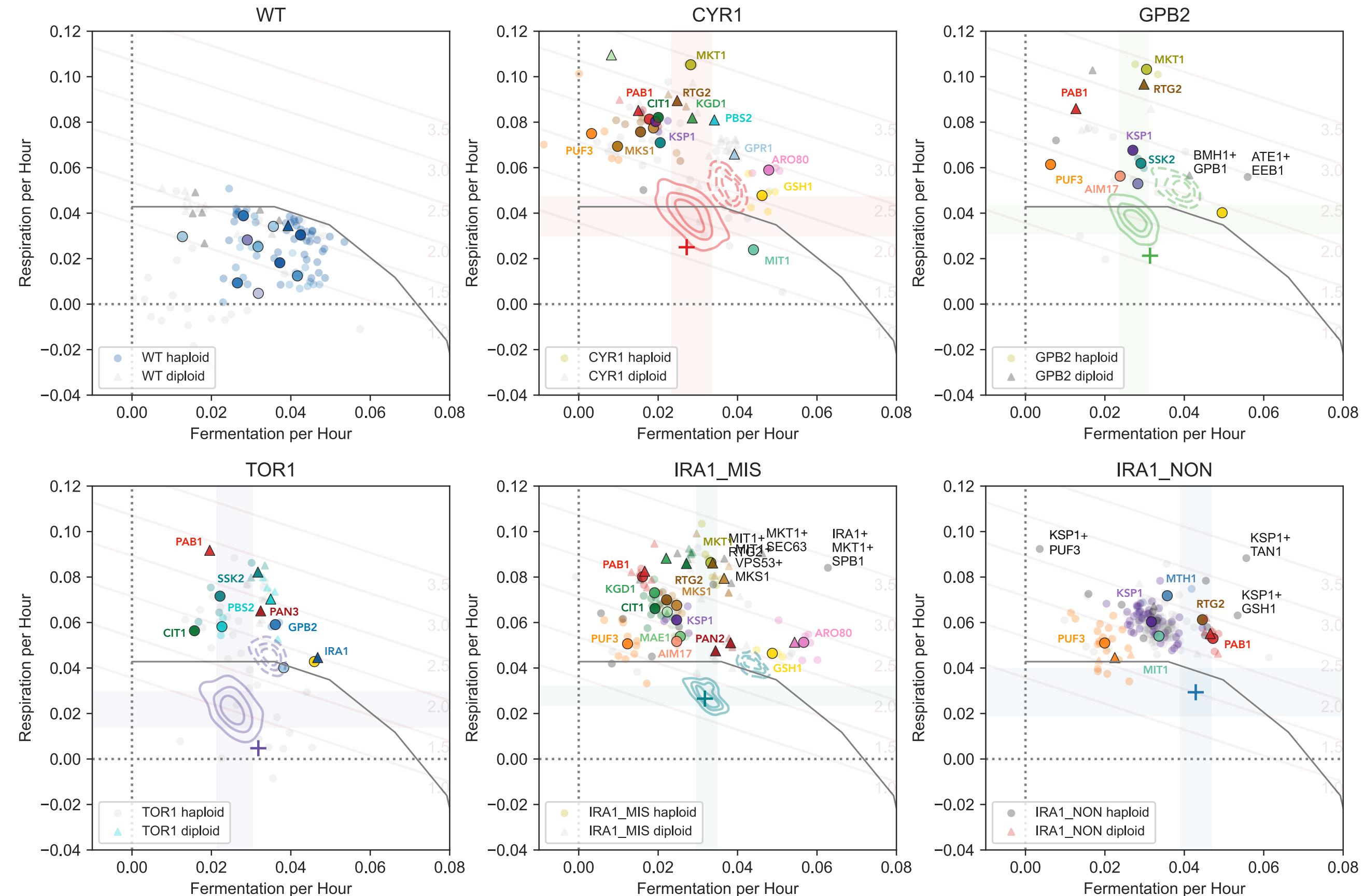
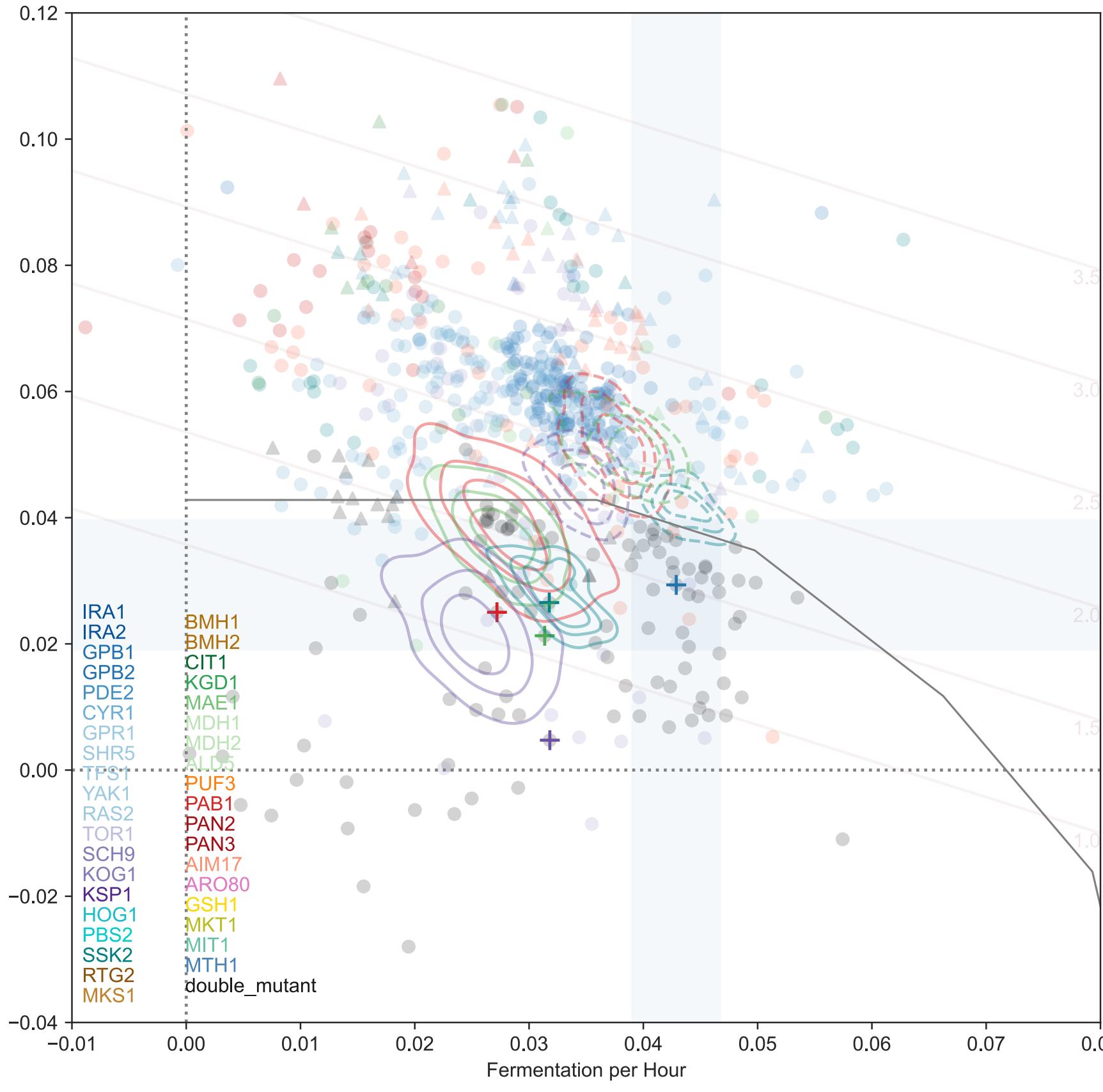
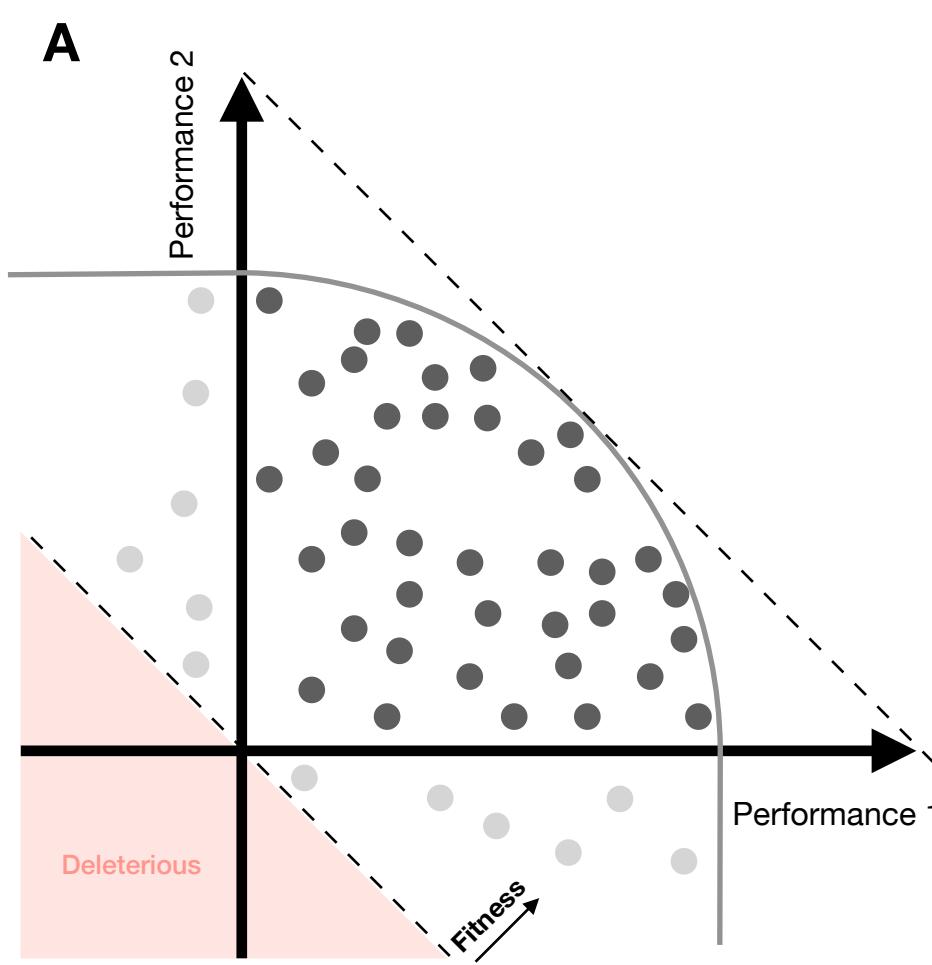


