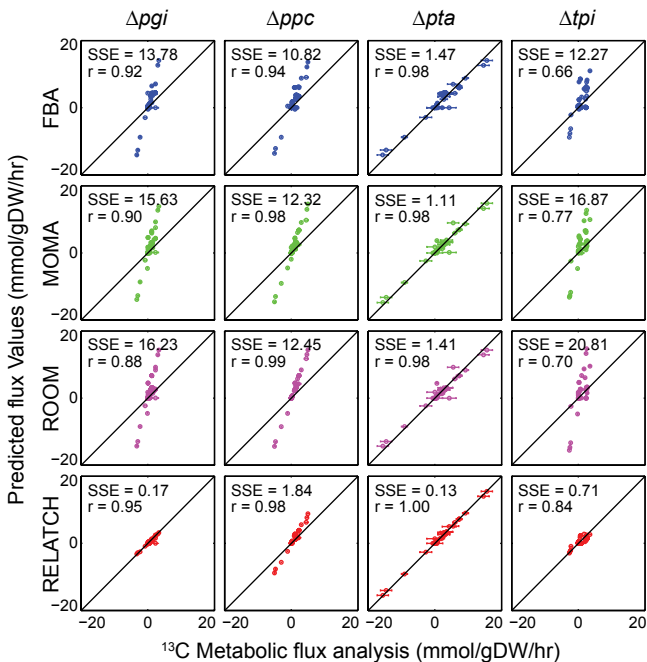
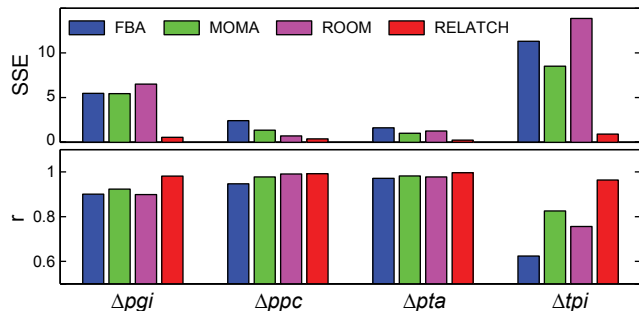


(a) Before adaptive evolution



(b) After adaptive evolution



(c) Largest relative flux changes in evolved strains

	Reaction	Wildtype / Evolved (mmol/gDW/hr)	Gene expression change (log ₂ ratio, p-value < 0.05)
Δpgi	PEP $\xrightarrow{\text{non-PTS}}$ PYR	1.40 / 0.00	<i>pykA</i> -2.28 <i>pykF</i> -1.82
	NADH + H ⁺ _[p] $\rightarrow$ NADPH	1.90 / 0.00	<i>pntA</i> ¹ -6.25 <i>pntB</i> ¹ -7.52
	NADPH $\rightarrow$ NADH	0.00 / 3.25	<i>sthA</i> ¹ +3.06
Δppc	AKG $\rightarrow$ SUCC	2.40 / 0.67	<i>sucA</i> -3.83 <i>sucB</i> -2.42 <i>sucC</i> -1.42 <i>sucD</i> -1.60
	ICIT $\rightarrow$ SUCC	0.00 / 1.75	<i>aceA</i> +1.49 <i>aceB</i> NC ² <i>glcB</i> +2.33
Δpta	PYR $\rightarrow$ PYR _{Ext}	0.00 / 5.21	No gene associated
Δtpi	DHAP $\rightarrow$ PYR	0.00 / 5.68	<i>mgsA</i> ³ NC ² <i>gloA</i> ³ +3.67 <i>gloB</i> -1.06 <i>dld</i> NC ²
	GLC _{Ext} $\xrightarrow{\text{non-PTS}}$ G6P	0.00 / 3.37	<i>galP</i> +8.14 <i>glk</i> +2.44

¹ 10 mutations found in these genes by whole-genome resequencing of 9 evolved strains

² No significant change ³ 10-fold higher *in vitro* enzyme activities in these enzymes