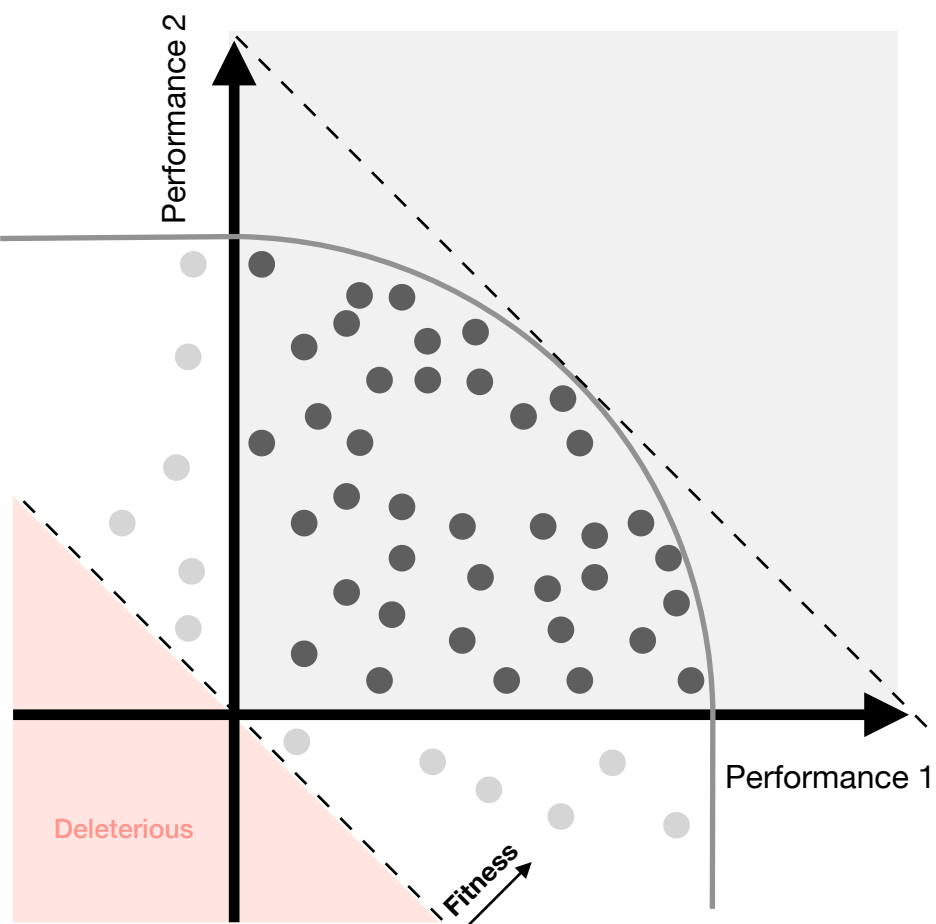
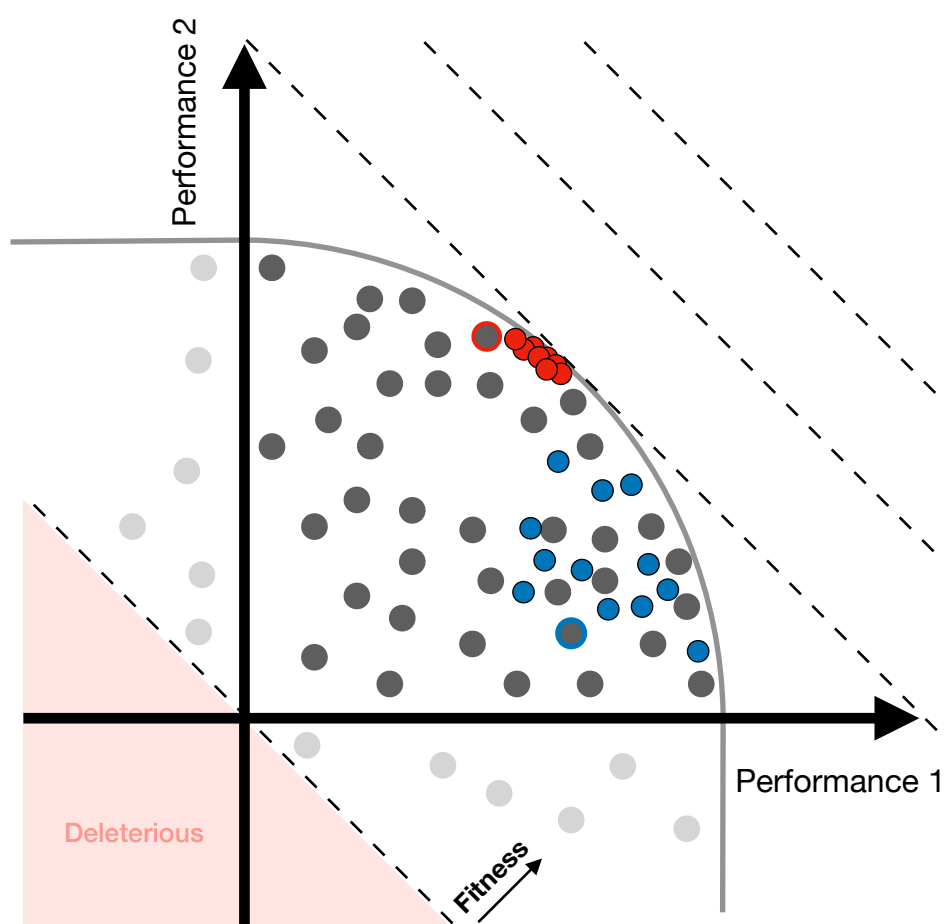