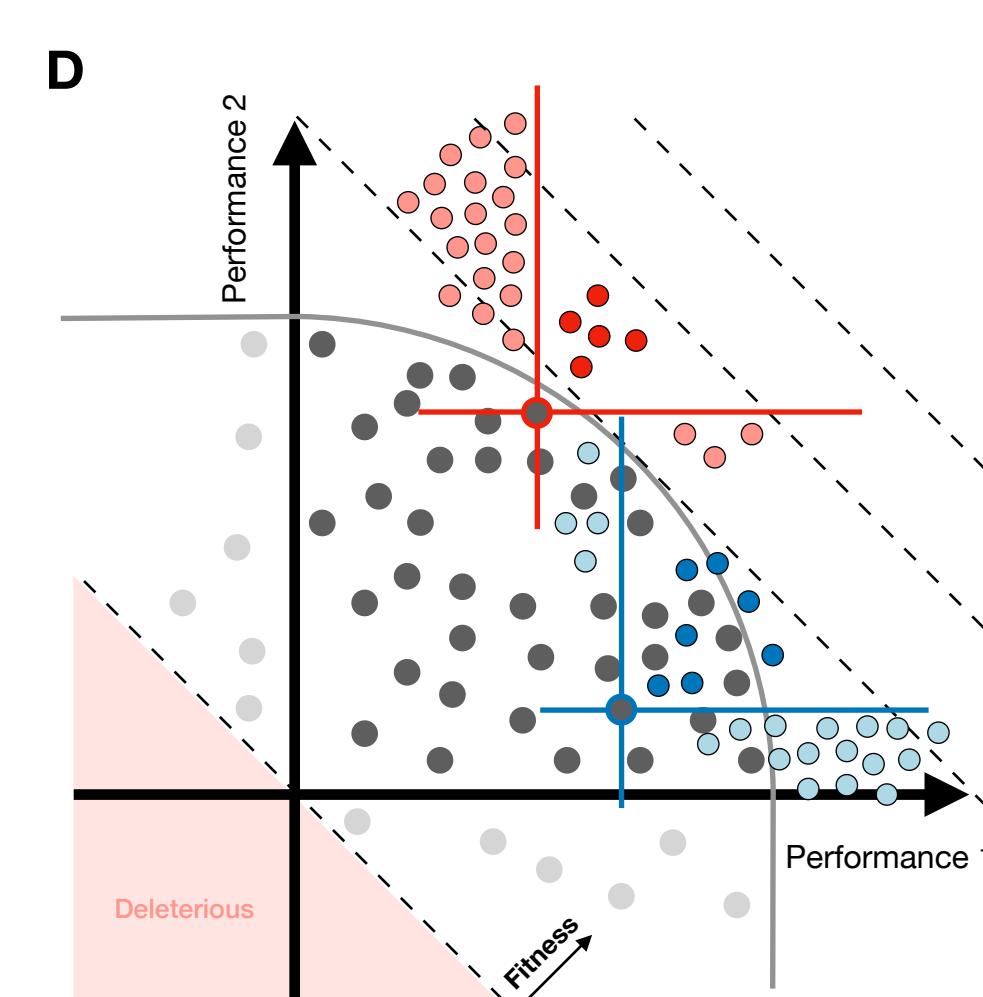
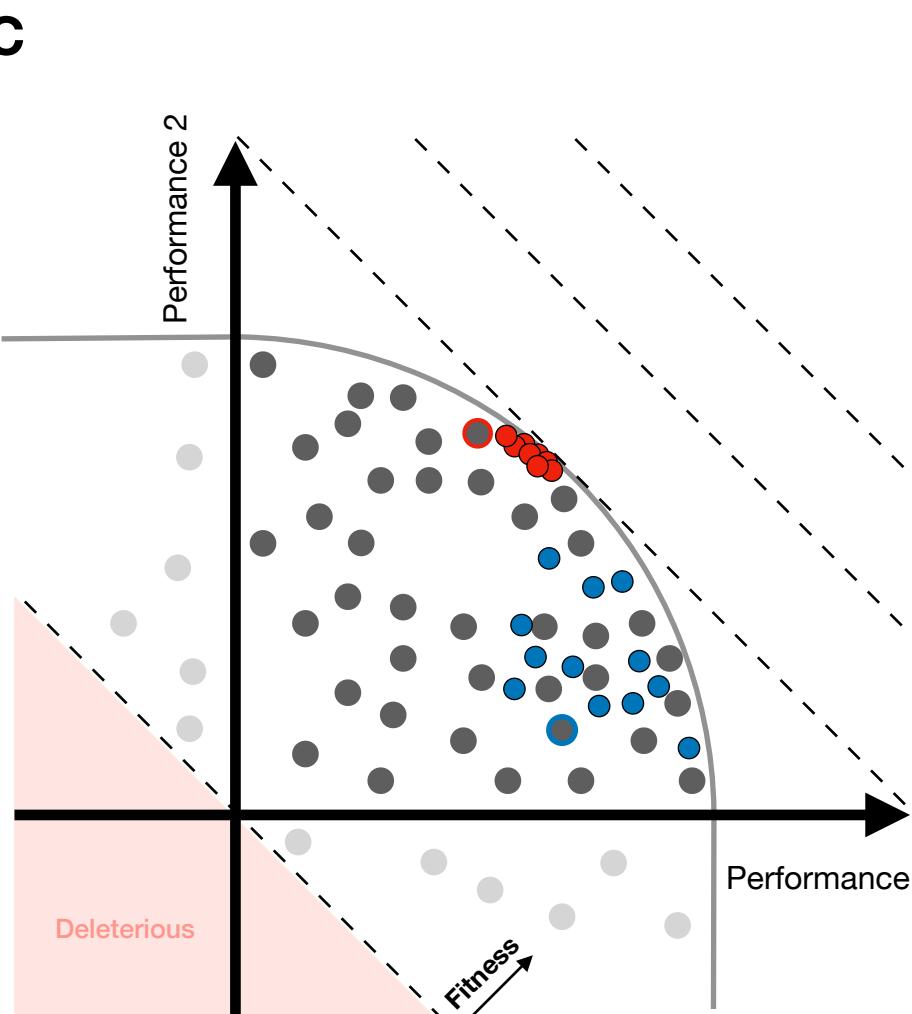
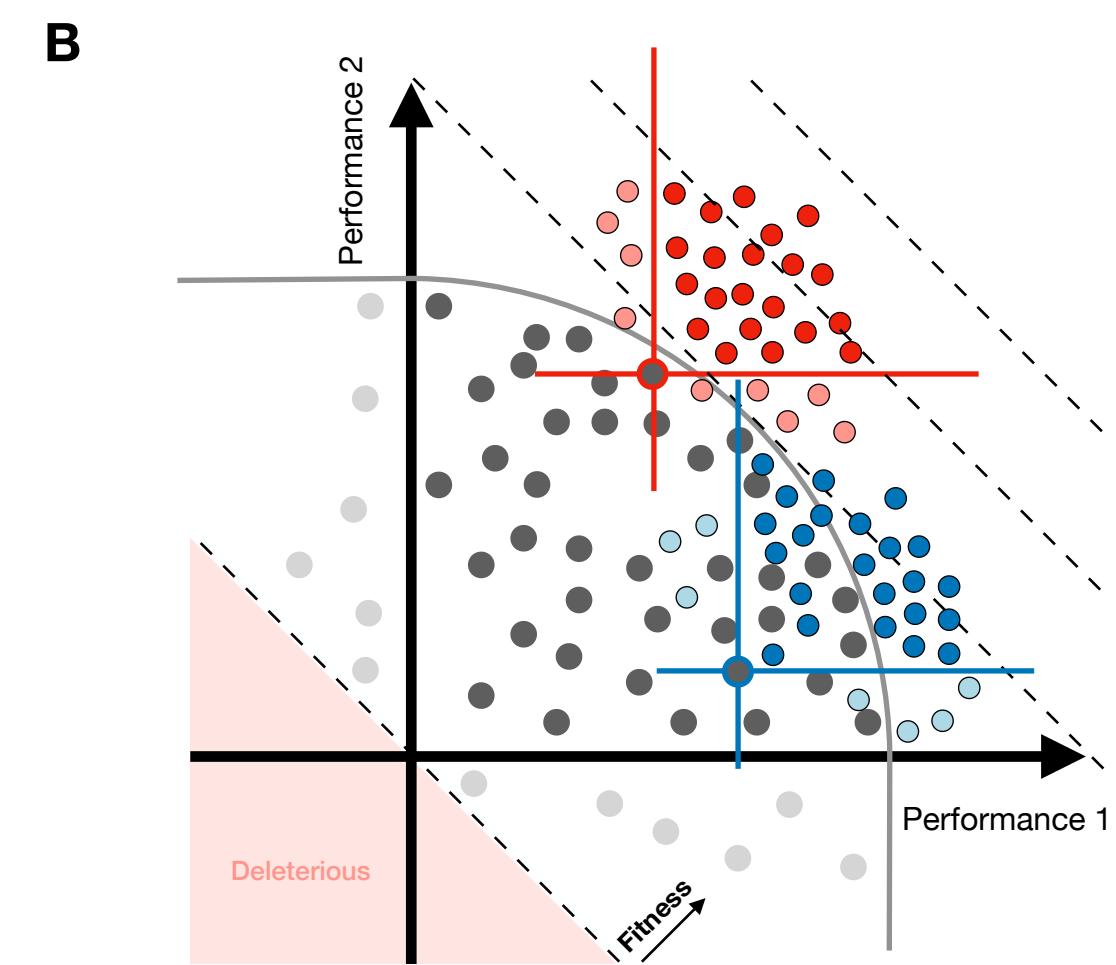
	WT Evo2D	WT Evo3D	TOR1 Evo2D	TOR1 Evo3D	GPB2 Evo2D	GPB2 Evo3D	CYR1 Evo2D	CYR1 Evo3D	IRA1_MIS Evo2D	IRA1_MIS Evo3D	IRA1_NON Evo2D	IRA1_NON Evo3D
Ras/PKA	30/77									1/34*		
	11/77		1/21									
	4/77				1/7*							
	14/77		2/21									
	11/77											
	3/77						1/28					
TOR/Sch9	1/77											
	1/77											
					1/7							
					1/7	1/8*	1/28	2/14	4/69		32/76	30/33
HOG							1/28					
					6/21							
					7/21	1/7	1/8	1/28				
RTG						1/8	4/28	2/14	9/69	1/34		1/76
							2/28	1/14	7/69	1/34*		
						1/7*	1/28					
TCA cycle												
							1/28		16/69	1/34*		
									3/69			
									4/69			
									2/69		2/76	
Mitochondrial Biogenesis								1/14	1/69*			2/33*
Others						1/8	4/28	2/14	7/69	7/34	24/76	1/33*
							1/28		3/69	5/34	12/76	
									2/69			
									1/69			
									2/69			



