# Statistics on hypercube orientations

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joint work with
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# Hypercube Definition

## Hypercube graph ($Q_n$)

Vertex set: binary words of length $n$
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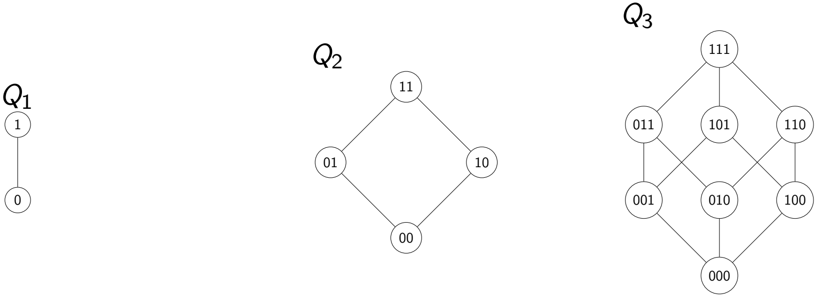

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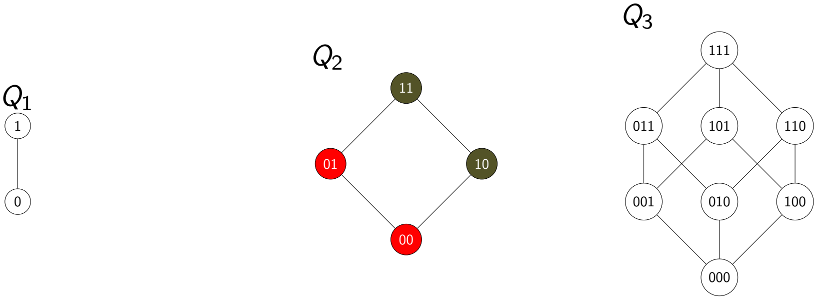
Alternate construction: take two copies of $Q_{n-1}$
Connect "corresponding" vertices.



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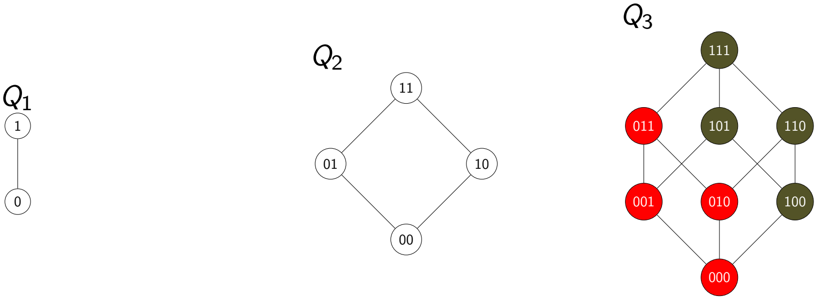
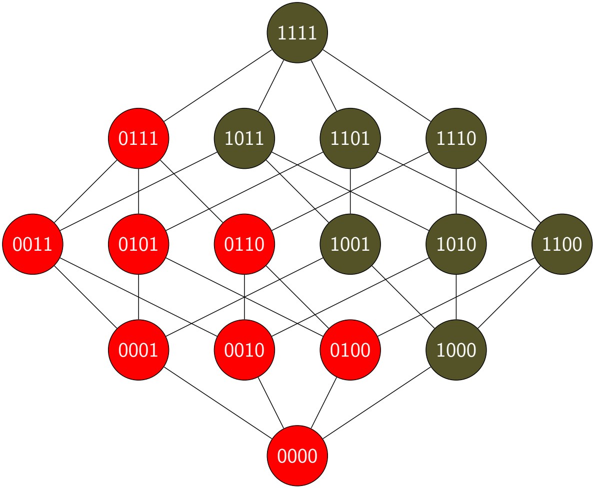


# Hypercube Construction

$Q_4$



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- $\chi(Q_n)(-1)$ acyclic orientations (Stanley, 2006)
  $2, 14, 1862, 193270310, \ldots$

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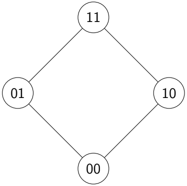
Goal: Consider acyclic orientations of $Q_n$.
Analyze joint distribution of two statistics motivated by theoretical biology.

