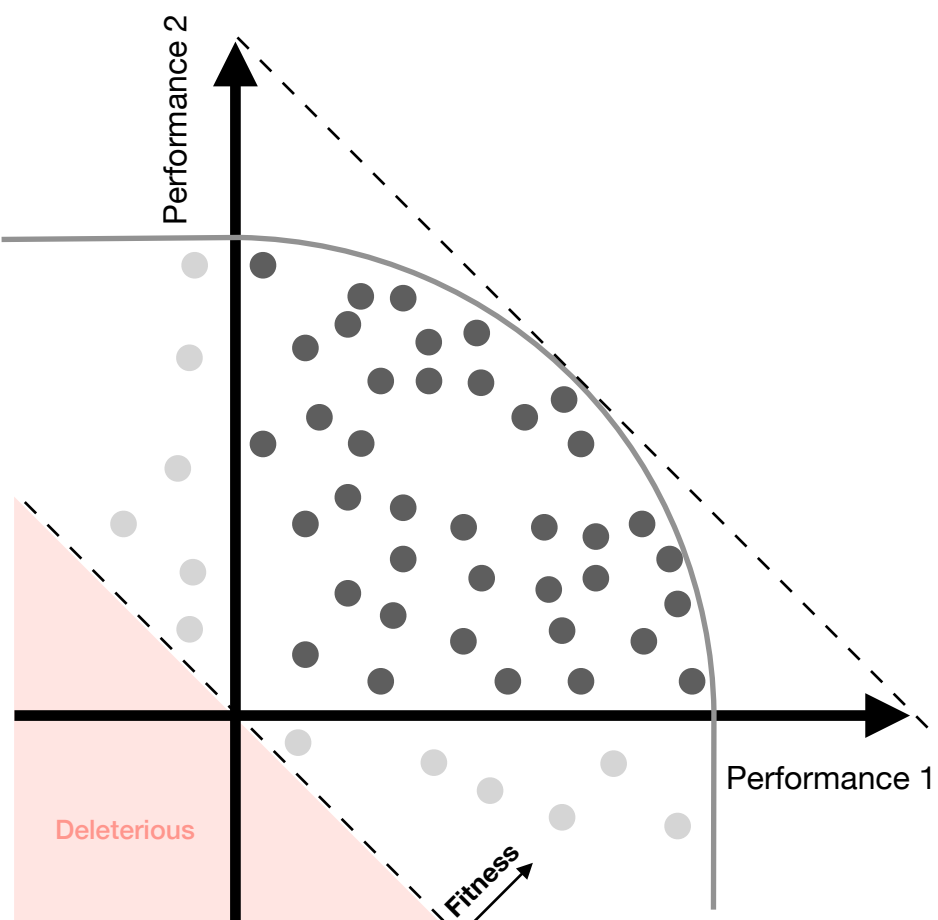
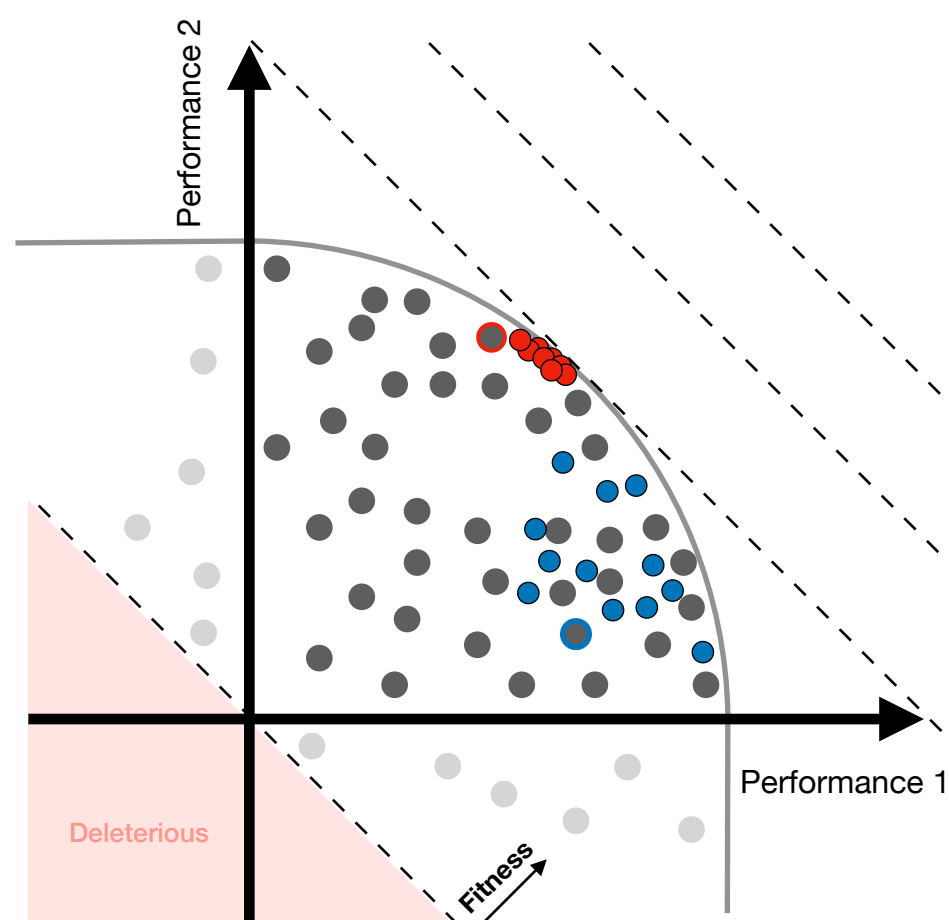
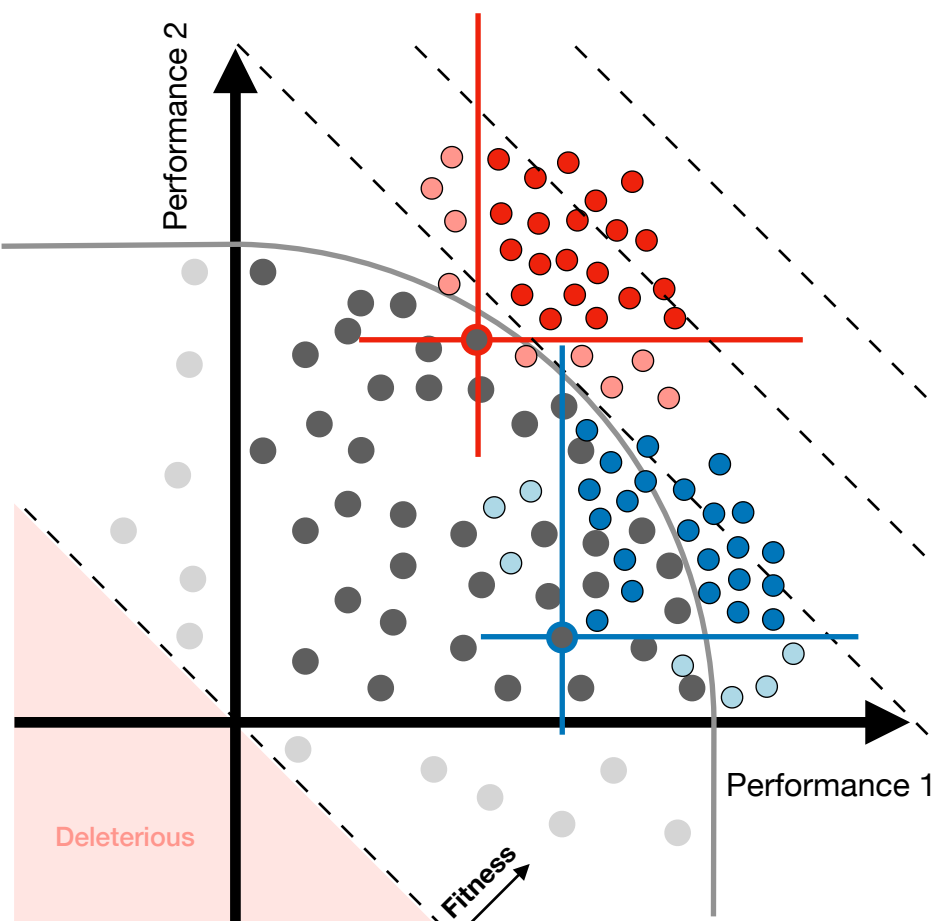


