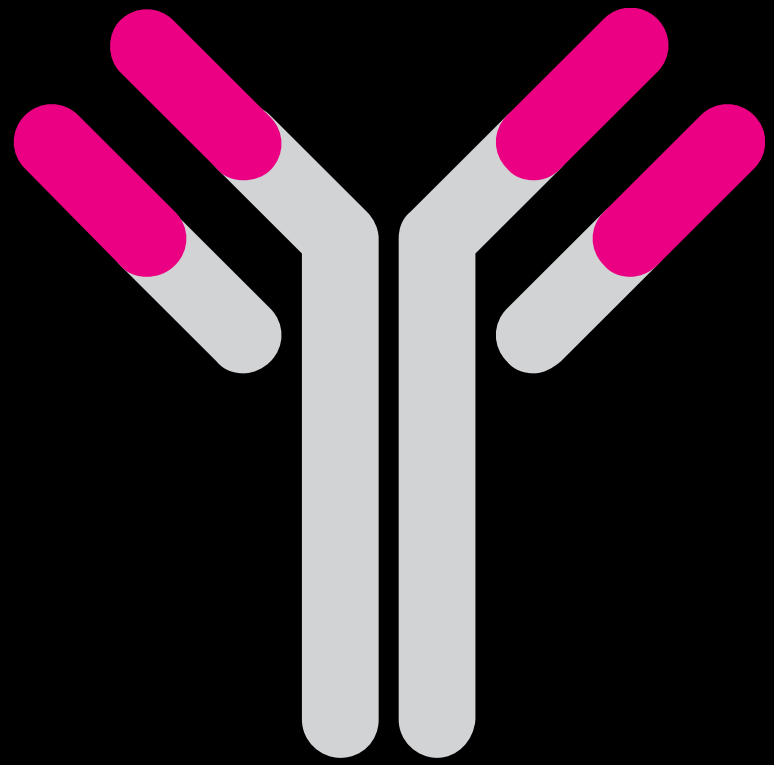
Antibody case study

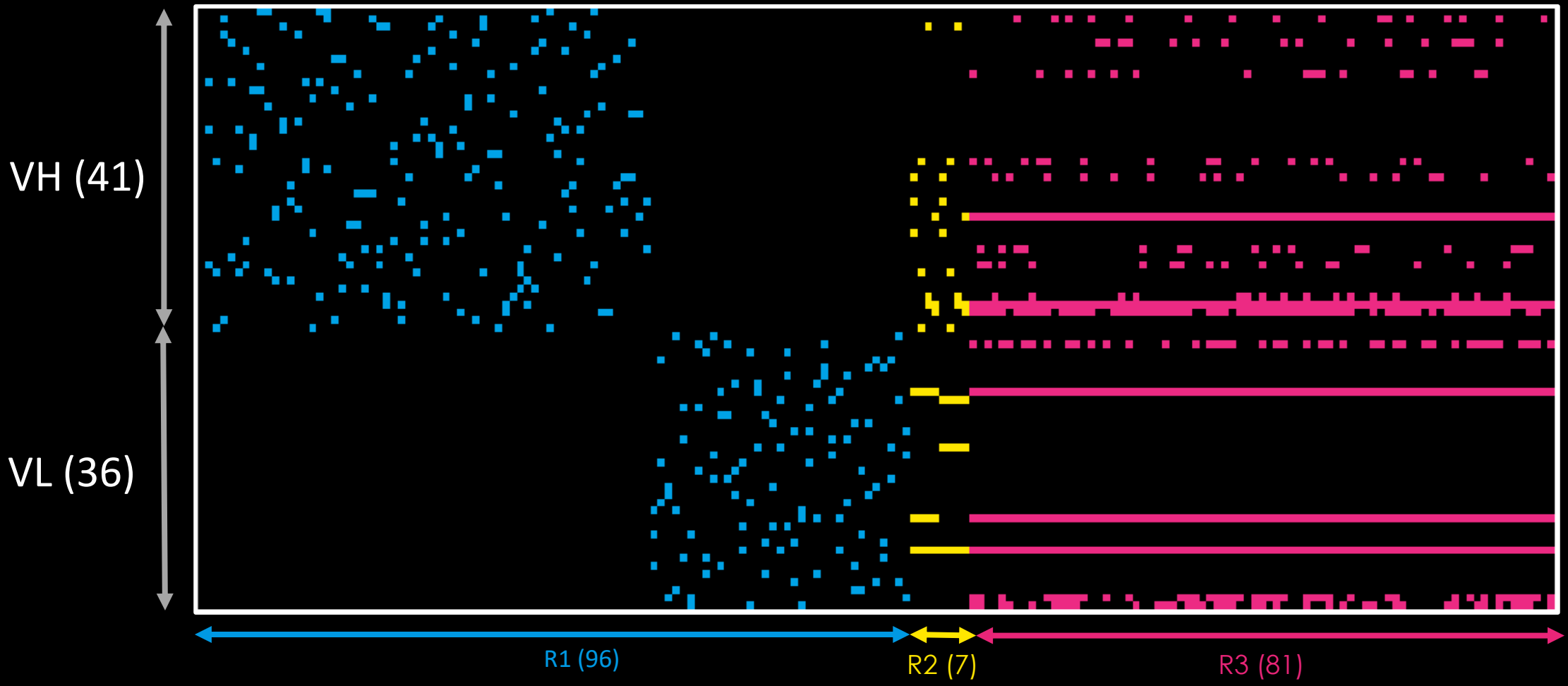
<u>Explored space:</u>

