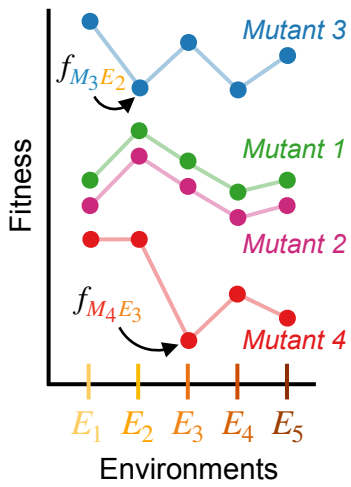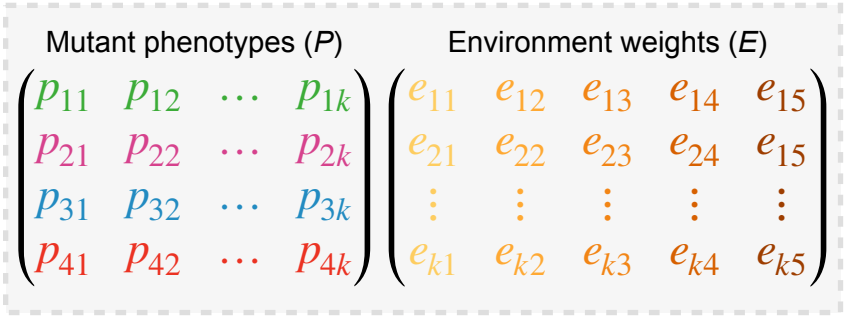**A** Measure fitness profiles of mutants across environments
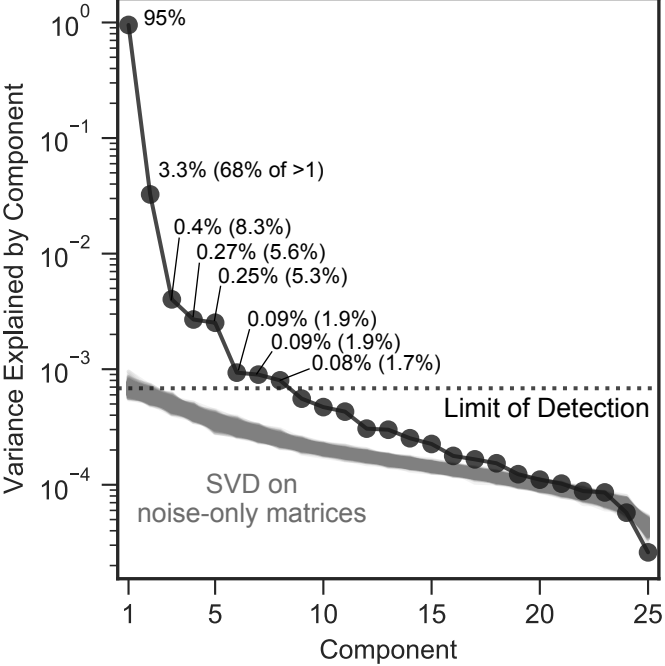
Infer mutant phenotypes and environment weights from fitness profiles using SVD

Mutant phenotypes (P)

$$\begin{pmatrix} p_{11} & p_{12} & \cdots & p_{1k} \\ p_{21} & p_{22} & \cdots & p_{2k} \\ p_{31} & p_{32} & \cdots & p_{3k} \\ p_{41} & p_{42} & \cdots & p_{4k} \end{pmatrix}$$

Environment weights (E)

$$\begin{pmatrix} e_{11} & e_{12} & e_{13} & e_{14} & e_{15} \\ e_{21} & e_{22} & e_{23} & e_{24} & e_{15} \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ e_{k1} & e_{k2} & e_{k3} & e_{k4} & e_{k5} \end{pmatrix}$$

$$f_{M_3E_2} = p_{31}e_{12} + p_{32}e_{22} + \ldots + p_{3k}e_{k2}$$
$$f_{M_4E_3} = p_{41}e_{13} + p_{42}e_{23} + \ldots + p_{4k}e_{k3}$$

Linear model of phenotype to fitness

B

95%

3.3% (68% of >1)

0.4% (8.3%)
0.27% (5.6%)
0.25% (5.3%)

0.09% (1.9%)
0.09% (1.9%)
0.08% (1.7%)

Limit of Detection

SVD on noise-only matrices

C

IRA1 nonsense

GPB2

TOR/Sch9 Pathway

Diploid

Diploid w/ add'l mutation

PDE2