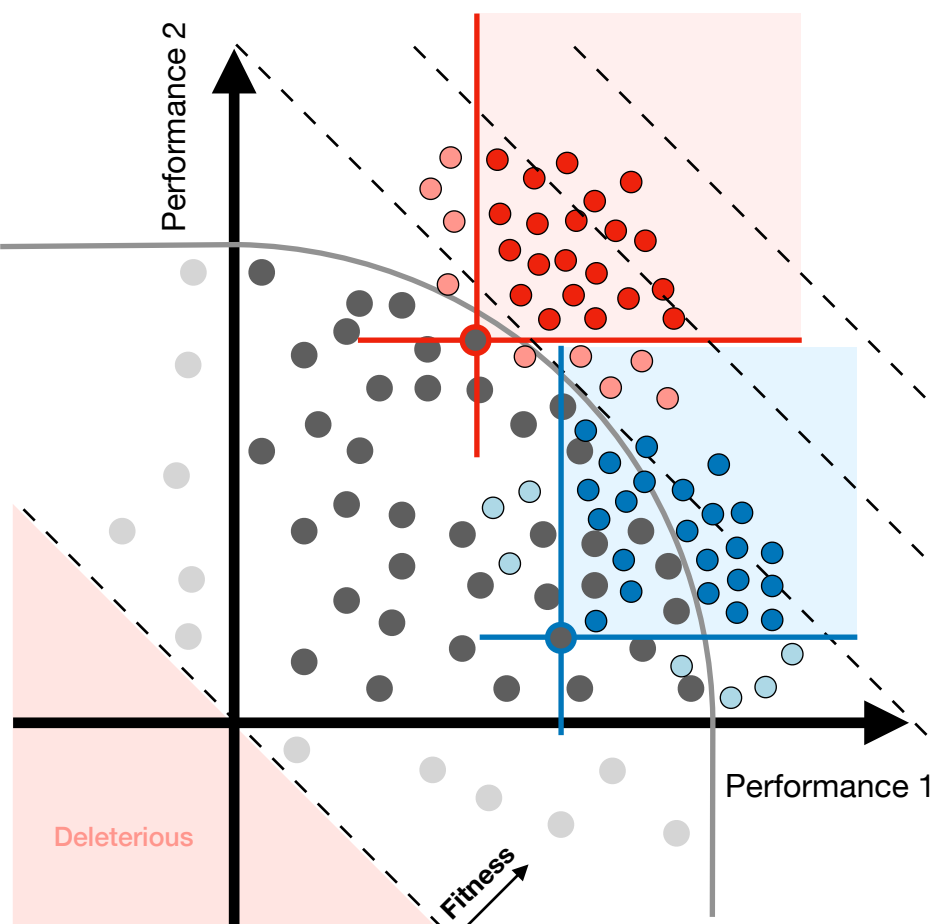


