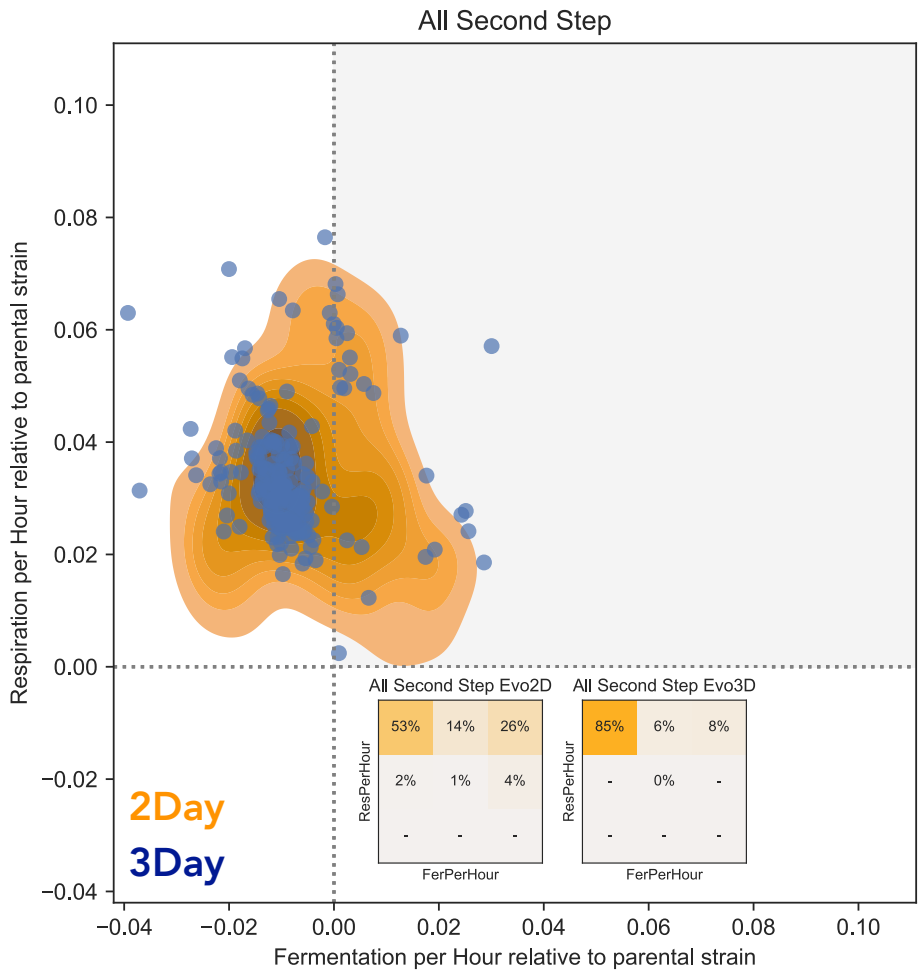|	Evo3D mutants	Number of pure diploids	Number of putative adaptive mutants
CYR1	35	8	20
GPB2	34	20	12
TOR1	2	-	2
IRA1 mis	32	3	28
IRA1 non	135	0	135
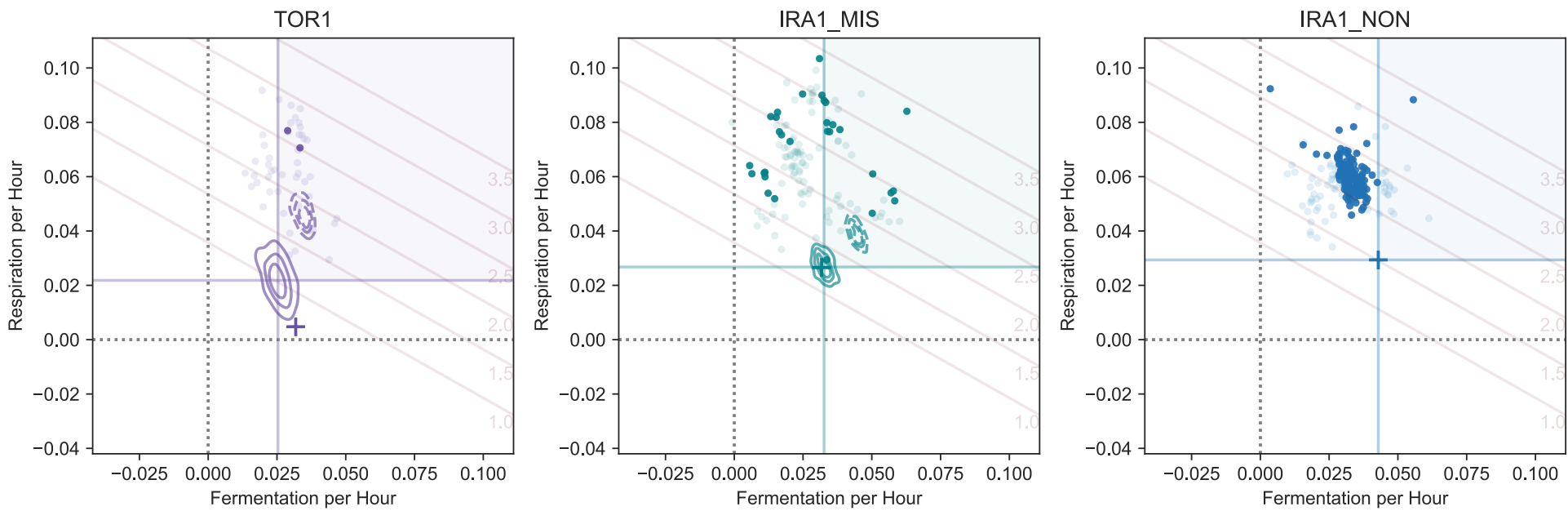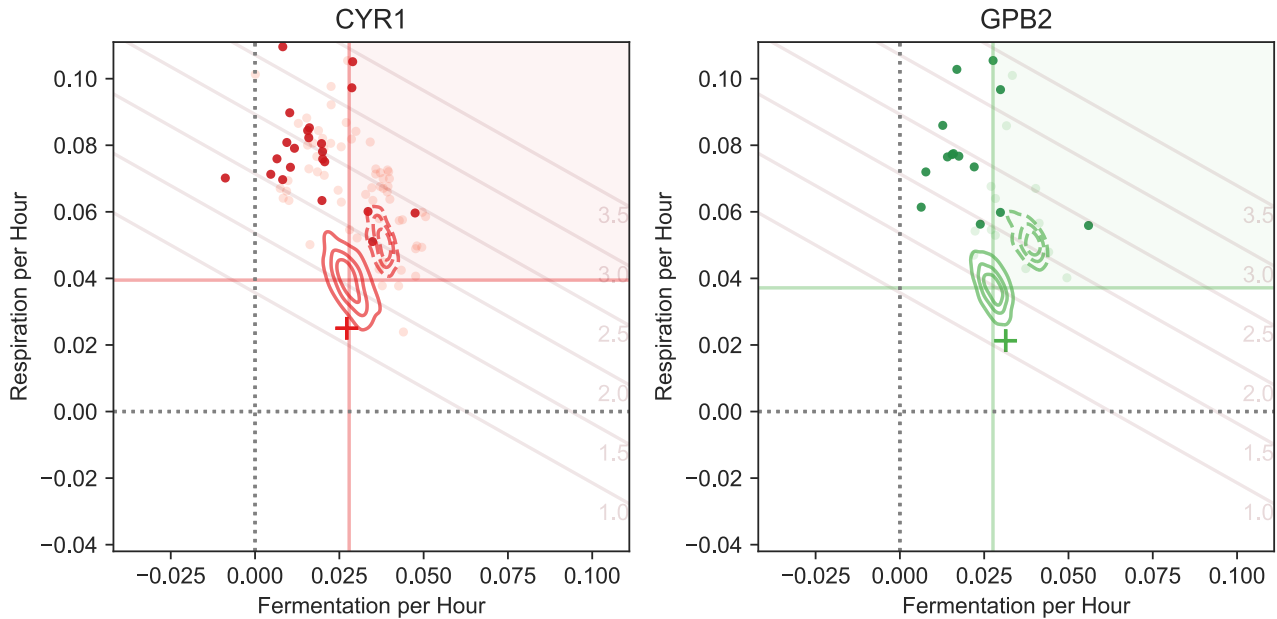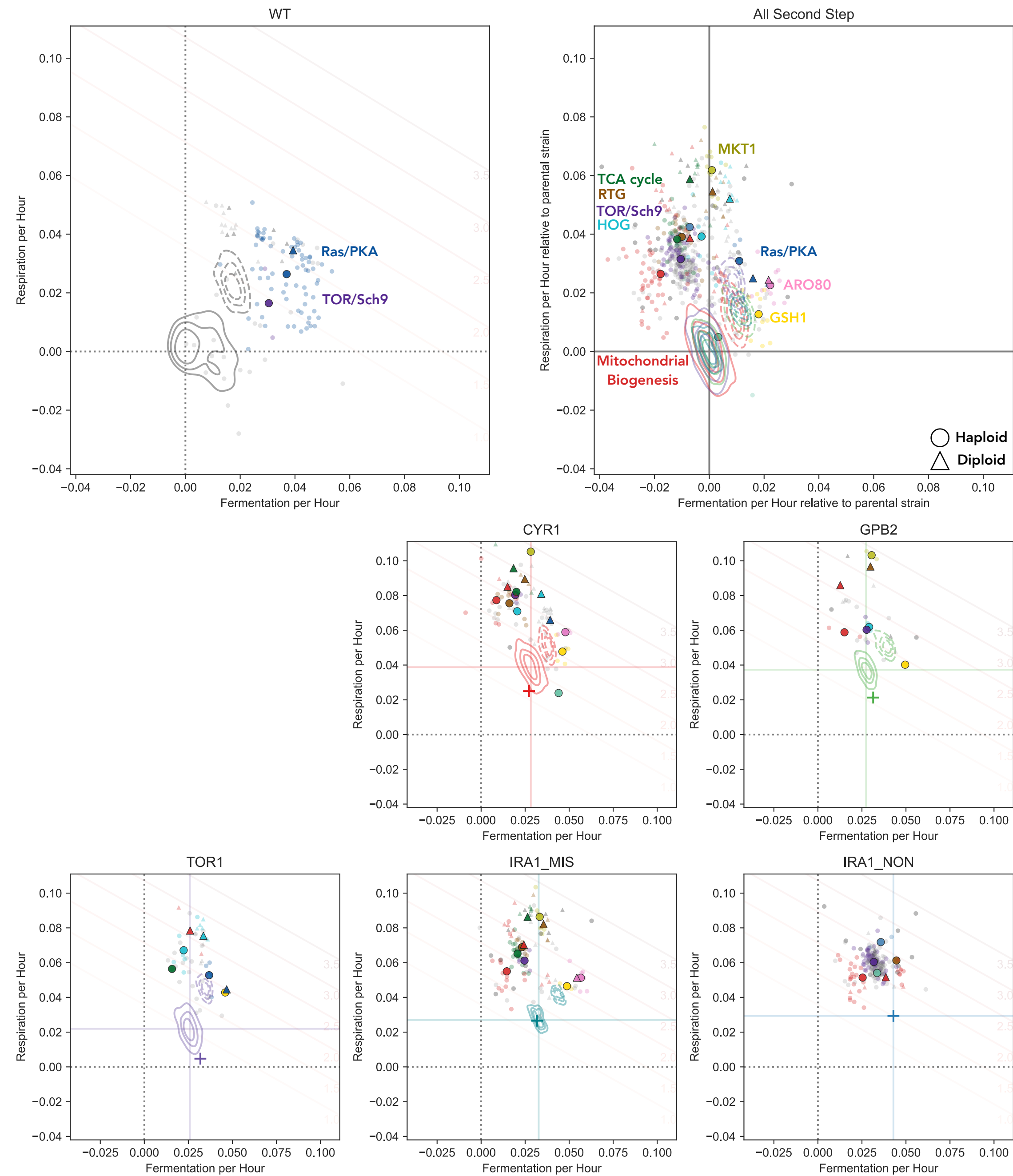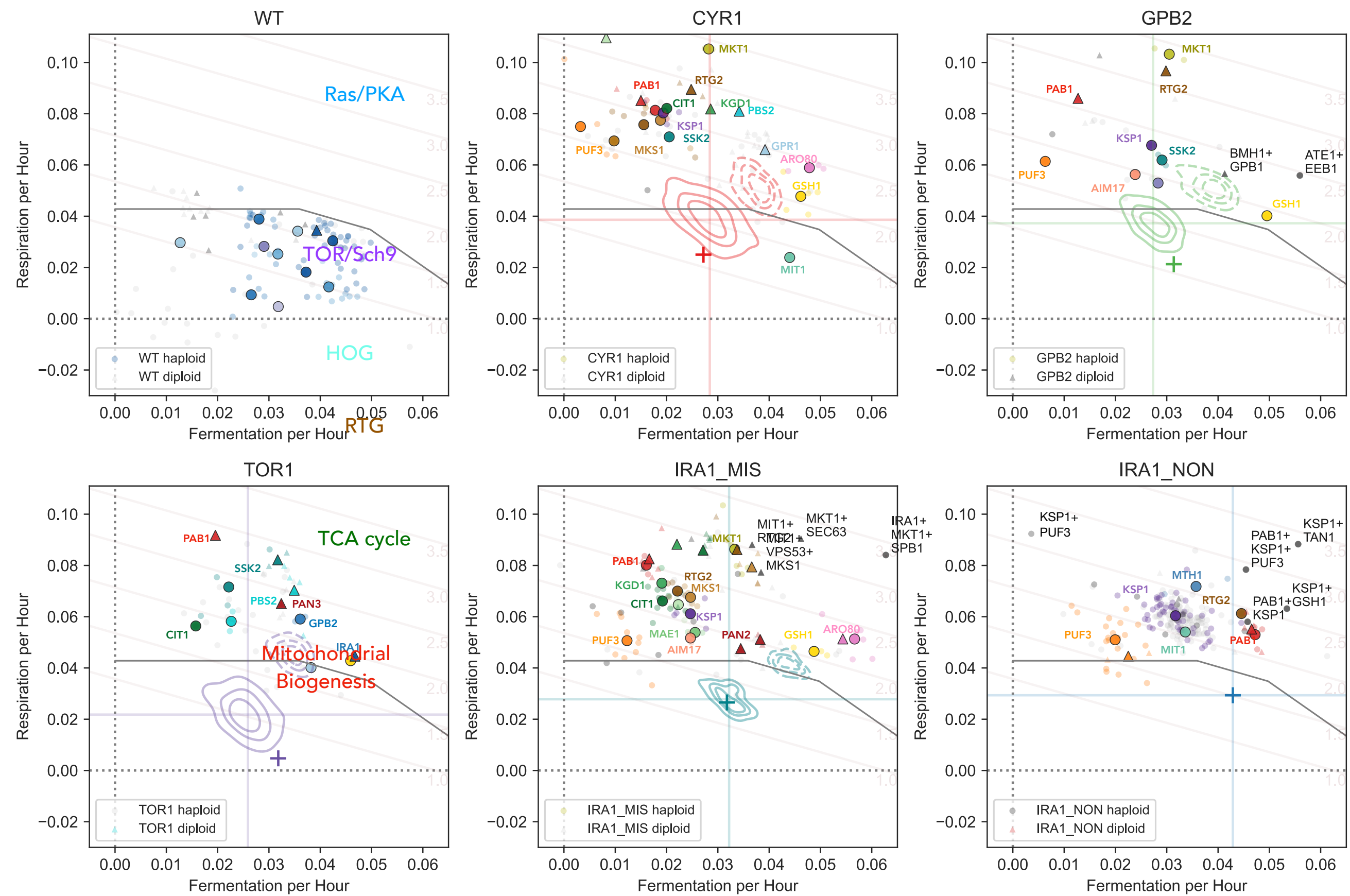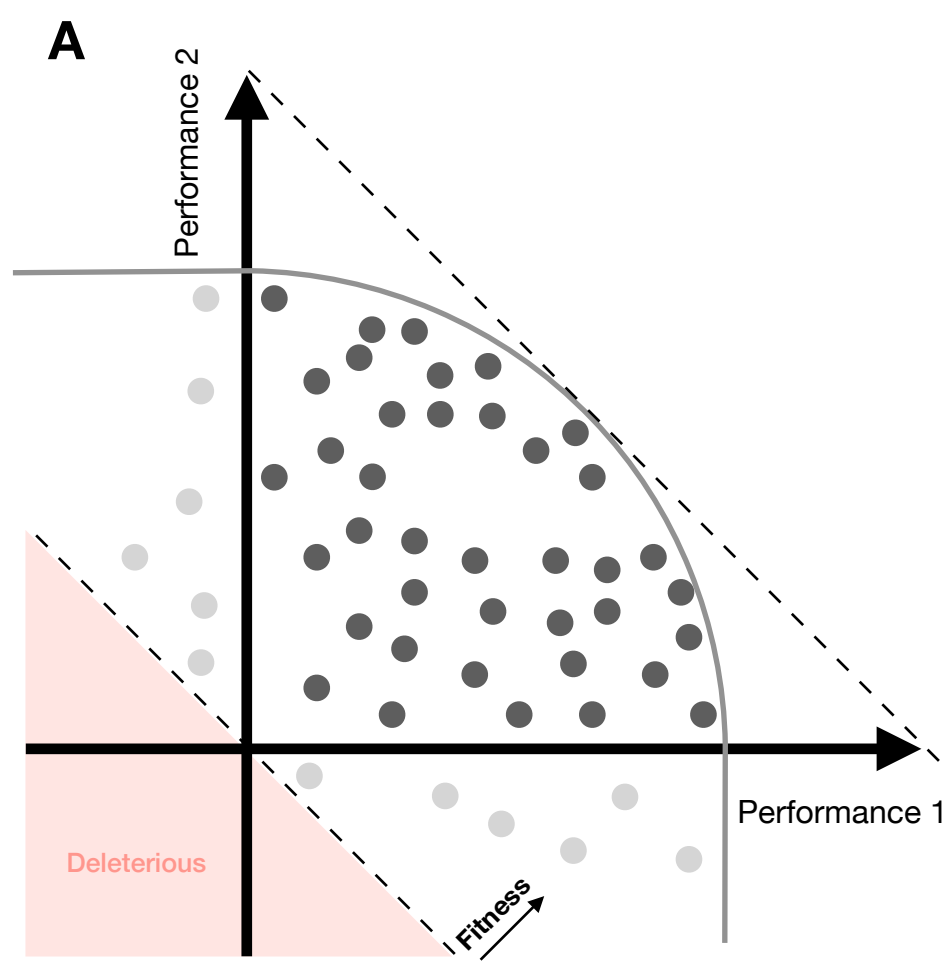
| Pathway	Gene	WT Evo2D	WT Evo3D	TOR1 Evo2D	TOR1 Evo3D	GPB2 Evo2D	GPB2 Evo3D	CYR1 Evo2D	CYR1 Evo3D	IRA1_MIS Evo2D	IRA1_MIS Evo3D	IRA1_NON Evo2D	IRA1_NON Evo3D