OLD VERSIONS BELOW

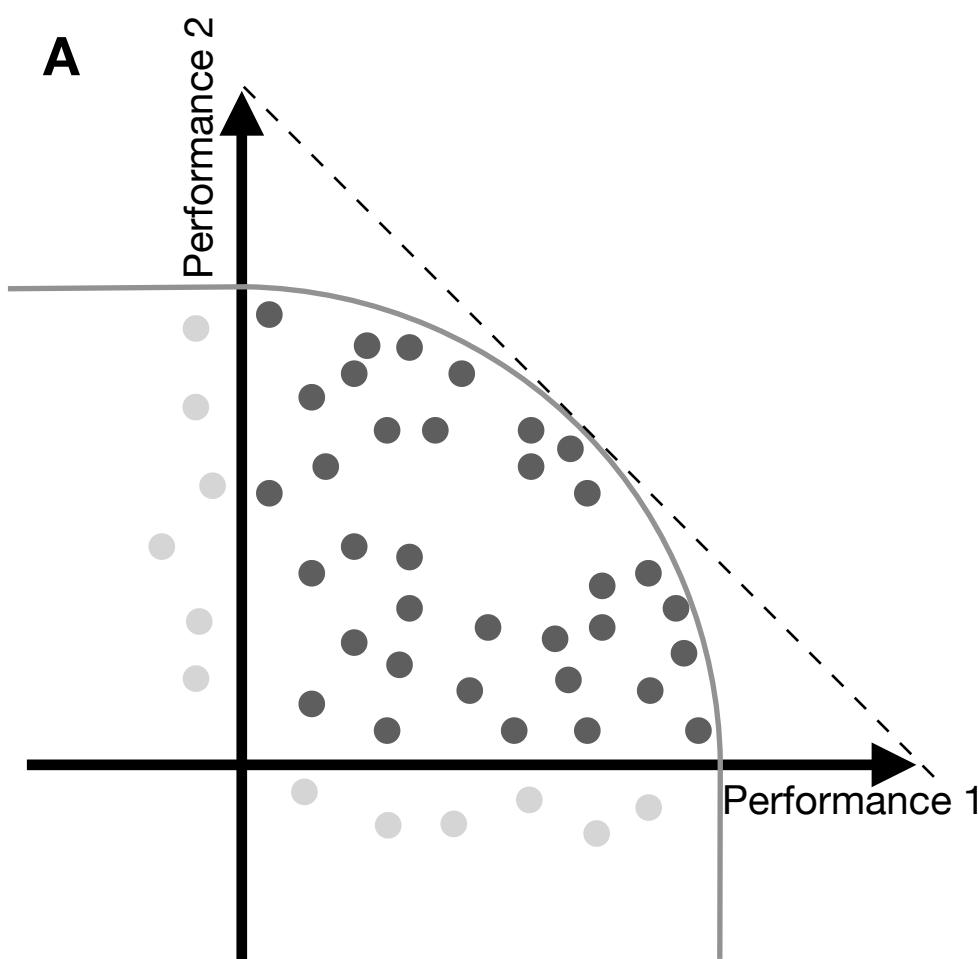


First-step mutations exhibit signs of adaptive pleiotropy (with most improving both performances at once) and tradeoffs (not achieving “perfect” extreme performance)