A

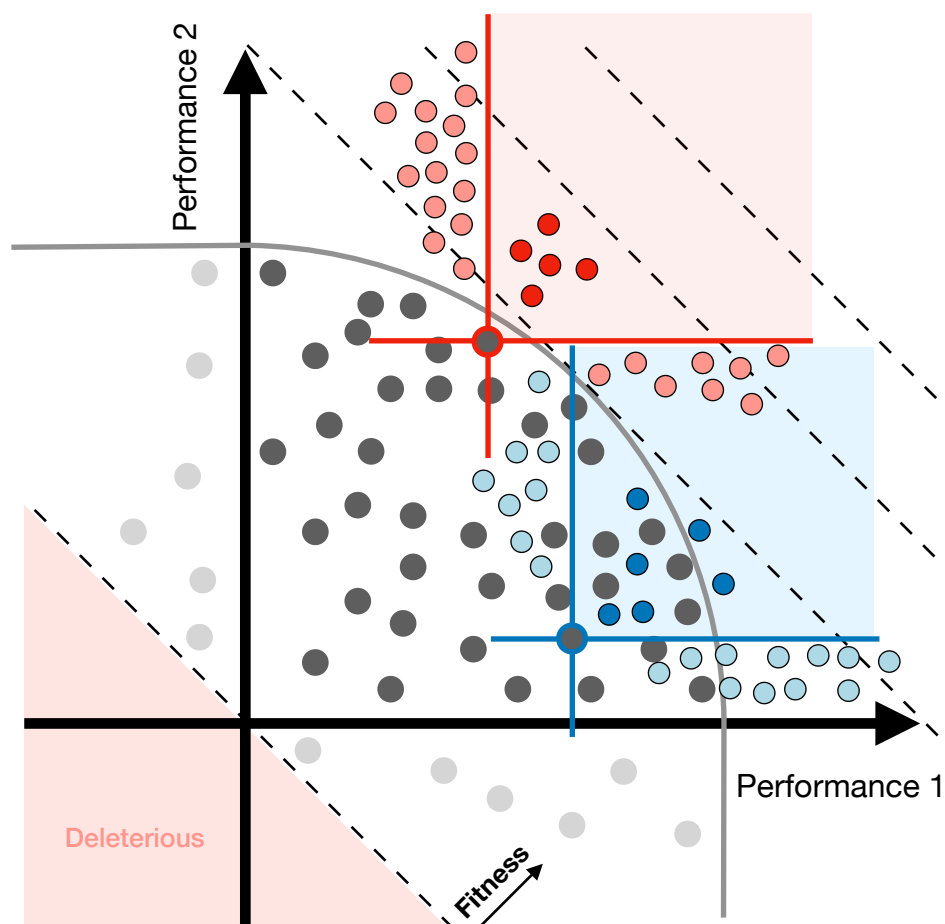
First-step mutations exhibit signs of adaptive pleiotropy and tradeoffs!

B

Tradeoffs are driven by functional constraints:
Second-step mutations cannot improve past these constraints

C

Only “constraint” is mutational distance:
Second-step adaptive mutants continue to show a pattern of adaptive pleiotropy

D

Accessibility of adaptive pleiotropic mutations is reduced:
Second-step mutations display new patterns of trait improvement