Ras/PKA	IRA1	30/77									1/34*		
	IRA2	11/77		1/21									
	GPB1	4/77				1/7*							
	GPB2	14/77		2/21									
	PDE2	11/77											
	CYR1	3/77						1/28					
	GPR1							1/28					
	RAS2	1/77		1/21									
	TFS1	1/77											
TOR/Sch9	TOR1	1/77											
	KOG1	1/77											
	SCH9					1/7							
	KSP1					1/7	1/8*	1/28	2/14	4/69		32/76	30/33
HOG	HOG1							1/28					
	PBS2			6/21									
	SSK2			7/21		1/7	1/8	1/28					
RTG	RTG2						1/8	4/28	2/14	9/69	1/34	1/76	
	MKS1							2/28	1/14	7/69	1/34*		
	BMH1					1/7*		1/28					
TCA cycle	CIT1			1/21				1/28		16/69	1/34*		
	KGD1							1/28		3/69			
	MDH1									4/69			
	MAE1									2/69		2/76*	
	ALD5								1/14	1/69*			2/33*
Mitochondrial Biogenesis	PUF3						1/8	4/28	2/14	7/69	7/34	24/76	1/33*
	PAB1			1/21			2/8	1/28	4/14	3/69	5/34	12/76	
	PAN2									2/69			
	PAN3			1/21						1/69			
	AIM17						1/8			2/69			
Others	MKT1					1/7	1/8	1/28	1/14	1/69*	9/34		
	ARO80							3/28	1/14	3/69	4/34		
	GSH1			1/21		1/7		5/28		2/69	1/34	1/76*	
	MIT1							1/28		2/69*	4/34*	2/76	
	MTH1											2/76	