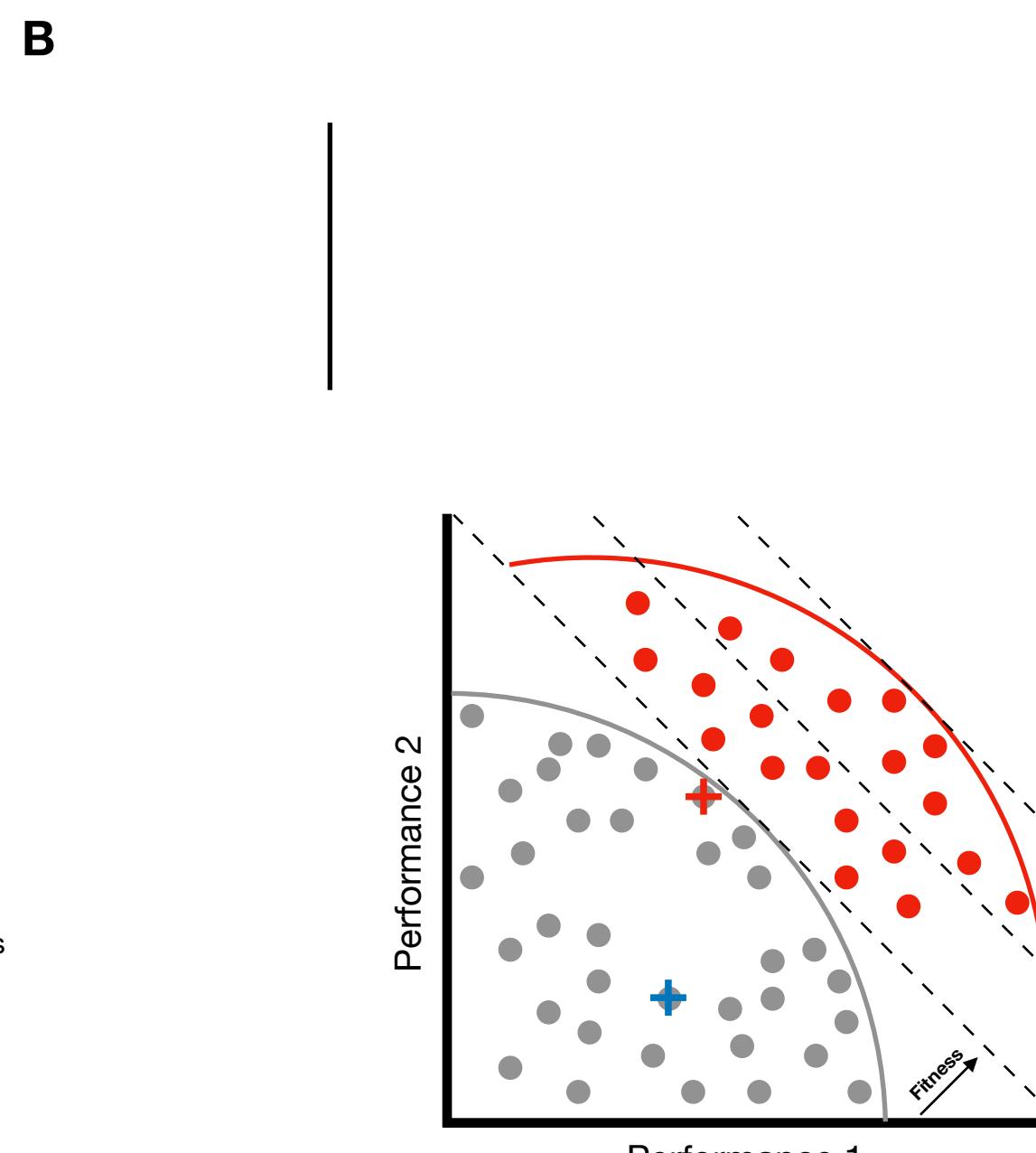


Tradeoffs represent functional/physiological constraints on the improvement of these performances

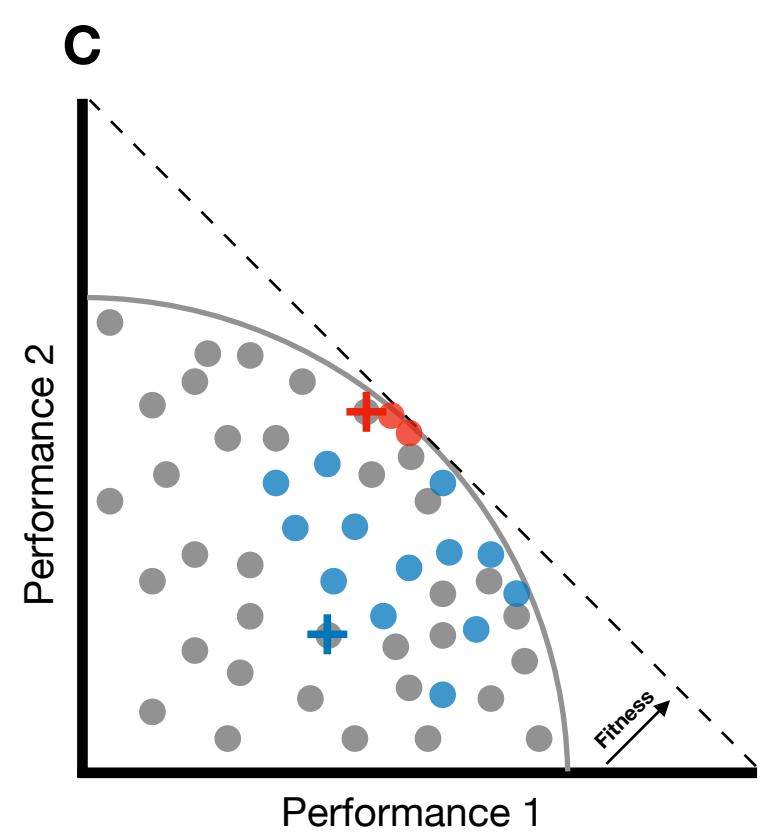
Klein et al., *bioRxiv* (2021); available at <https://doi.org/10.1101/2021.05.10.443801>; this version posted May 10, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under a [CC-BY-ND 4.0 International license](https://creativecommons.org/licenses/by-nd/4.0/).



