All supplementary plots and tables show results for the following 7 sets of parameter values:
A) $\mu=10^{-6}, \theta=0.01, \lambda=1 / 2$ and 2 dimensions. This is identical to the figures in the main text
B) $\mu=10^{-4}, \theta=1, \lambda=1 / 2$ and 2 dimensions
C) $\mu=10^{-6}, \theta=0.01, \lambda=2$ and 2 dimensions
D) $\mu=10^{-6}, \theta=0.01, \lambda=1 / 4$ and 2 dimensions
E) $\mu=10^{-6}, \theta=0.01, \lambda=1 / 2$ and 3 dimensions
F) $\mu=10^{-6}, \theta=0.01, \lambda=1 / 2$ and 4 dimensions
G) $\mu=10^{-6}, \theta=0.01, \lambda=1 / 2$ and 7 dimensions

Figure S1. Phenotypic distribution of homozygous alleles as in Figure 1 for all sets of parameter values. For simulations containing more than two dimensions (plots E-G), only the first two dimensions are shown.

Figure S2. Epistasis as a function of overdominance as in Figure 3 for all sets of parameter values.

Figure S3. Maximum pairwise distance statistic as in Figure 4 for all sets of parameter values.

Figure S4. Maximum distance from optimal trajectory statistic as in Figure 5 for all sets of parameter values.

Figure S5. Effective number of paths statistic as in Figure 6 for all sets of parameter values.

Figure S6. Mean path divergence statistic as in Lobkovsky et. al. (2011) for all sets of parameter values.

Table S1. Pairwise Epistasis ( $\mathrm{n}=5,000$ )

Table S2. Conditional Mutations

Table S3. Backwards Predictability P Values

Table S4. Epistasis and Predictability P values










Table S1

| Parameter | X2 p-value | Ploidy | Sign | Reciprocal Sign |  | Ancestral Deleterious |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | Haploid |  | 52.30\% | 31.00\% | 16.00\% |
| A | 8.8E-128 | Diploid |  | 53.00\% | 21.40\% | 2.80\% |
|  |  | Haploid |  | 74.70\% | 68.80\% | 47.20\% |
| B | 5.8E-252 | Diploid |  | 76.40\% | 65.10\% | 6.20\% |
|  |  | Haploid |  | 12.60\% | 3.50\% | 0.80\% |
| C | 1.3E-015 | Diploid |  | 12.00\% | 1.30\% | 0.00\% |
|  |  | Haploid |  | 61.40\% | 51.00\% | 38.00\% |
| D | 2.8E-151 | Diploid |  | 65.80\% | 49.40\% | 17.20\% |
| E |  | Haploid |  | 53.20\% | 38.10\% | 23.00\% |
| E | 7.7E-125 | Diploid |  | 51.40\% | 26.70\% | 3.30\% |
| F | 3.3E-139 | Haploid |  | 52.90\% | 38.00\% | 23.80\% |
| F | 3.3E-139 | Diploid |  | 50.60\% | 25.40\% | 2.90\% |
| G | 2.5E-145 | Haploid |  | 54.20\% | 38.90\% | 24.50\% |
| G | 2.5E-145 | Diploid |  | 48.80\% | 23.20\% | 2.20\% |

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Table S2

| Parameter | X2 p-value | Ploidy <br> Plaploid | All <br> A |
| :---: | :---: | :--- | :--- |
| A | $1.50 \mathrm{E}-14$ | Diploid <br> Diplo | $26.3 \%$ |
| B | $1.30 \mathrm{E}-79$ | Haploid | $48.1 \%$ |
|  | Diploid | $40.8 \%$ |  |
| C | $4.50 \mathrm{E}-06$ | Haploid | $3.4 \%$ |
|  | Diploid | $4.6 \%$ |  |
| D | $2.80 \mathrm{E}-34$ | Haploid | $27.4 \%$ |
|  |  | Diploid | $36.1 \%$ |
| E | $1.40 \mathrm{E}-07$ | Haploid | $18.3 \%$ |
|  |  | Diploid | $21.5 \%$ |
| F | $8.20 \mathrm{E}-05$ | Haploid | $17.4 \%$ |
|  | Diploid | $19.7 \%$ |  |
| G | $9.46 \mathrm{E}-01$ | Haploid | $17.6 \%$ |
|  |  | Diploid | $17.5 \%$ |

Initial Mutation Initial Mutation Not Overdominant Overdominant
NA NA
62.4
NA
18.2\%
82.9\%
.
NA
27.2\%