OLD VERSIONS BELOW

A

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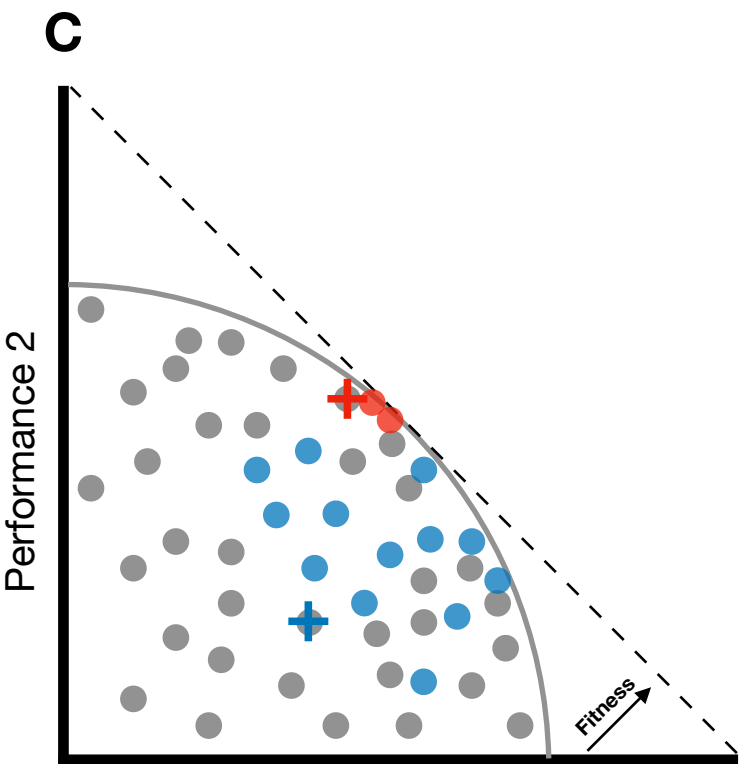
B