# Fitness Landscapes

Vocab:

- *genotype*: genetic makeup of an organism
- *wild type*: genotype of majority of a population
  represented by $0 \cdots 0$ vertex
- *mutant*: has one or more gene mutations compared to wild type
  represented by vertex with 1s
- *mutational neighbor*: genotypes differing by exactly one mutation



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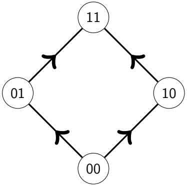

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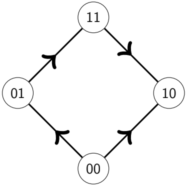
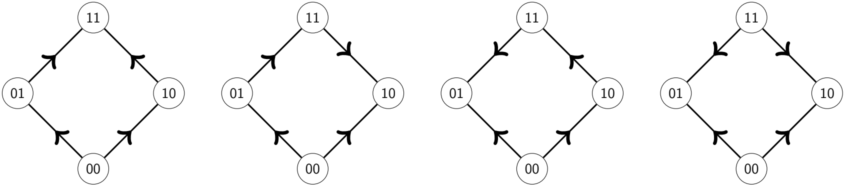


# Fitness Landscapes

*Fitness landscapes* are represented by acyclic orientations of a hypercube.

Simplifying assumption: Wild type is less fit than any mutant.



# Fitness Landscape Features

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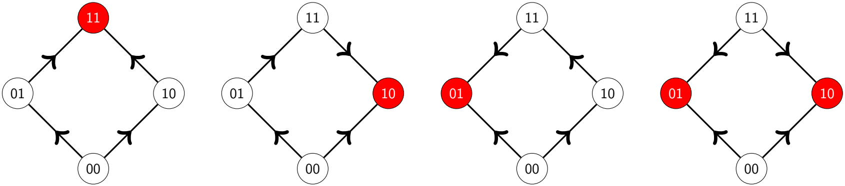
Important features:

- peaks: vertex where all edges point inward



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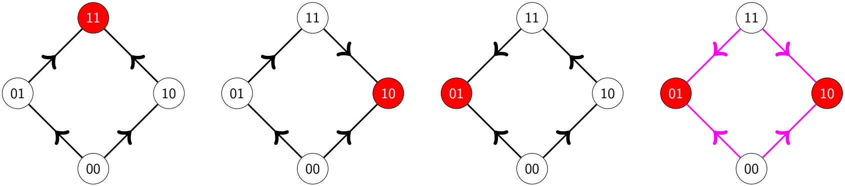

# Fitness Landscape Features

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Important features:

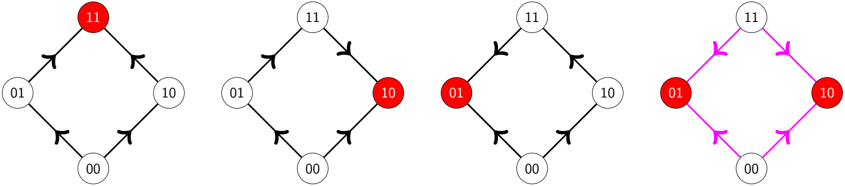
- peaks: vertex where all edges point inward
- reciprocal sign epistasis (RSE): 4-cycle with alternating direction edges

Known: RSEs are necessary for multi-peak landscapes (Poelwijk et. al., 2011)

Questions:

- What pairs of (number of peaks, number of RSEs) are possible?
- In a single peak landscape, what is the maximum possible number of RSEs?

# Dimension 2



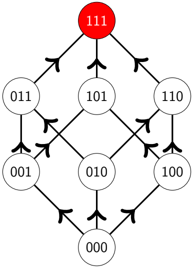

| RSEs\peaks | 1 | 2 |
|---|---|---|
| **0** | 3 | 0 |
| **1** | 0 | 1 |

# Dimension 3 (Exact count, 340 possible orientations)

| RSEs\peaks | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| 0 | 91 | 0 | 0 | 0 |
| 1 | 84 | 42 | 0 | 0 |
| 2 | 0 | 93 | 0 | 0 |
| 3 | 0 | 12 | 8 | 0 |
| 4 | 0 | 0 | 9 | 0 |
| 5 | 0 | 0 | 0 | 0 |
| 6 | 0 | 0 | 0 | 1 |

