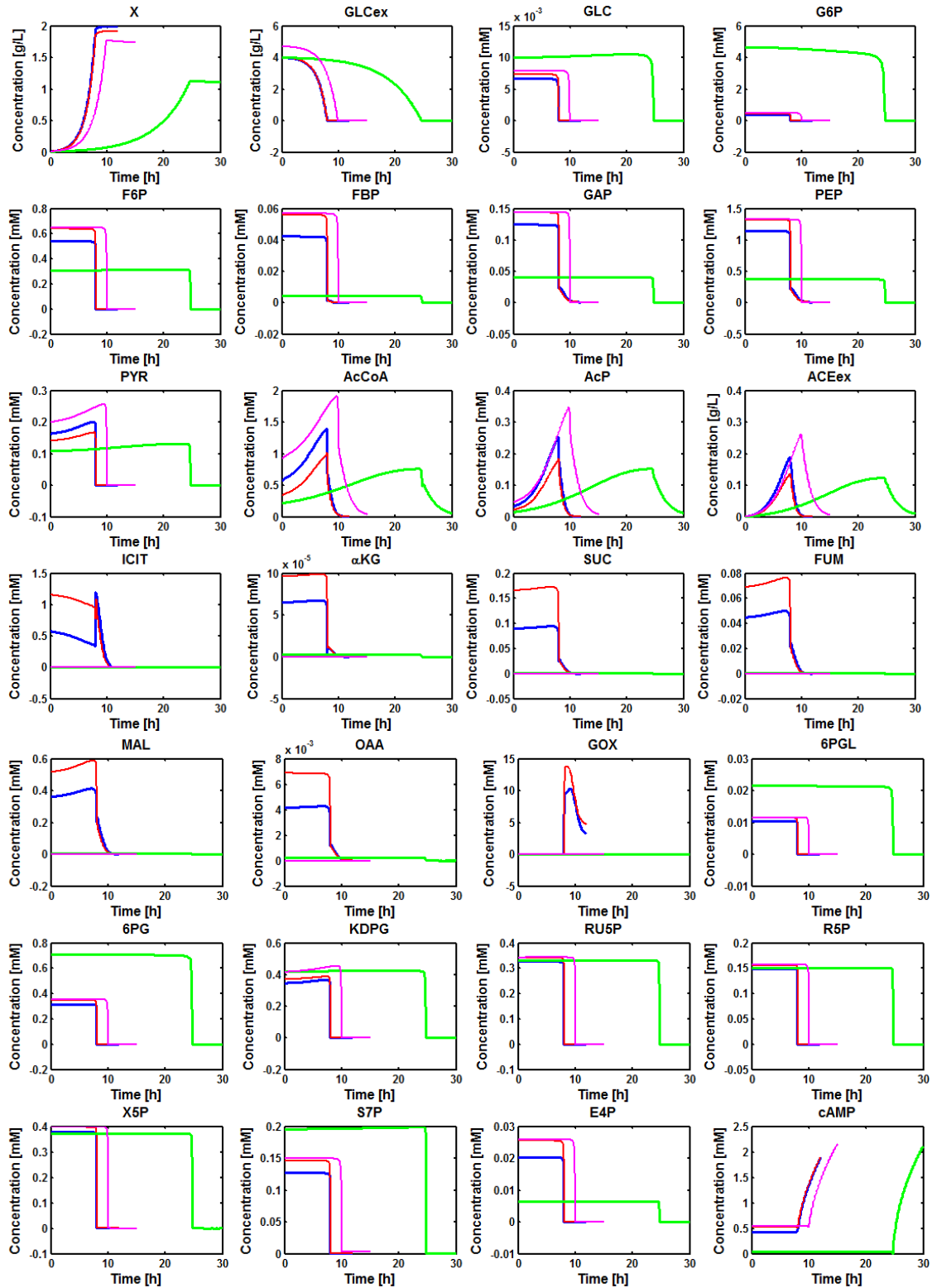