VH = ~10^{12}
VL = ~10^{10}

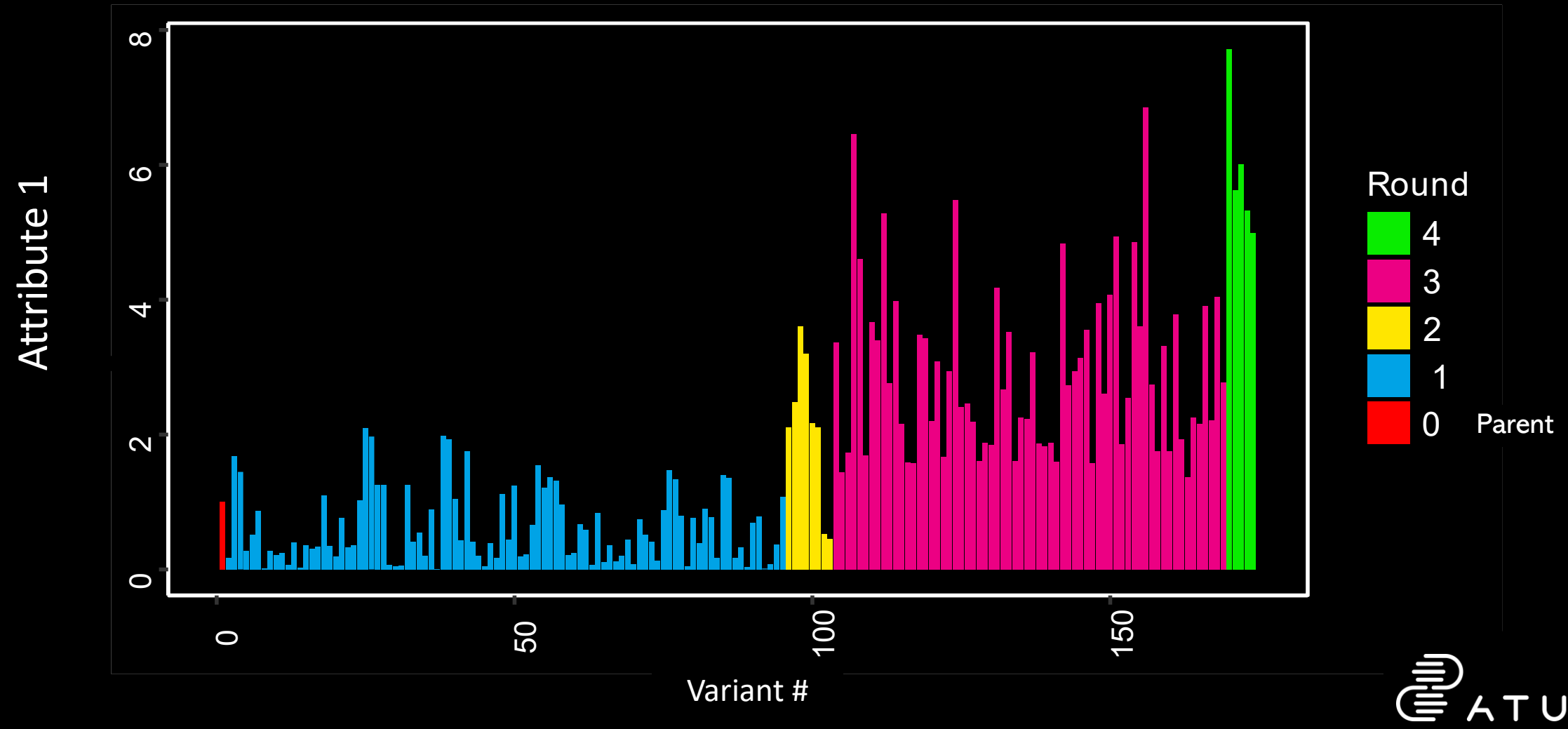
Total: 10^{22}



Variable matrix



Improvement by round