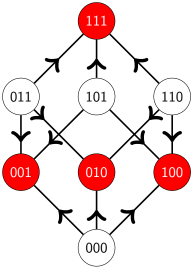
# Extreme Constructions

All Ups




1 peak
0 RSEs

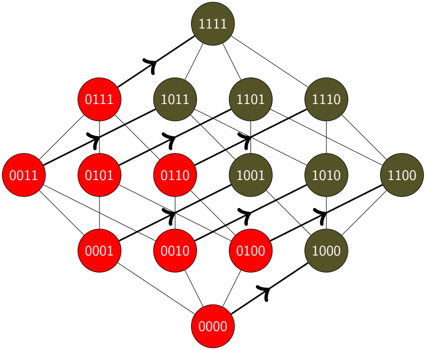
Alternating




$2^{n-1}$ peaks
$2^{n-3}(n-1)n$ RSEs

# Standard Gluing

Take two copies of $Q_{n-1}$, connect corresponding vertices with up arrow.




Observe: If lower $Q_{n-1}$ has $p_1$ peaks and $r_1$ RSEs,
and upper $Q_{n-1}$ has $p_2$ peaks and $r_2$ RSEs,
then glued $Q_n$ has $p_2$ peaks and $r_1 + r_2$ RSEs.

# Scaling up

## Dimension 3 options

| RSEs\ peaks | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| 0 | X | | | |
| 1 | X | X | | |
| 2 | | X | | |
| 3 | | X | X | |
| 4 | | | X | |
| 5 | | | | |
| 6 | | | | X |

## Dimension 4 gluing

| RSEs\ peaks | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| 0 | X | | | | | | | |
| 1 | X | X | | | | | | |
| 2 | X | X | | | | | | |
| 3 | X | X | X | | | | | |
| 4 | X | X | X | | | | | |
| 5 | X | X | X | | | | | |
| 6 | X | X | X | X | | | | |
| 7 | X | X | X | X | | | | |
| 8 | | X | X | X | | | | |
| 9 | | X | X | X | | | | |
| 10 | | | X | X | | | | |
| 11 | | | | | | | | |
| 12 | | | | X | | | | |
| 13 | | | | | | | | |
| 14 | | | | | | | | |
| 15 | | | | | | | | |
| 16 | | | | | | | | |
| 17 | | | | | | | | |
| 18 | | | | | | | | |
| 19 | | | | | | | | |
| 20 | | | | | | | | |
| 21 | | | | | | | | |
| 22 | | | | | | | | |
| 23 | | | | | | | | |
| 24 | | | | | | | | |

# Dimension 4

Dimension 4 gluing

All options from gluing two $Q_3$s

| RSEs\ peaks | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| 0 | X | | | | | | | |
| 1 | X | X | | | | | | |
| 2 | X | X | | | | | | |
| 3 | X | X | X | | | | | |
| 4 | X | X | X | | | | | |
| 5 | X | X | X | | | | | |
| 6 | X | X | X | X | | | | |
| 7 | X | X | X | X | | | | |
| 8 | | X | X | X | | | | |
| 9 | | X | X | X | | | | |
| 10 | | | X | X | | | | |
| 11 | | | | | | | | |
| 12 | | | | X | | | | |
| 13 | | | | | | | | |
| 14 | | | | | | | | |
| 15 | | | | | | | | |
| 16 | | | | | | | | |
| 17 | | | | | | | | |
| 18 | | | | | | | | |
| 19 | | | | | | | | |
| 20 | | | | | | | | |
| 21 | | | | | | | | |
| 22 | | | | | | | | |
| 23 | | | | | | | | |
| 24 | | | | | | | | |