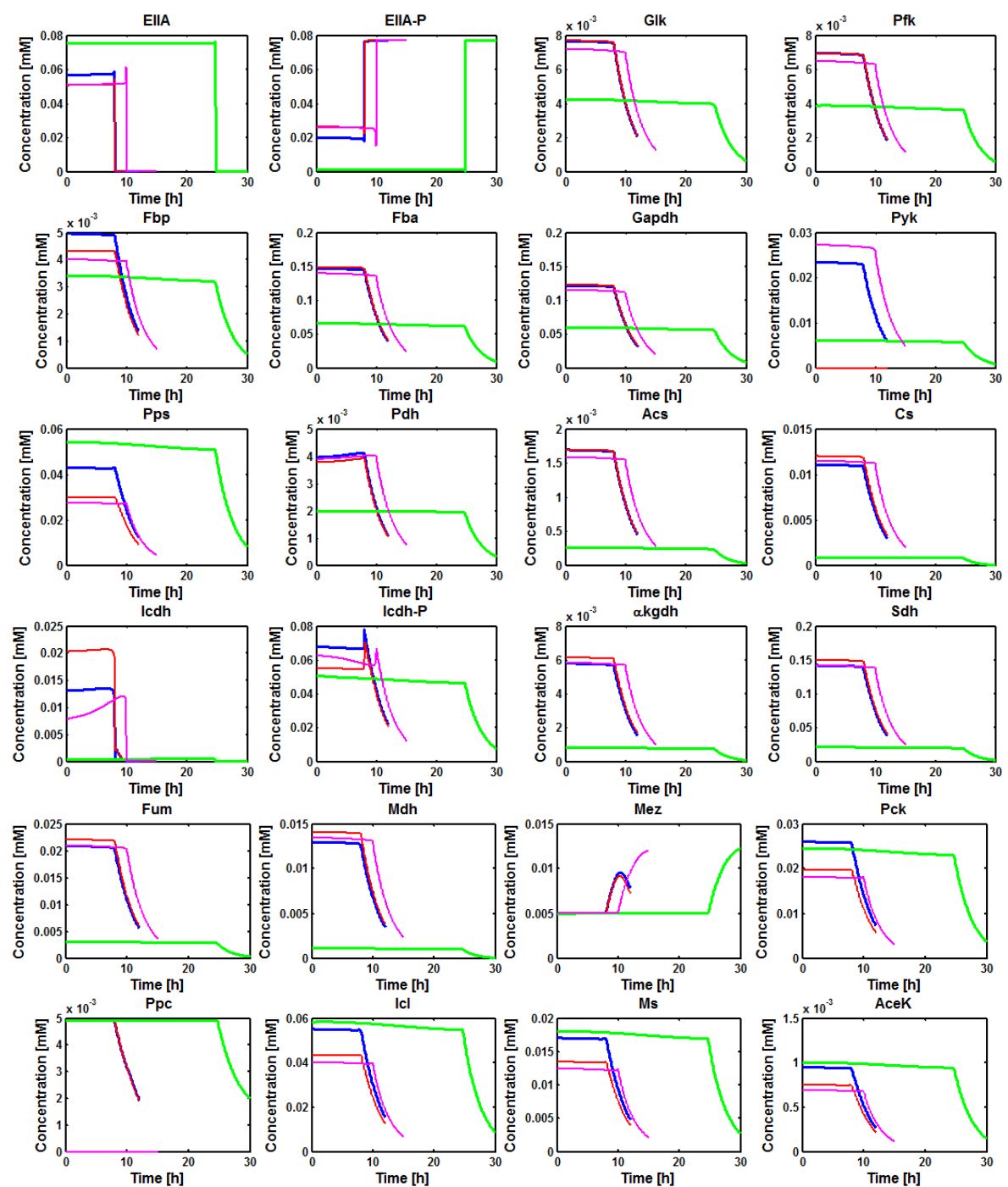