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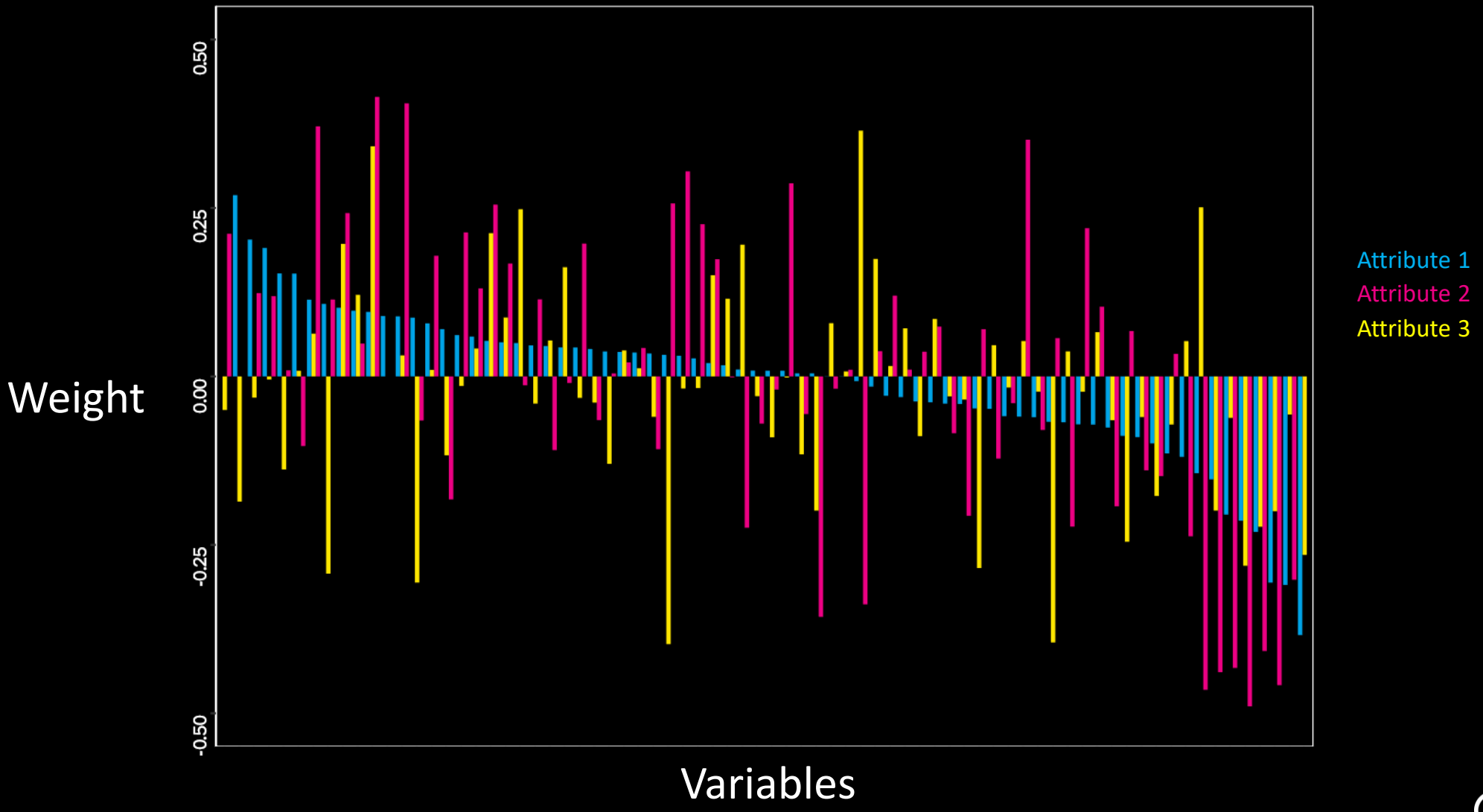
Multi-dimensional variable weight plot