First-step mutations exhibit signs of adaptive pleiotropy (with most improving both performances at once) and tradeoffs (not achieving “perfect” extreme performance)

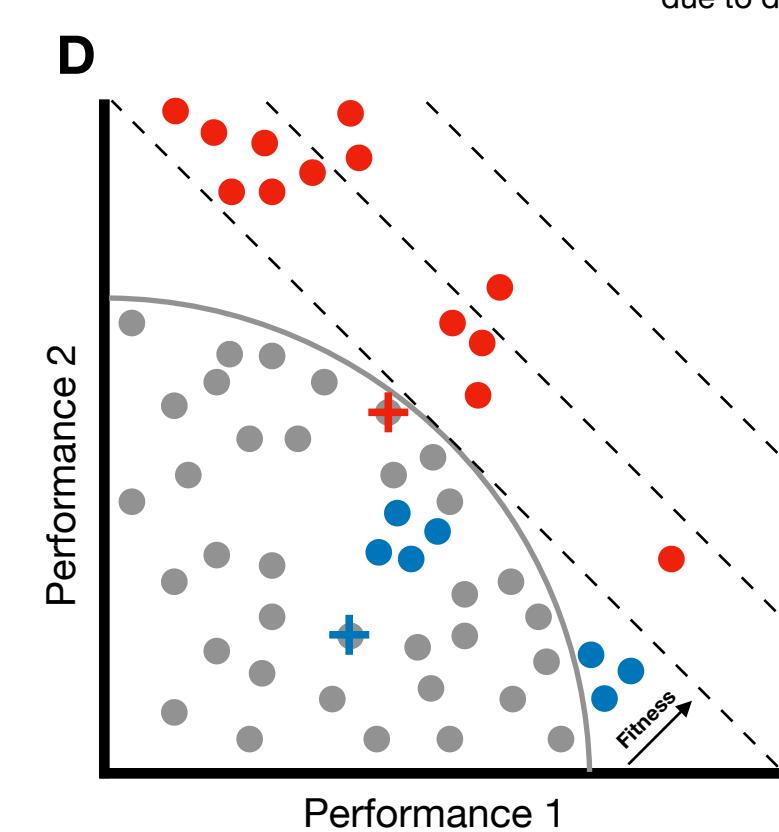


If tradeoffs don't represent any functional or genetic constraints but instead just mutational distance, then further adaptive steps should continue to improve as the first, albeit more slowly due to diminishing returns...



