This talk is based on joint work with Chenette, Philipps, Pudwell

Occurrences of a specific pattern in hypercube orientations

Manda Riehl

Math, then bio?

Bio, then math

Fitness Landscapes (Crona and Wiesner)

The typical allele (unmutated type) will be called the *wild type*. Populations have members with mutations, and those mutants can have better or worse tness for their environment.

Over generations, we expect the population tness to increase from the pressures of natural selection.

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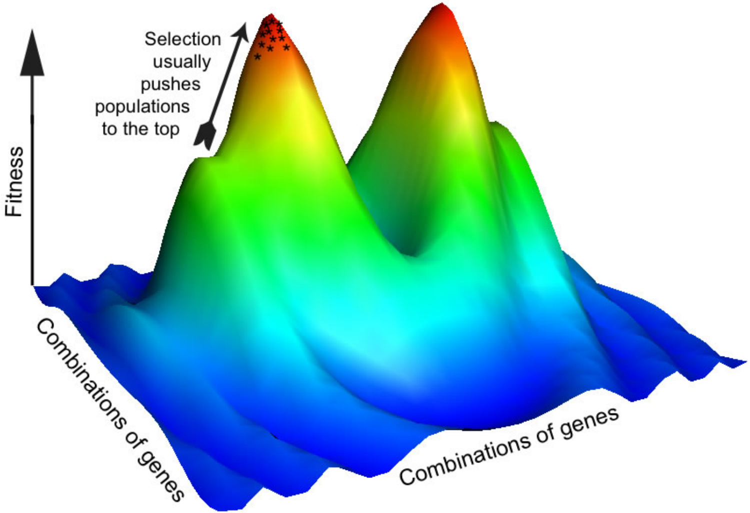
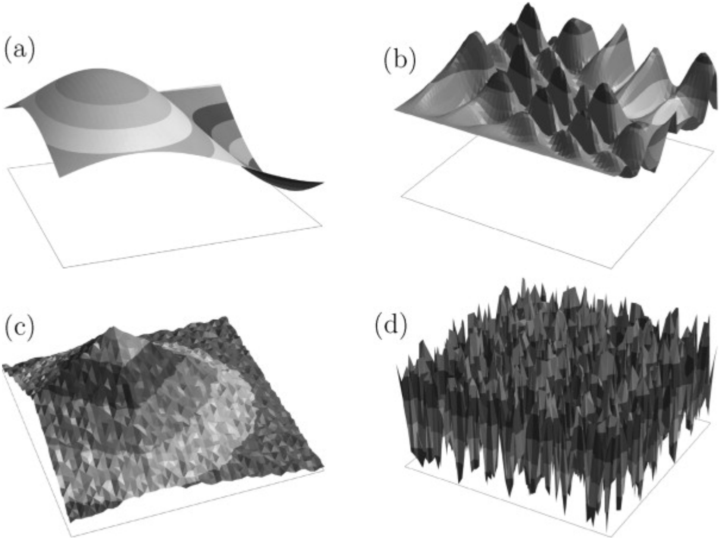
Fitness Landscapes



Which landscape is most likely?



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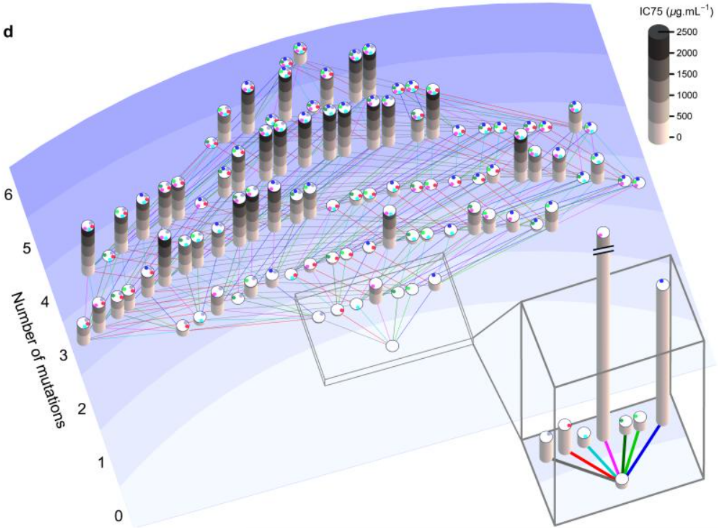
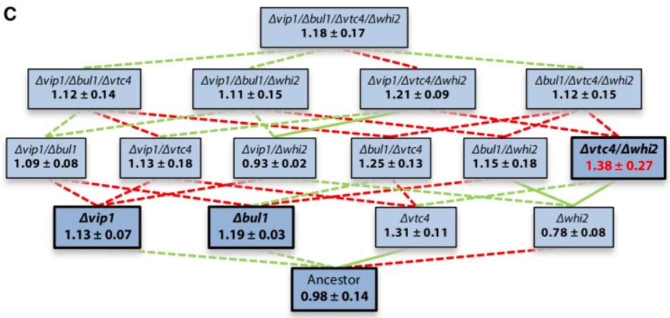