Dimension 4 heat map

10,000 randomly generated orientations

| RSEs\peaks | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 8 | 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 28 | 36 | 1 | 0 | 0 | 0 | 0 | 0 |
| 3 | 50 | 137 | 8 | 0 | 0 | 0 | 0 | 0 |
| 4 | 52 | 380 | 59 | 0 | 0 | 0 | 0 | 0 |
| 5 | 27 | 597 | 369 | 7 | 0 | 0 | 0 | 0 |
| 6 | 16 | 473 | 792 | 47 | 0 | 0 | 0 | 0 |
| 7 | 2 | 275 | 1002 | 192 | 0 | 0 | 0 | 0 |
| 8 | 1 | 213 | 795 | 420 | 0 | 0 | 0 | 0 |
| 9 | 0 | 55 | 643 | 631 | 29 | 0 | 0 | 0 |
| 10 | 0 | 17 | 249 | 625 | 64 | 0 | 0 | 0 |
| 11 | 0 | 0 | 99 | 569 | 99 | 0 | 0 | 0 |
| 12 | 0 | 4 | 11 | 208 | 140 | 1 | 0 | 0 |
| 13 | 0 | 0 | 9 | 71 | 89 | 13 | 0 | 0 |
| 14 | 0 | 0 | 0 | 40 | 68 | 45 | 0 | 0 |
| 15 | 0 | 0 | 0 | 8 | 50 | 18 | 0 | 0 |
| 16 | 0 | 0 | 0 | 0 | 26 | 39 | 0 | 0 |
| 17 | 0 | 0 | 0 | 0 | 0 | 15 | 0 | 0 |
| 18 | 0 | 0 | 0 | 0 | 16 | 7 | 20 | 0 |
| 19 | 0 | 0 | 0 | 0 | 0 | 6 | 6 | 0 |
| 20 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 21 | 0 | 0 | 0 | 0 | 0 | 0 | 10 | 0 |
| 22 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 23 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 24 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |

# Motivating Question

What is the largest number of RSEs in a single peak landscape?

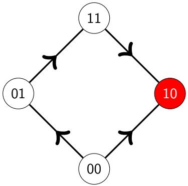
Strategy: Find a topological order of vertices with nice properties.

# Topological Orders

## Definition

A *topological order* of an oriented graph is a list of all the vertices such that each edge is directed from an earlier vertex to a later vertex in the list.

Example:




has topological order 00, 01, 11, 10.

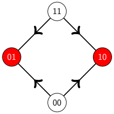
## Theorem

A directed graph is acyclic if and only if it has a topological order.

# Topological Orders

Observations:

- Topological orders aren't always unique!




has orders (00, 11, 01, 10), (11, 00, 01, 10), (00, 11, 10, 01), and (11, 00, 10, 01).

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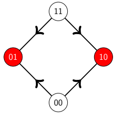
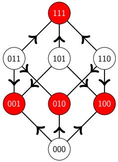



has orders (00, 11, 01, 10), (11, 00, 01, 10), (00, 11, 10, 01), and (11, 00, 10, 01).

- The alternating construction has a topological order of the form (even vertices, odd vertices)




has order (000, 011, 101, 110, 001, 010, 100, 111).

# Topological Orders

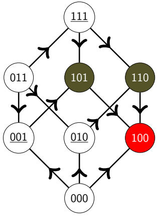
Observations:

- If a topological order $(v_1, \ldots, v_n)$ corresponds to a single peak orientation, then for all $v_i$ with $i < n$, there exists $v_j$ with $j > i$ such that $v_i$ is adjacent to $v_j$.(*)

Goal: Find a topological order of the form:

(even vertices, odd vertices, connected cover(*))

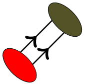
Example:




000, 011, <u>010</u>, <u>001</u>,
<u>111</u>, 101, 110, 100

# Strategic Topological Order Search Results

Maximum number of RSEs in a $n$-dimensional single peak orientation



| dimension | RSEs by gluing (% of all 4-cycles) | RSEs by search (% of all 4-cycles) |
|---|---|---|
| 2 | 0 (0) | 0 (0) |
| 3 | 1 (16.7) | 1 (16.7) |
| 4 | 7 (29.2) | |
| 5 | | |
| 6 | | |
| 7 | | |

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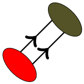

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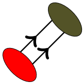

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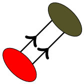

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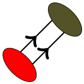

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| 7 | 359 (53.4) | (in progress) |

Theorem: As $n \to \infty$, the percent of 4-cycles that can be RSEs in a single-peak landscape approaches 100%.

# References


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# Thanks for listening!

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