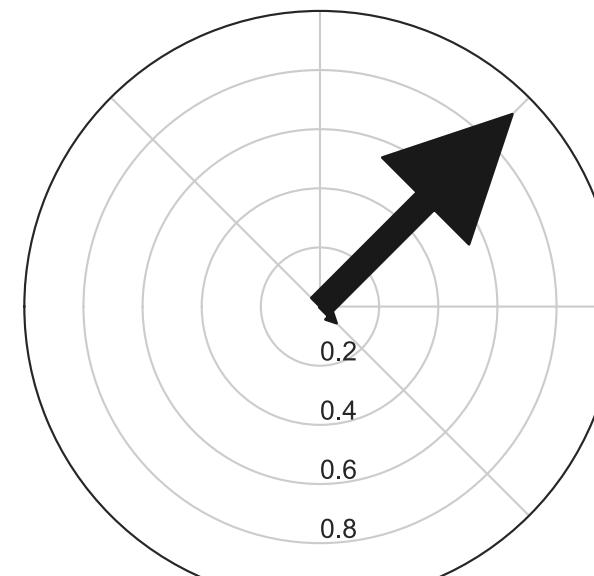
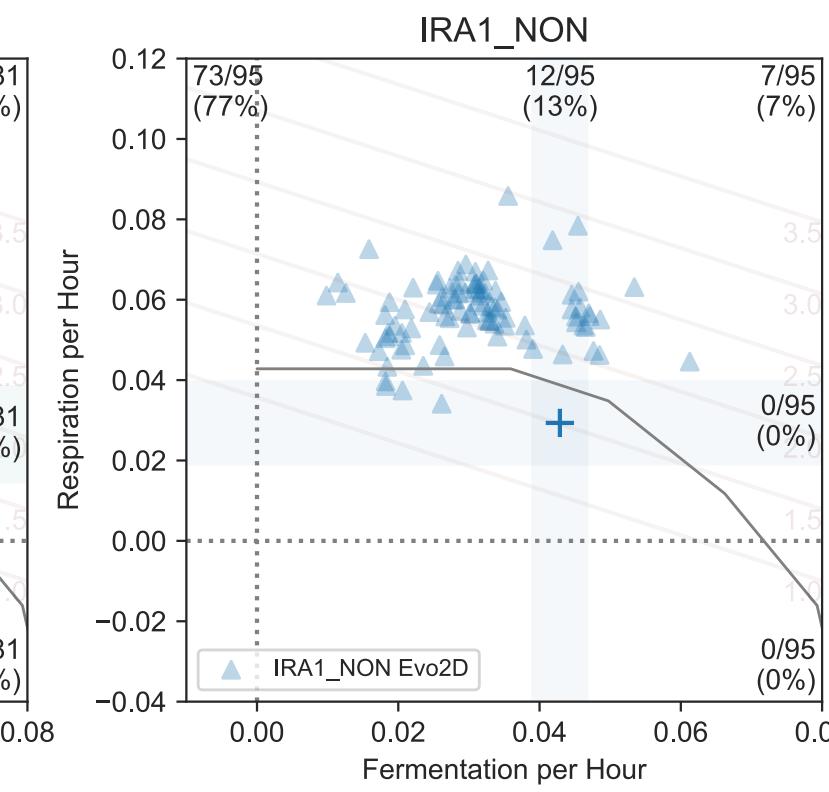
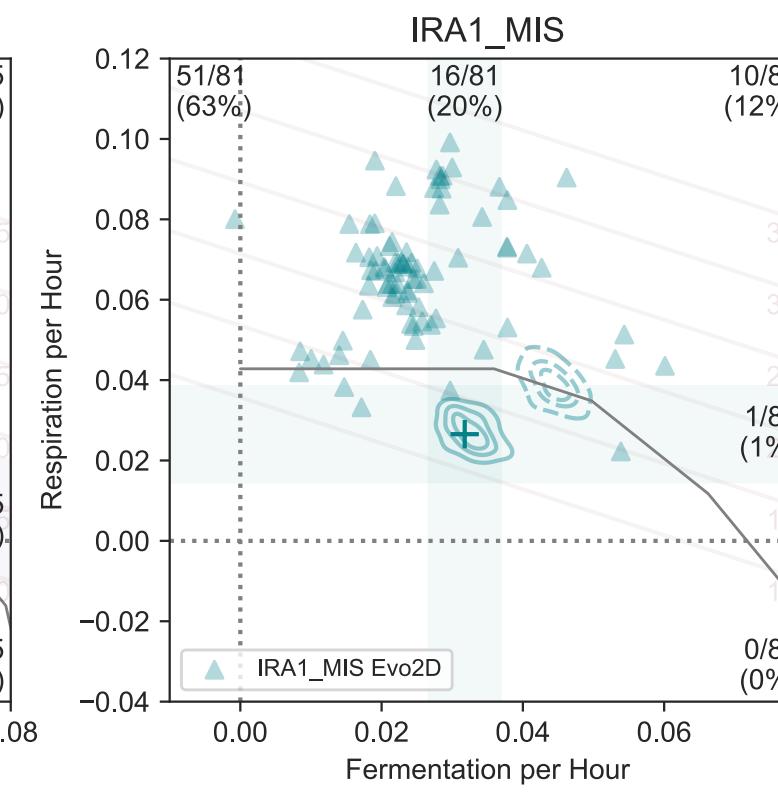
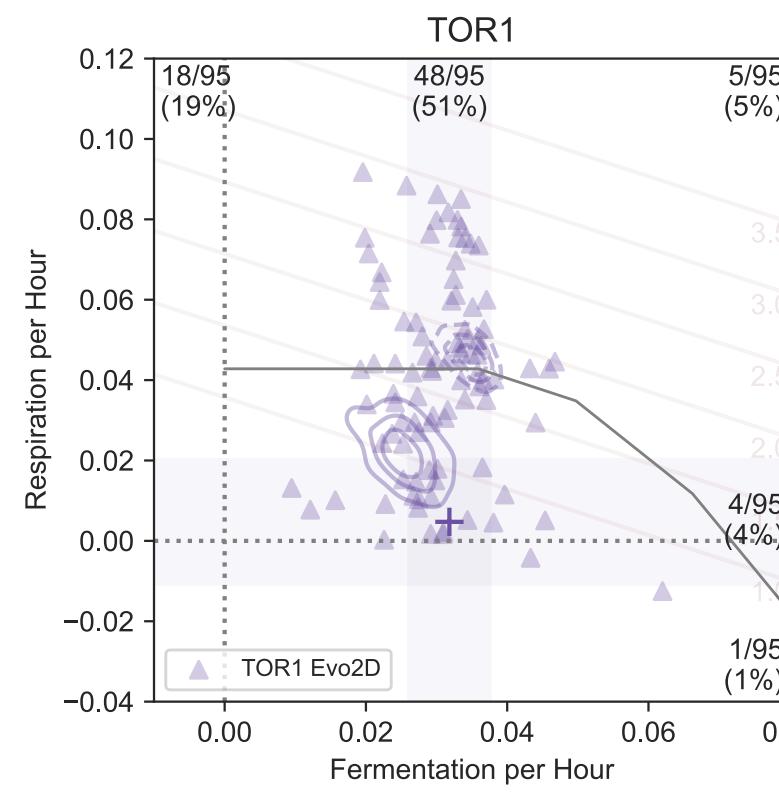
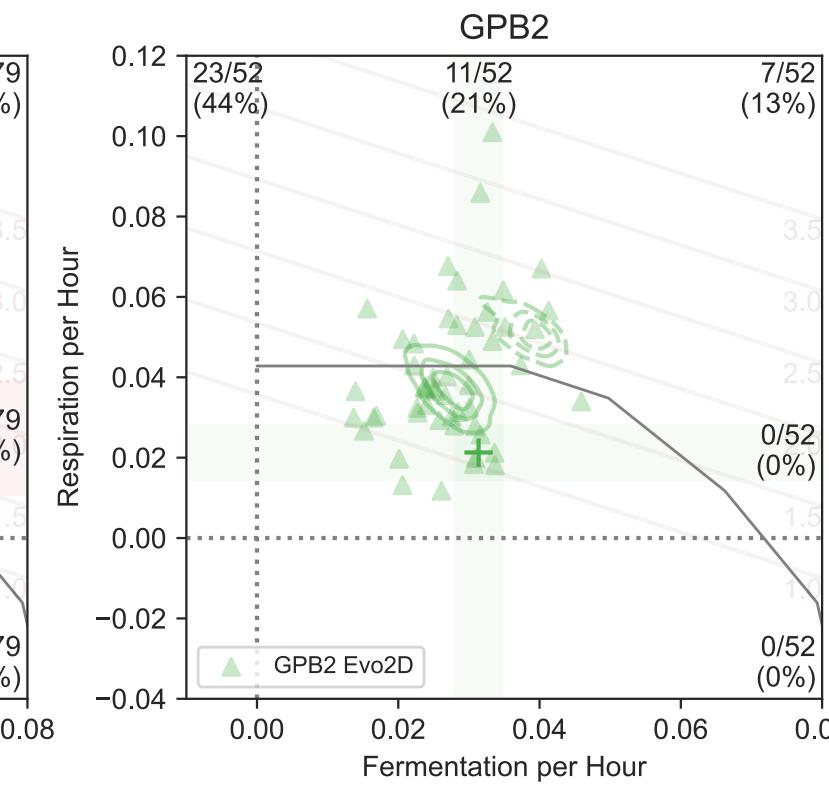