d
IC75 (μg.mL^{-1})
2500
2000
1500
1000
500
0
6
5
4
3
2
1
0
Number of mutations


C
Δvip1/Δbul1/Δvtc4/Δwhi2
1.18 ± 0.17
Δvip1/Δbul1/Δvtc4
1.12 ± 0.14
Δvip1/Δbul1/Δwhi2
1.11 ± 0.15
Δvip1/Δvtc4/Δwhi2
1.21 ± 0.09
Δbul1/Δvtc4/Δwhi2
1.12 ± 0.15
Δvip1/Δbul1
1.09 ± 0.08
Δvip1/Δvtc4
1.13 ± 0.18
Δvip1/Δwhi2
0.93 ± 0.02
Δbul1/Δvtc4
1.25 ± 0.13
Δbul1/Δwhi2
1.15 ± 0.18
Δvtc4/Δwhi2
1.38 ± 0.27
Δvip1
1.13 ± 0.07
Δbul1
1.19 ± 0.03
Δvtc4
1.31 ± 0.11
Δwhi2
0.78 ± 0.08
Ancestor
0.98 ± 0.14

Discrete Landscapes

Here we have 3 genes, with increasing tness marked with arrows.

It's acyclic!

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Here we have 3 genes, with increasing tness marked with arrows.
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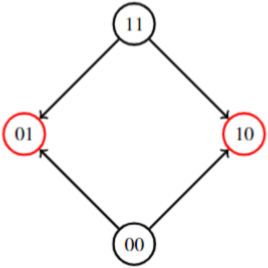
Which animal is this?

Reciprocal Sign Epistasis (RSE)

Two mutations, each bene cial, but both is worse than either individually



Or two mutations, each deleterious, but together bene cial.

Both are square faces of a hypercube with no maximal path of nontrivial length.

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Both are square faces of a hypercube with no maximal path of nontrivial length.

One early theorem in this area by Poelwijk et.al. states:

Theorem

A tness landscape cannot have more than one peak without an occurrence of RSE.

Extension of Poelwijk

Theorem (CPPR '21)

In any dimension, a lattice with k peaks contains at least k 1 RSEs.

Sketch of proof:

By induction: Take an n-dimensional acyclic hypercube Q_n with $k > 2$ peaks. Pick two of them, identify the sub-lattice between them, call it Q , with one peak at the bottom and the other at the top.Q has at least 1 RSE, and in that RSE some label has a bit 0 change to 1 in position i.

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Define Q^0_{n-1} to be the hypercube with 0 in position i and Q^1_{n-1} with 1.

Q^0_{n-1} has $j > 0$ peaks (therefore at least $j - 1$ RSE), and Q^1_{n-1} has $k - j > 0$ peaks (therefore at least $k - j - 1$ RSE.

So total we have at least

$(j - 1) + (k - j - 1) + 1 = k - 1$ RSEs.

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Visual Example

Visual Example

Visual Example

Visual Example

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We computationally study which combinations of peaks and RSEs are possible. Our results can therefore be described as theorems on the joint distribution of two patterns (peaks and RSEs) in acyclic Boolean lattices, and likewise nding the maximum number of RSEs can be considered a form of pattern packing.

Our primary focus is on which combinations of peak counts and RSE counts are possible, in other words the nonzero entries in the joint distribution of the two patterns peak and RSE.

		Peaks				
		0	1	2	3	4
	0	0	91	0	0	0
	1	0	84	42	0	0
	2	0	0	93	0	0
RSEs	3	0	0	12	8	0
	4	0	0	0	9	0
	5	0	0	0	0	0
	6	0	0	0	0	1

Table: For dimension 3, number of acyclic orientations with each (number of RSEs, number of peaks).

Theorem (CPPR '21)

Single-peaked n-dimensional lattices exist with r_n RSEs, where

$$r_n = 2^{n-3}(n^2 - 5n + 8) - 1. \tag{1}$$

Notably, the most significant term in this expression is $2^{n-3}n^2$. The total number of faces is $2^{n-3}(n^2 - n)$, which has the same most significant term. This means that, in high enough dimensions, an arbitrarily large proportion of the faces in a lattice can be RSEs while still having only one peak.

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Theorem (CPPR '21)

A single-peaked n-dimensional lattice cannot have more than

$$2^{n-3}(n^2 - n - 2\lfloor n/2 \rfloor) \tag{2}$$

RSE faces.

Conjecture (CPPR '21)

The maximum number of RSEs in a single-peaked n-dimensional lattice is $2^{n-3}(n^2 - 4n + 4)$.

n	2	3	4	5	6	7	8
Lower bound (known to be possible)	0	1	7	31	111	351	1023
Conjectured maximum	0	1	8	36	128	400	1152
Upper bound (more is impossible)	0	4	16	64	192	576	1536

Theorem (CPPR '21)

For $n \quad 4$, an n-dimensional lattice with $2^{n \quad 1} \quad (n \quad 1)$ peaks can have $2^{n \quad 2 \; \frac{n}{2} \qquad \frac{n}{2}}$ RSEs but not $2^{n \quad 2 \; \frac{n}{2} \qquad \frac{n}{2}} \quad 1$ RSEs.