C

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

A

Performance 2

Performance 1

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

B

Performance 2

Performance 1

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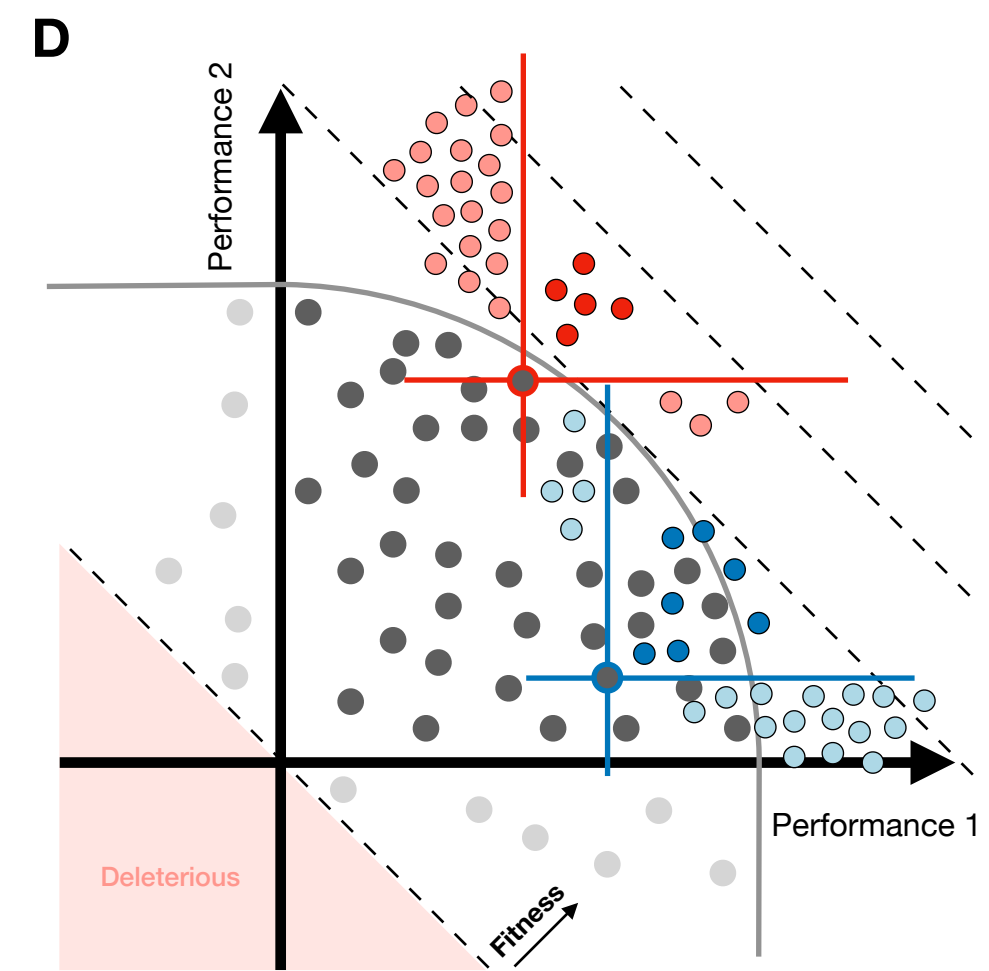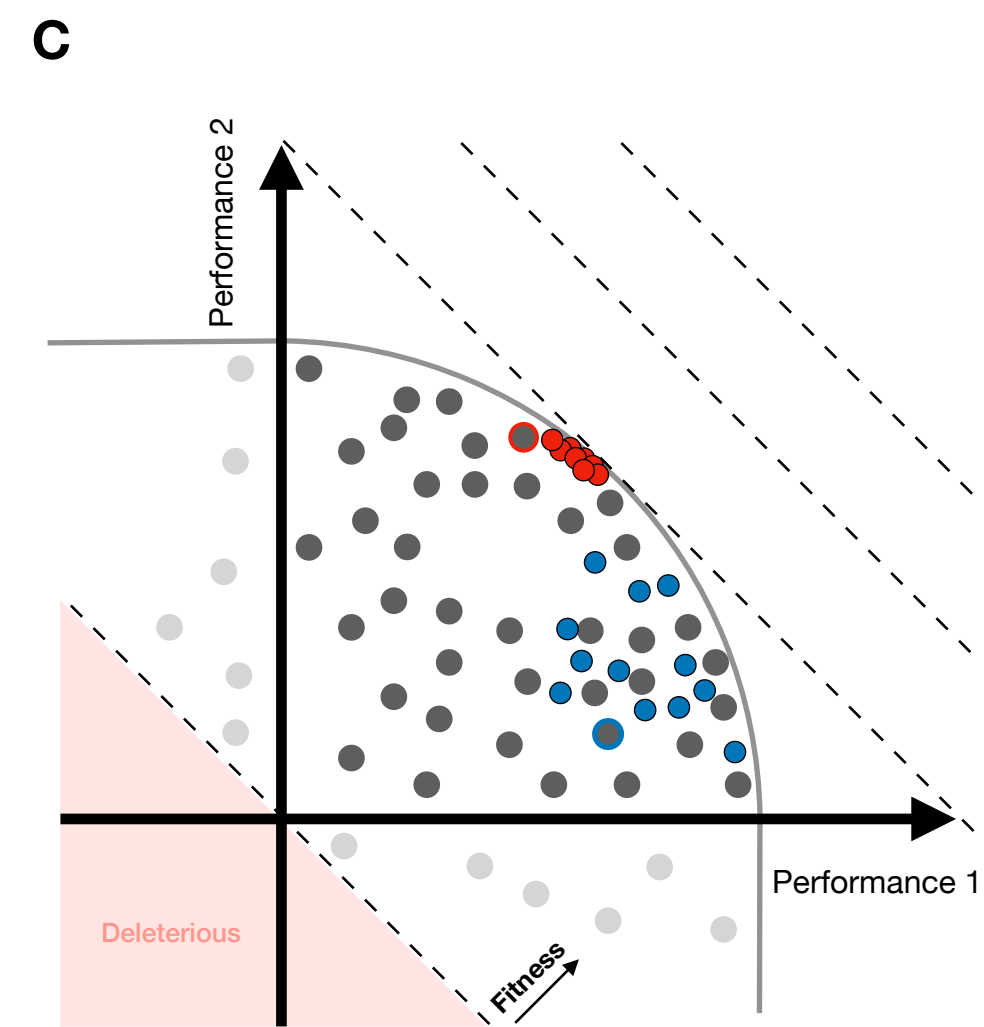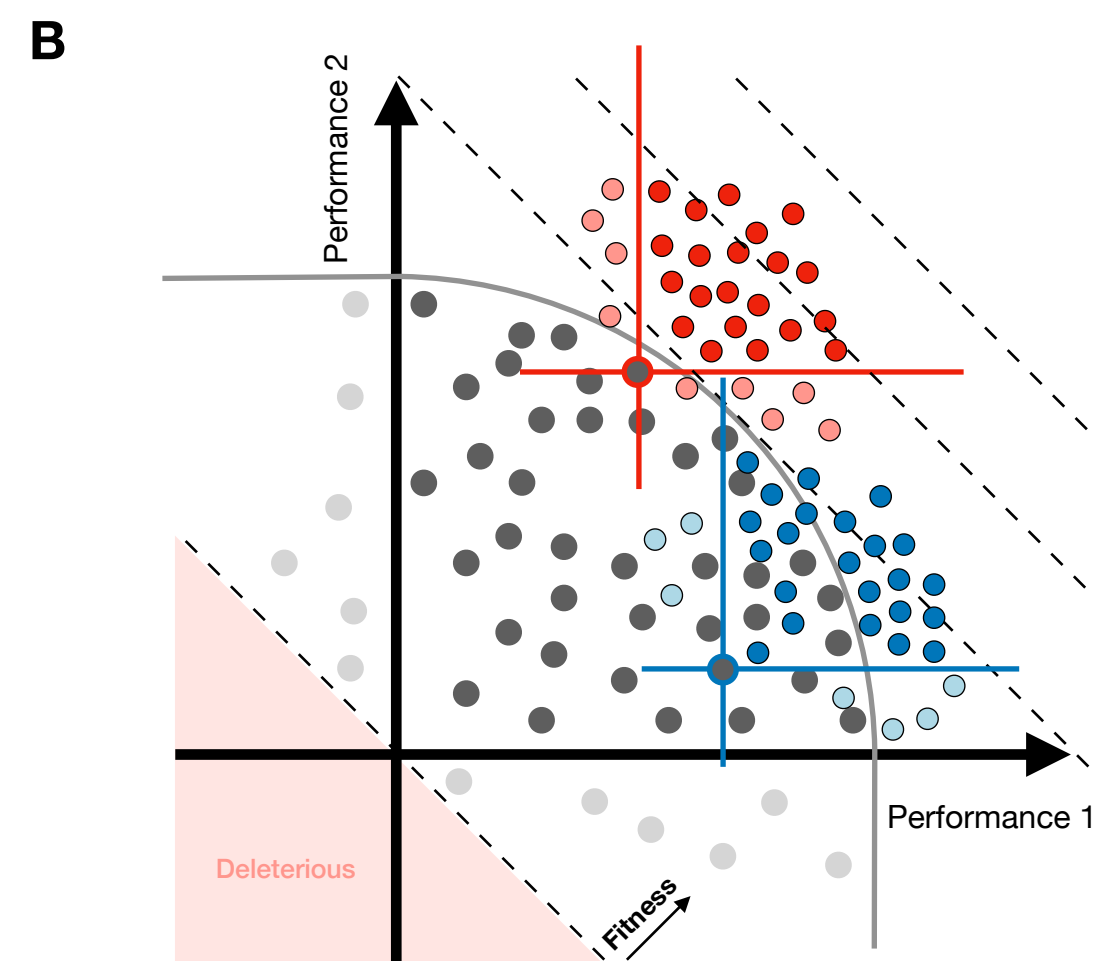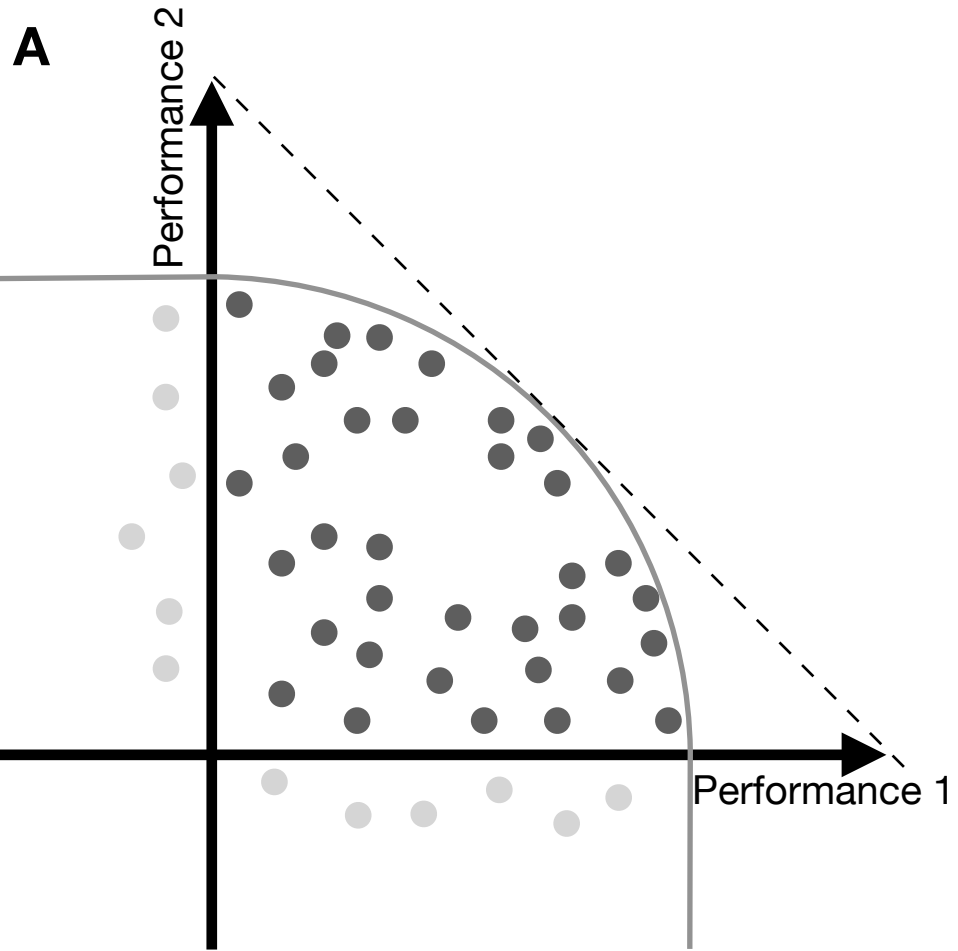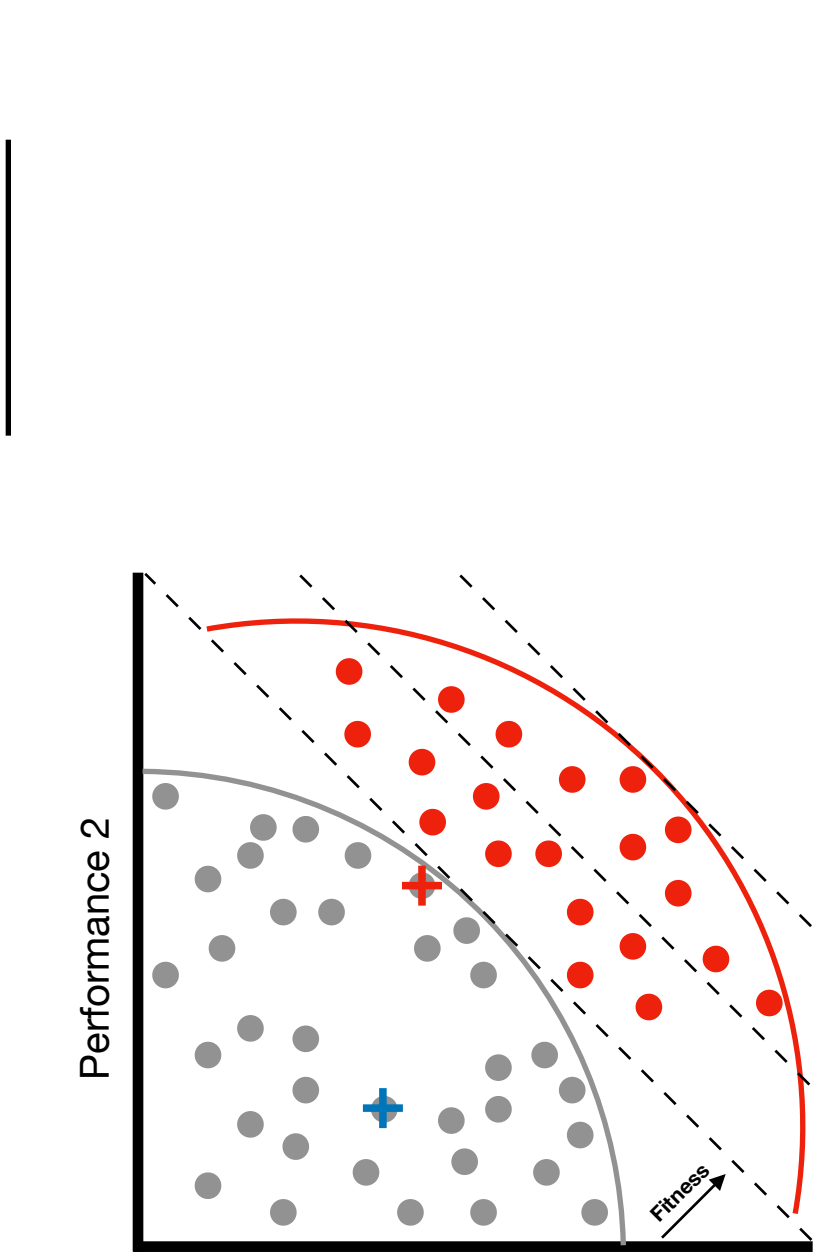
If tradeoffs don't represent any functional or genetic