NA
65.5\%

NA
61.4\%

NA
61.9\%

NA
60.9\%
30.4\%

NA
3.7\%

NA
28.0\%

NA
14.0\%

NA
12.1\%

NA
10.3\%

Table S3


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Table S4
$P$ values from chi-square contingency table tests

|  | Hap vs Dip across all 4 levels of Epistasis | Diploid Sign Epi. One overdom vs no overdom | Diploid recip sign epi one overdom vs no overdom | Diploid anc del epi one overdom vs no overdom | Diploid sign epi two overdom vs no overdom | diploid recip sign epi two overdom vs no overdom | Diploid anc del epi two overdom vs no overdom | conditional mutation haploid vs diploid | initial mutation vs diploid not overdom initial mutation |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| A | $8.84 \mathrm{E}-128$ | $2.03 \mathrm{E}-103$ | $6.20 \mathrm{E}-70$ | $3.20 \mathrm{E}-01$ | $2.37 \mathrm{E}-61$ | 2.02E-137 | $4.75 \mathrm{E}-49$ | $1.52 \mathrm{E}-14$ | $2.09 \mathrm{E}-290$ |
| B | $5.80 \mathrm{E}-252$ | 2.23E-71 | 1.50E-66 | $2.36 \mathrm{E}-04$ | $3.93 \mathrm{E}-28$ | $2.55 \mathrm{E}-69$ | 5.87E-59 | $1.28 \mathrm{E}-79$ | $0.00 \mathrm{E}+00$ |
| C | $1.34 \mathrm{E}-15$ | 5.72E-54 | $6.21 \mathrm{E}-16$ | $0.00 \mathrm{E}+00$ | $1.31 \mathrm{E}-03$ | 7.47E-02 | $0.00 \mathrm{E}+00$ | $4.53 \mathrm{E}-06$ | 1.15E-100 |
| D | $2.75 \mathrm{E}-151$ | 8.36E-85 | $1.42 \mathrm{E}-80$ | $4.95 \mathrm{E}-01$ | $3.50 \mathrm{E}-77$ | $6.26 \mathrm{E}-155$ | $1.11 \mathrm{E}-76$ | $2.80 \mathrm{E}-34$ | 1.90E-177 |
| E | $7.71 \mathrm{E}-125$ | 3.76E-157 | $1.70 \mathrm{E}-86$ | 5.70E-02 | $1.29 \mathrm{E}-56$ | $5.26 \mathrm{E}-101$ | 2.28E-46 | $1.39 \mathrm{E}-07$ | $0.00 \mathrm{E}+00$ |
| F | 3.27E-139 | $6.21 \mathrm{E}-168$ | 1.17E-94 | $2.66 \mathrm{E}-01$ | $1.43 \mathrm{E}-62$ | 4.06E-127 | $1.22 \mathrm{E}-44$ | $8.25 \mathrm{E}-05$ | $0.00 \mathrm{E}+00$ |
| G | 2.51E-145 | $6.20 \mathrm{E}-171$ | $2.71 \mathrm{E}-80$ | $2.99 \mathrm{E}-01$ | 1.99E-61 | 5.47E-114 | 4.87E-24 | $9.46 \mathrm{E}-01$ | $0.00 \mathrm{E}+00$ |

p values from two-tailed t tests

|  | max pairwise dist $p$ value | max dist from optimal p value | Dip vs Hap Effective num paths $p$ valuje | cor dip effective num paths and num overdom | cor $p$ value dip effective num paths and num overdom | mean path <br> divergence $p$ <br> value |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| A | 9.97E-22 | $0.00 \mathrm{E}+00$ | $4.06 \mathrm{E}-20$ | -0.345 | $1.40 \mathrm{E}-19$ | $4.89 \mathrm{E}-10$ |
| B | $1.36 \mathrm{E}-66$ | 7.66E-220 | $1.38 \mathrm{E}-79$ | -0.302 | 2.15E-44 | $3.45 \mathrm{E}-40$ |
| C | $4.98 \mathrm{E}-27$ | $4.21 \mathrm{E}-91$ | 5.12E-31 | -0.425 | 4.52E-101 | $5.11 \mathrm{E}-12$ |
| D | $6.42 \mathrm{E}-21$ | $0.00 \mathrm{E}+00$ | $3.31 \mathrm{E}-15$ | -0.282 | $1.86 \mathrm{E}-06$ | $4.42 \mathrm{E}-06$ |
| E | $4.42 \mathrm{E}-17$ | $0.00 \mathrm{E}+00$ | $2.15 \mathrm{E}-23$ | -0.393 | $6.80 \mathrm{E}-22$ | $5.63 \mathrm{E}-09$ |
| F | $9.75 \mathrm{E}-07$ | $3.71 \mathrm{E}-196$ | $6.41 \mathrm{E}-19$ | -0.331 | $2.68 \mathrm{E}-13$ | $1.63 \mathrm{E}-07$ |
| G | $3.94 \mathrm{E}-04$ | 7.81E-111 | 3.86E-09 | -0.287 | $4.68 \mathrm{E}-09$ | $9.85 \mathrm{E}-04$ |