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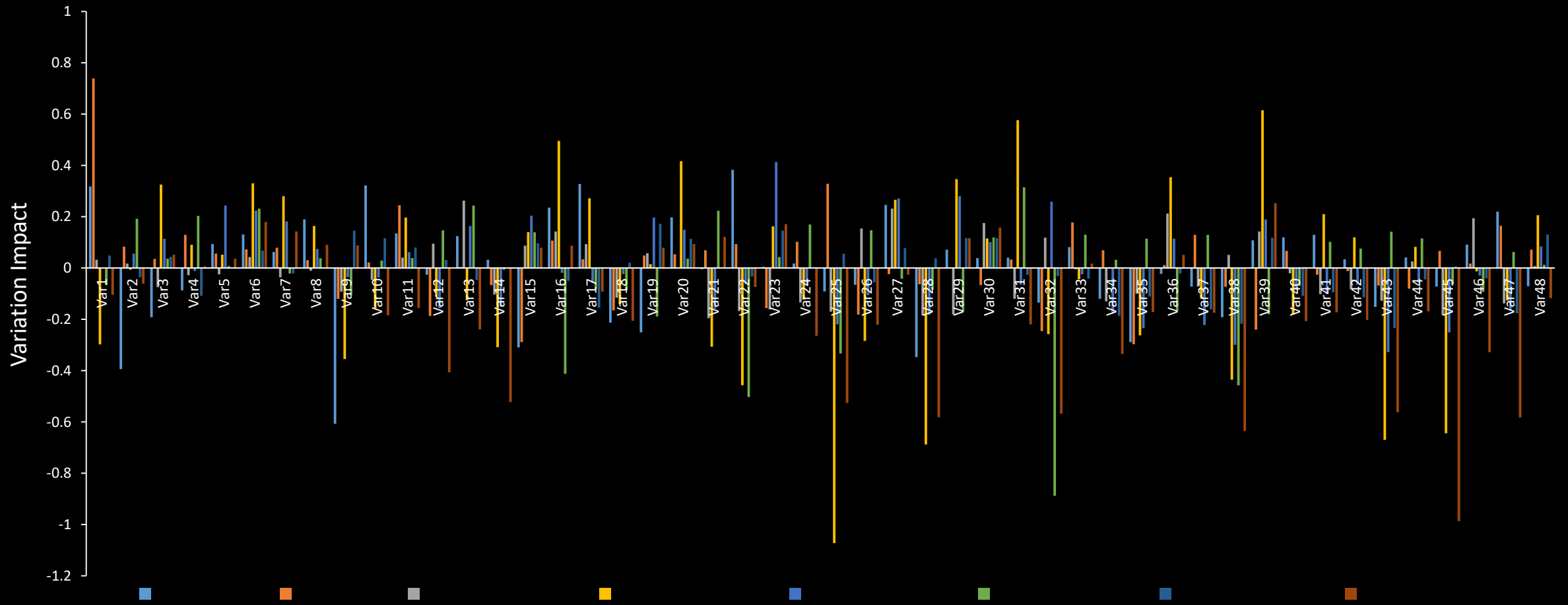