Theorem

For $n \quad 4$, if an n-dimensional lattice has at least $2^{n} \; {}^{2} \; {}^{n}_{2} \quad (n \quad 1) \quad (n \quad 2)$ RSEs, then it must have exactly:

- $2^{n} \; {}^{2} \; {}^{n}_{2}$ *(every face),*
- $2^{n} \; {}^{2} \; {}^{n}_{2} \quad (n \quad 1)$, *or*
- $2^{n} \; {}^{2} \; {}^{n}_{2} \quad (n \quad 1) \quad (n \quad 2)$

RSEs.

We also came up with a variety of explicit construction algorithms, mostly involving adding connecting edges between two smaller lattices, to give an explicit examples of a wide variety of RSE/peak combinations.

RSEs n Peaks	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
0	g	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
1	g	G	X	X	X	X	X	X	X	X	X	X	X	X	X	X
2	g	G	G	X	X	X	X	X	X	X	X	X	X	X	X	X
3	g	G	G		X	X	X	X	X	X	X	X	X	X	X	X
4	g	G	G	P		X	X	X	X	X	X	X	X	X	X	X
5	g	G	G	G			X	X	X	X	X	X	X	X	X	X
6	g	G	G	G				X	X	X	X	X	X	X	X	X
7	g	G	G	G	P				X	X	X	X	X	X	X	X
8	g	G	G	G	G					X	X	X	X	X	X	X
9	g	G	G	G	G						X	X	X	X	X	X
10	g	G	G	G	G	P						X	X	X	X	X
11	g	G	G	G	G	P							X	X	X	X
12	g	G	G	G	G	G								X	X	X
13	g	G	G	G	G	G									X	X
14	g	G	G	G	G	G	P									X
15	g	G	G	G	G	G	P									X
16	g	G	G	G	G	G	P									X
17	B	G	G	G	G	G	P									X
18	B	G	G	G	G	G	G	P								X
19	B	G	G	G	G	G	G	P								X
20	B	G	G	G	G	G	G	P								X
21	B	g	G	G	G	G	G	P								X
22	B	g	G	G	G	G	G	P								X
23	B	g	G	G	G	G	G	P	P							X
24	B	g	G	G	G	G	G	G	P							X
25	B	B	G	G	G	G	G	G	P							X
26	B	B	G	G	G	G	G	G	P							X
27	B	B	G	G	G	G	G	G	P							X
28	B	B	g	G	G	G	G	G	P							X
29	B	B	g	G	G	G	G	G	P	P						X
30	B	B	B	G	G	G	G	G	P	P						X
31	B	B	B	G	G	G	G	G	P	P						X
32	B	B	B	G	G	G	G	G	P	P						X
33	F	B	B	G	G	G	G	G	P	P						X
34		B	B	g	G	G	G	G	P	P						X
35		F	B	g	G	G	G	G	P	P	P					X
36		B	B	B	G	G	G	G	P	P	P					X
37		F	B	B	G	G	G	G	P	P	P					X
38		F	F	B	G	G	G	G	P	P	P					X
39		F	F	B	g	G	G	G	P	P	P					X
40		F	F	F	g	G	G	G	P	P	P					X
41			F	F	F	G	P	G	P	P	P					X
42		F	F	F	g	G	G	G	P	P	P	P				X
43			F	F	F	G	G	G	P	P	P	P				X
44			F	F	F	P	P	P	P	P	P	P				X
45				F	F	O	G	G	P	P	P	P				X
46				F	F	O	P	P	P	P	P	P				X
47				F	F	O	P	P	P	P	P	P				X
48					F	F	P	G	P	P	P	P				X
49					F	F	O	P	P	P	P	P				X
50						F	O	P	P	P	P	P				X
51					F		O	P	P	P	P	P	P			X
52						F	F	P	P	P	P	P	P			X
53						F	O	P	P	P	P	P	P			X
54							F	P	P	P	P	P	P			X
55								O	P	P	P	P	P			X
56							F	F	P	P	P	P	P			X
57								O	O	P	P	P	P			X
58									P	P	P	P	P			X
59									O	P	P	P	P			X
60								O		P	P	P	P	P		X
61									O		P	P	P	P		X
62										P	P	P	P	P		X
63										O	P	P	P	P		X
64											P	P	P	P		X
65	X											P	P	P		X
66	X										O	P	P	P		X
67	X											P	P	P		X
68	X												P	P		X
69	X											X	P	P		X
70	X											O		P	P	X
71	X												P		P	X
72	X													P		X
73	X													P	P	X
74	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
75	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
76	X														P	X
77	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
78	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
79	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
80	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	P

Thank you all! Thank you Lara!

A 3 drug cycle alternating the antibiotics cefepime, ceftazidime, and cefprozil