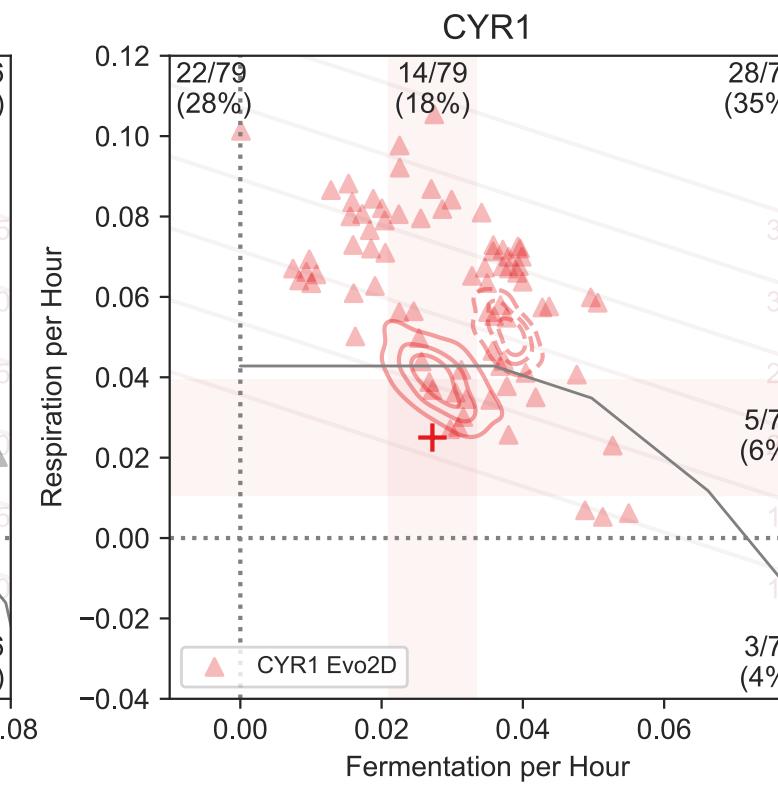
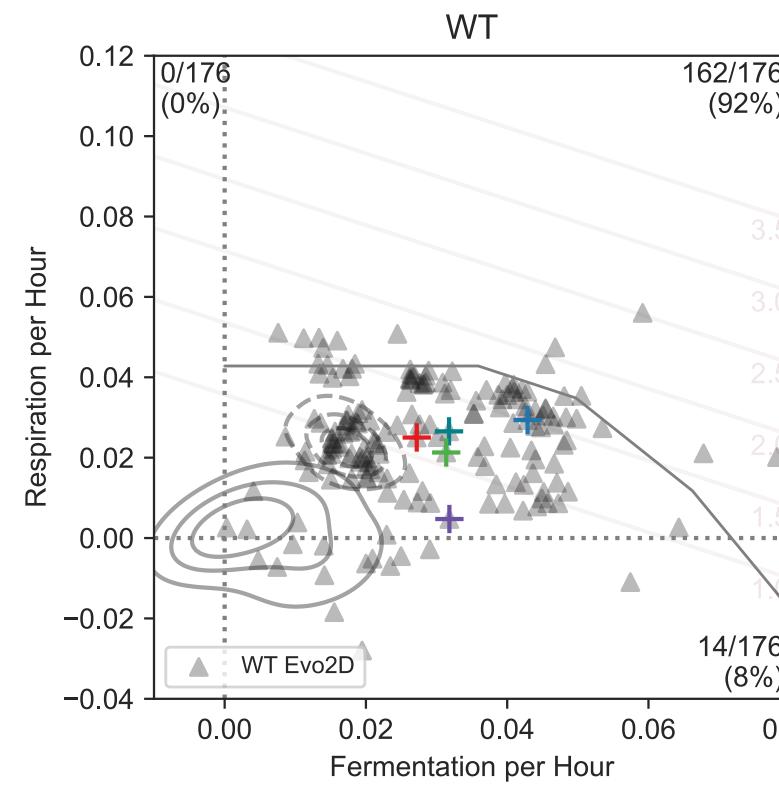
Tradeoffs represent functional/physiological constraints on the improvement of these performances