constraints but instead just mutational distance, then further adaptive steps should continue to improve as the first, albeit more slowly due to diminishing returns…
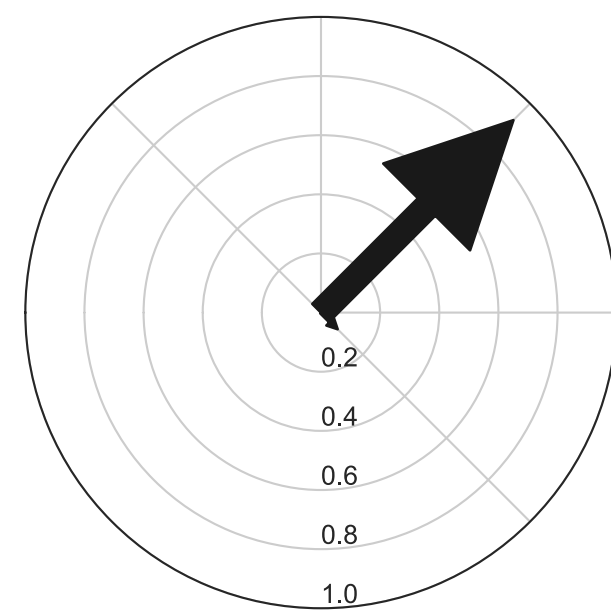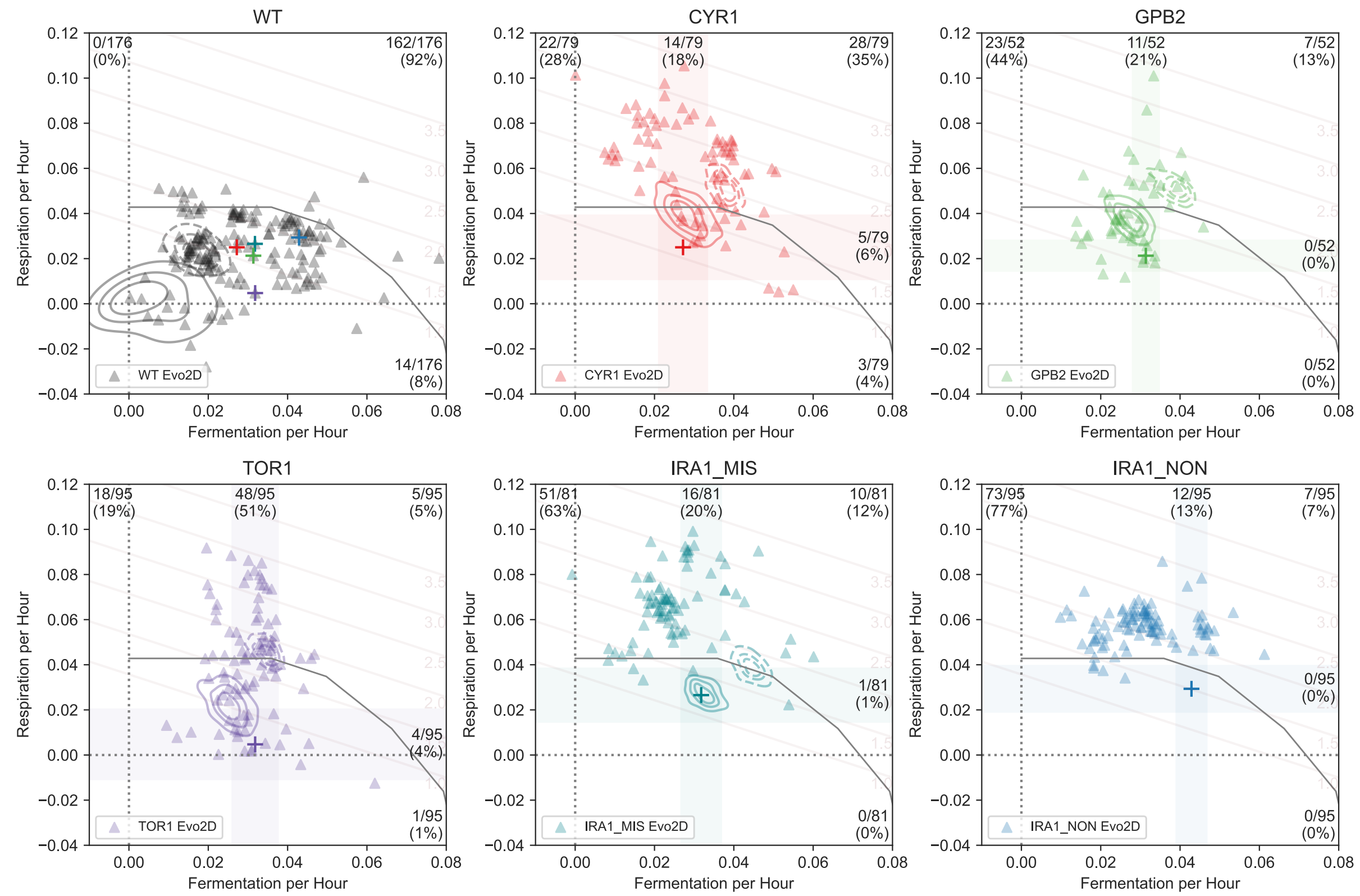
C