**A**

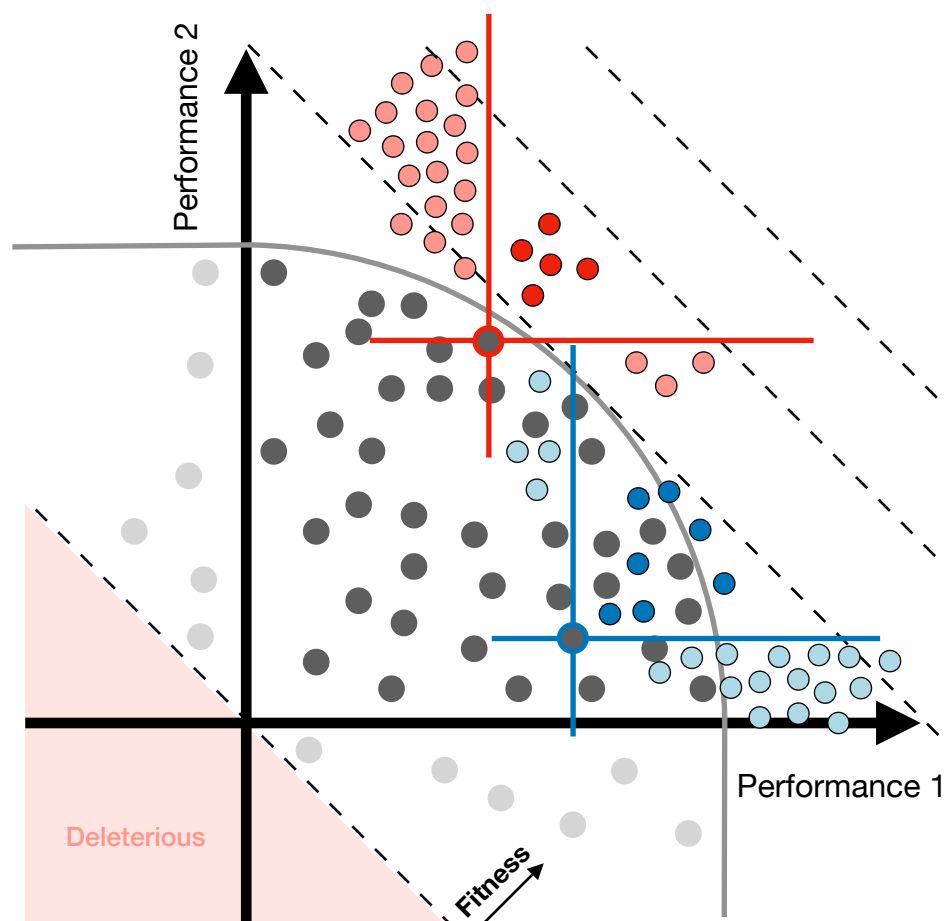
**First-step mutations** exhibit signs of adaptive pleiotropy and tradeoffs!

**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