If true, further steps might move within or along these limits but cannot break through them

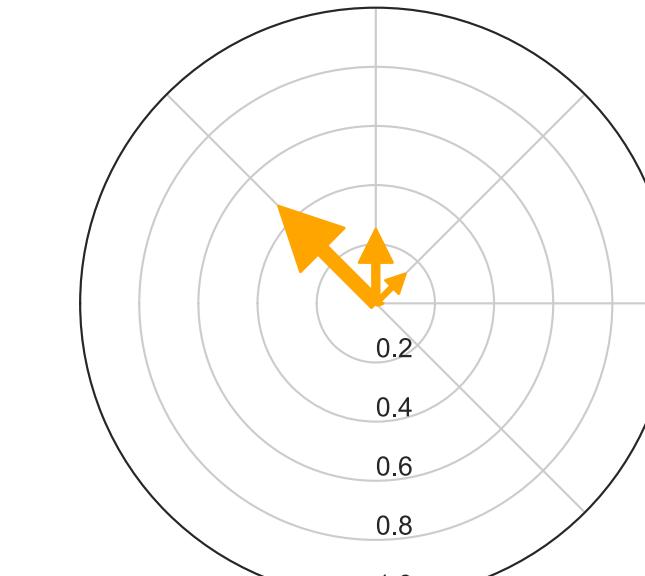


Tradeoffs reflect constraints imposed by genetic wiring, the accessibility of adaptive solutions and their pleiotropic effects.

Further adaptive steps may display new patterns of genetic wiring, and these shifts in genetic wiring and pleiotropy may be dependent on the background of the first step



First step



All second step