Performance 2

Performance 1

Fitness

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
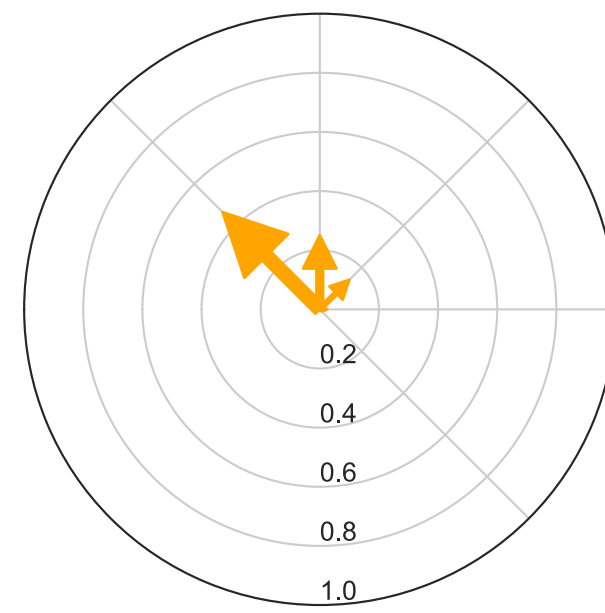
D

Performance 2

Performance 1

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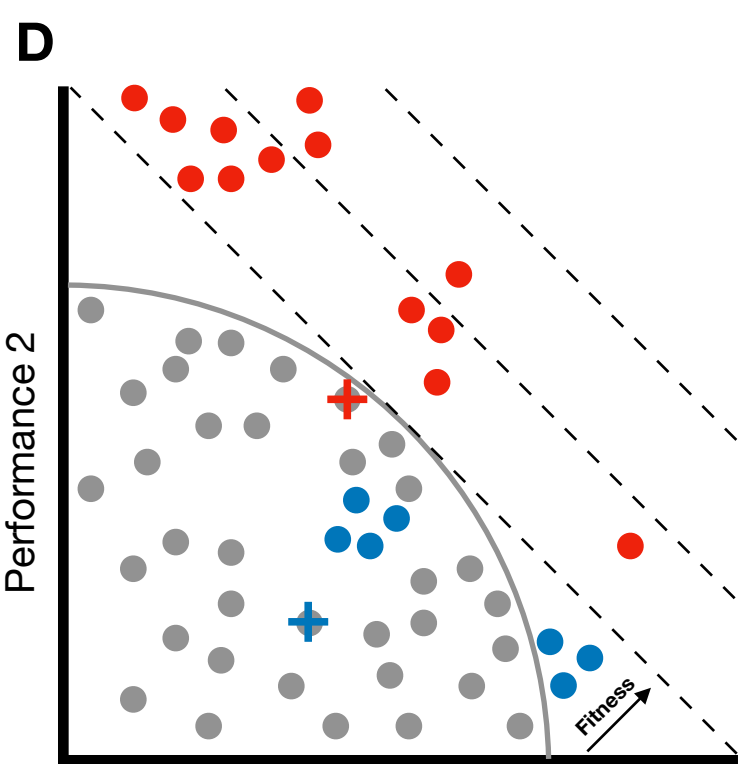
Tradeoffs reflect constraints imposed by genetic wiring, the accessibility of adaptive solutions and their pleiotropic effects.

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