8 unique attributes / assay measurements

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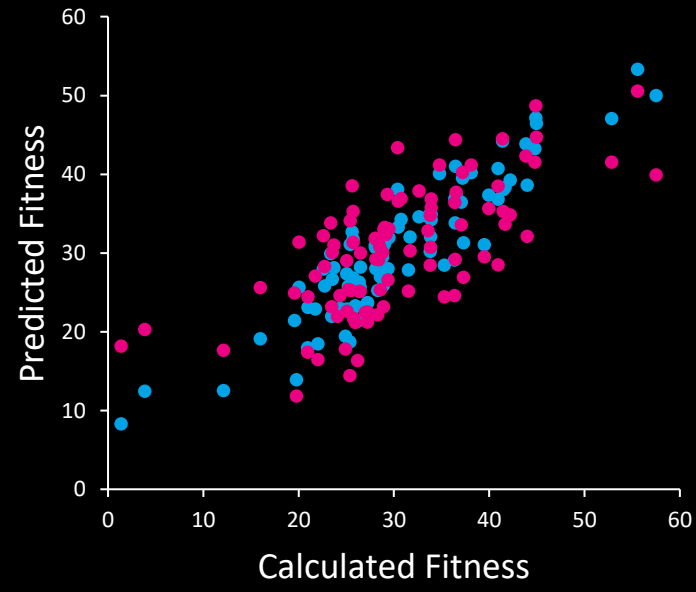
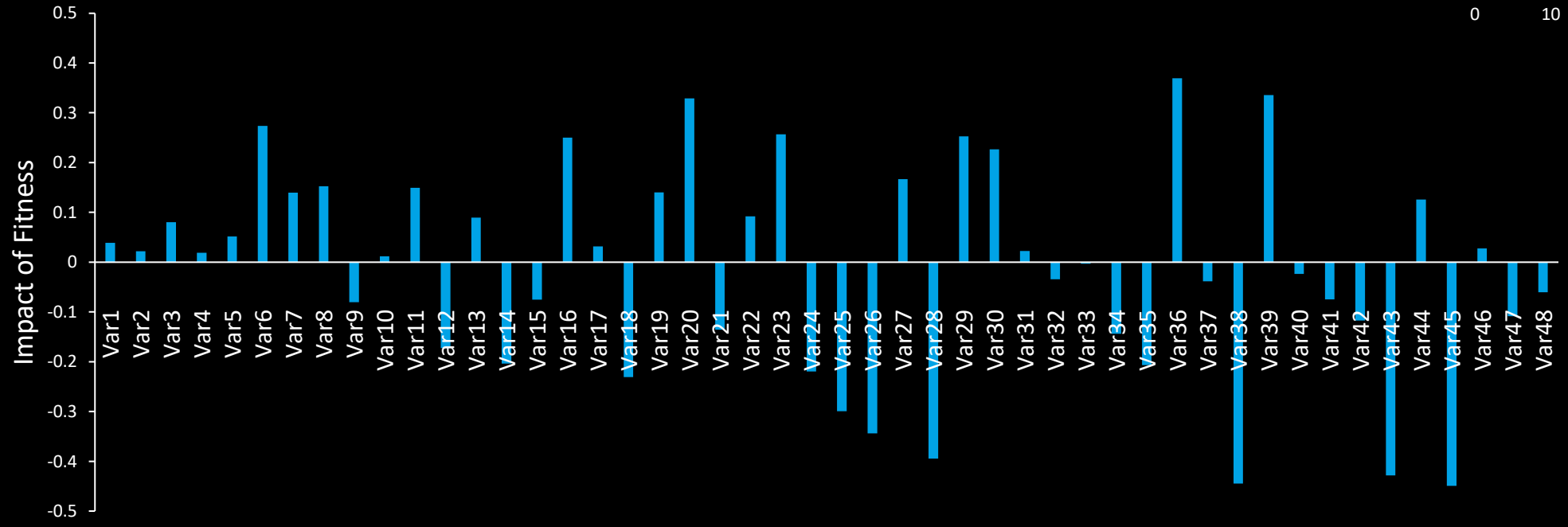
Multi-dimensional Fitness

Fitness = 6x Function A
1x Function B
3x Function C
5x Function D
2x Function E
2x Function F
5x Function G
5x Function H





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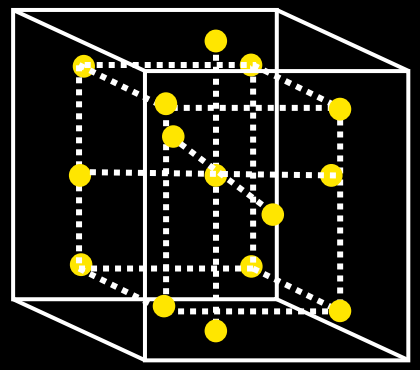
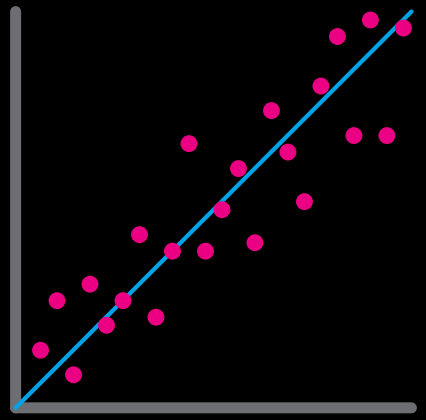
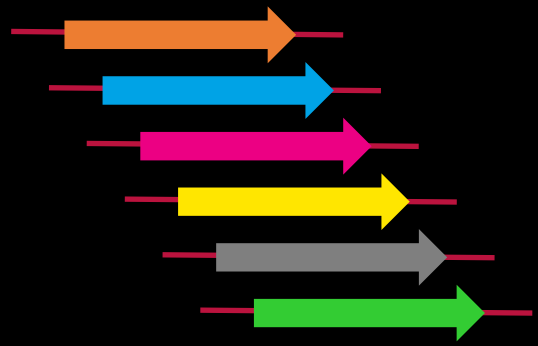
Design of Experiment



