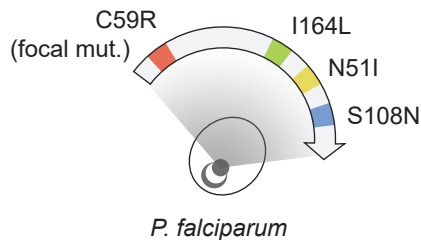


A**B**

Genetic backgrounds

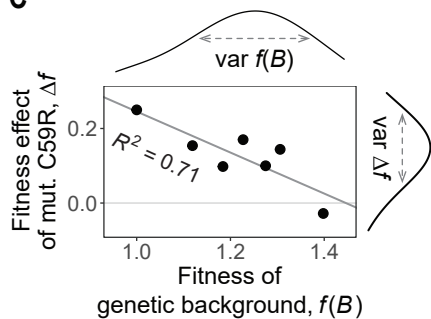
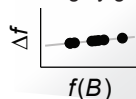
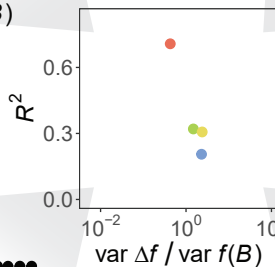
Fitness: $f(B)$

Focal mutation in backgrounds



Fitness effect of focal mutation:

$$\Delta f = f(B + \text{C59R}) - f(B)$$

C**D**Low epistasis,
but largely globalHigh epistasis,
global

Focal mutation

No epistasis
(additive fitness effect)High epistasis,
idiosyncratic