Learn



GPS platform



Build

Test

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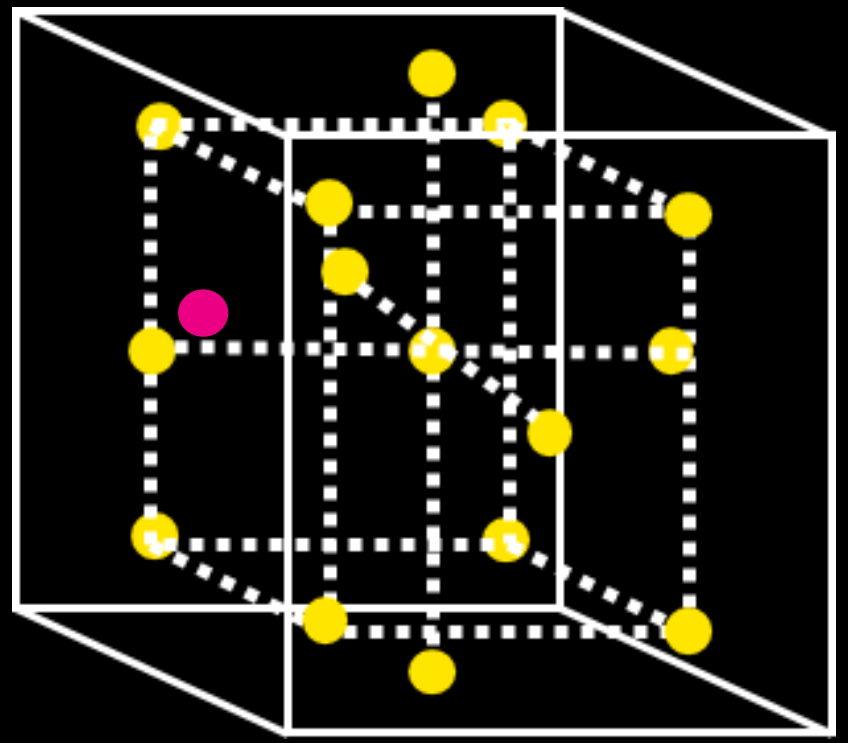
Life is multi-dimensional



Winner

- ✓ Cell based assay
- ✓ Antigen binding
- ✓ Cross reactivity
- ✓ Aggregation
- ✓ Thermostability
- ✓ Humanized
- ✓ Solubility
- ✓ IP
- ✓ …And more

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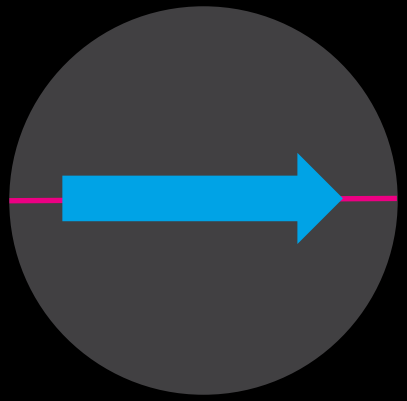
The GPS Platform



gene GPS

ORF codon optimization

vector GPS

Expression vector element optimization

protein GPS

Protein attribute optimization

ATUM

ATUM

- Gene synthesis, vectors
  - Large, complex, routine
  - Host optimized
- Protein production
  - 96-well to 100’s of grams
  - mAbs to others
  - Mammalian, e. coli, other
- Protein analytics
  - MS, HPLC, CE, other
  - Developability
- Cell based assays
  - FACS, signaling, other
  - Primary immune cells
- **Cell Line Development**

ATUM

Thank You

Technology presented is protected by issued US patents 11162102, 11060109, 11060098, 11060086, 10435696, 10435696, 10344285, 10287590, 10253321, 10233454, 10041077, 9771402, 9580697, 9574209, 9534234, 9493521, 9428767, 9290552, 9206433, 9102944, 8975042, 8825411, 8635029, 8412461, 8401798, 8323930, 8158391, 8126653, 8005620, 7805252, 7561973, 7561972 and pending applications

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