Simulation results

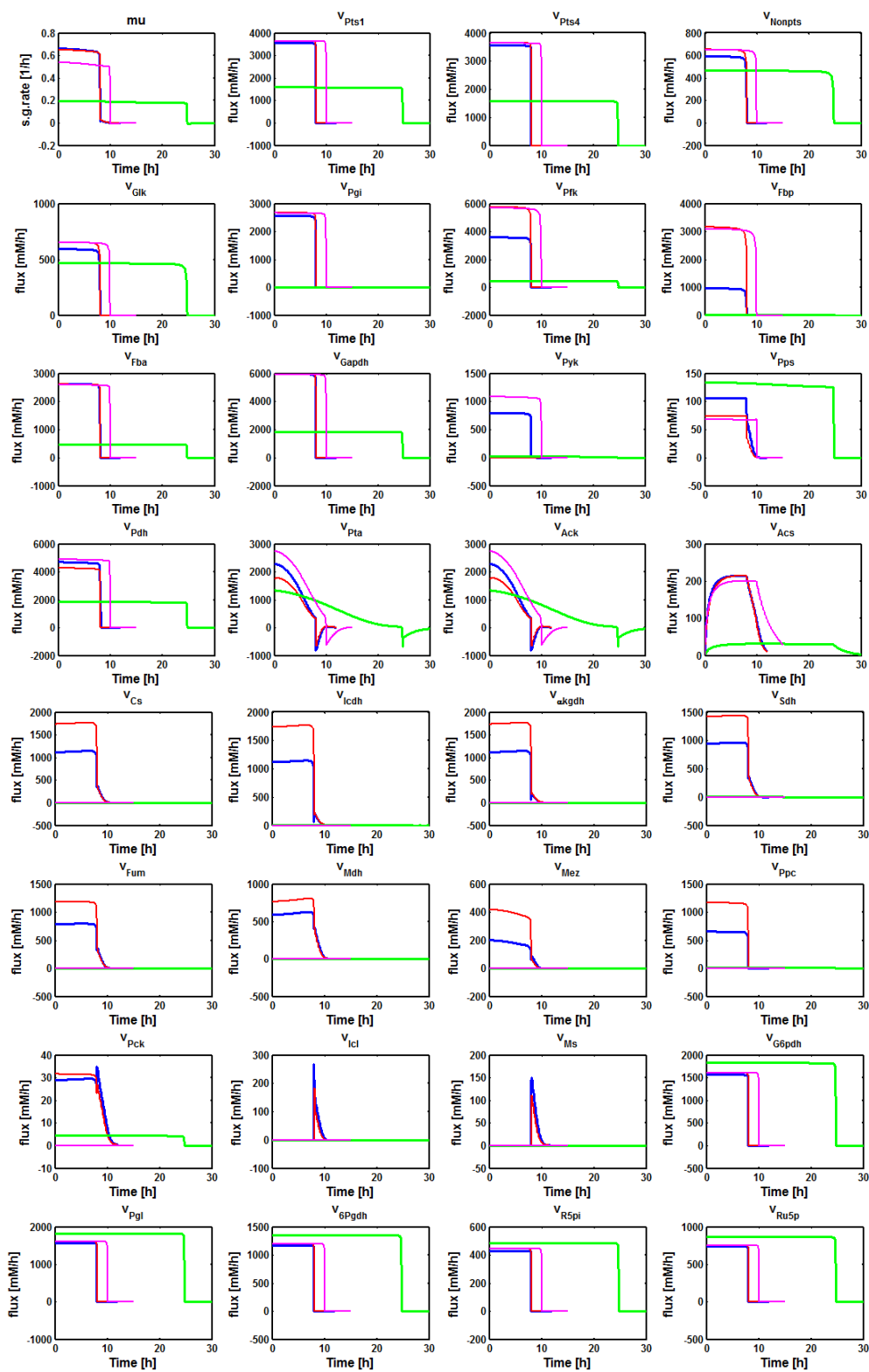
A



B



C



C (continue...)

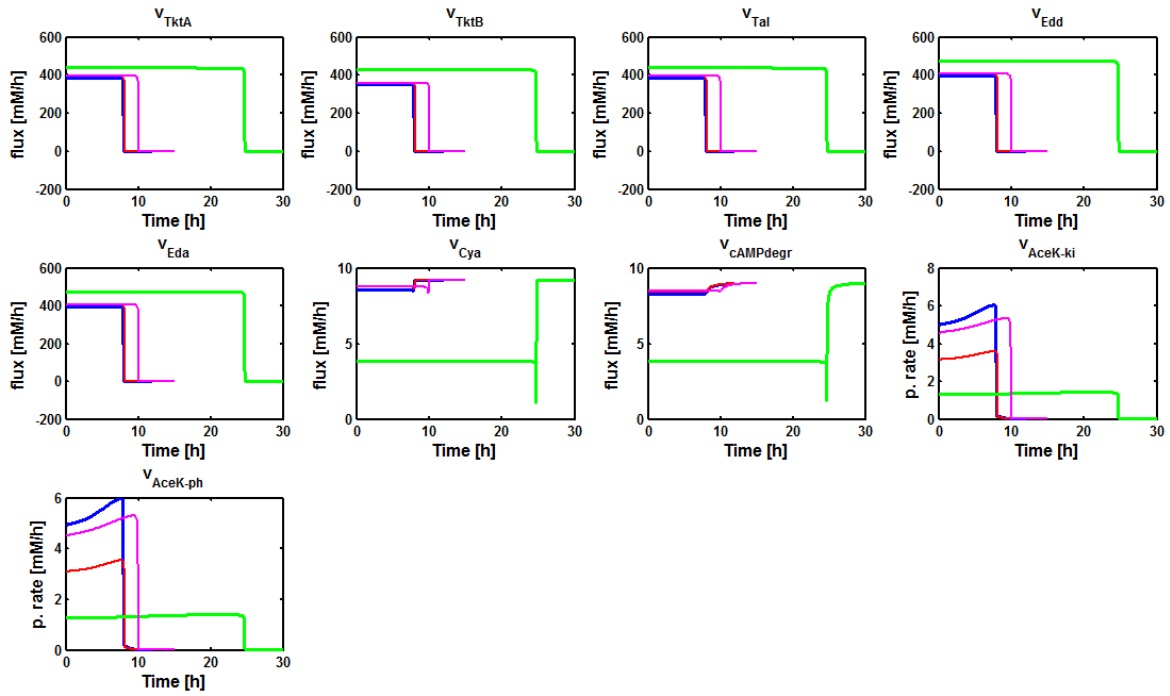


Figure S1: Simulated time course of WT, $\Delta pykF$, Δpgi and Δppc

The blue, red, green, and magenta lines indicate WT, $\Delta pykF$, Δpgi and Δppc , respectively.

A. Metabolite concentrations; **B.** Enzyme concentrations; **C.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

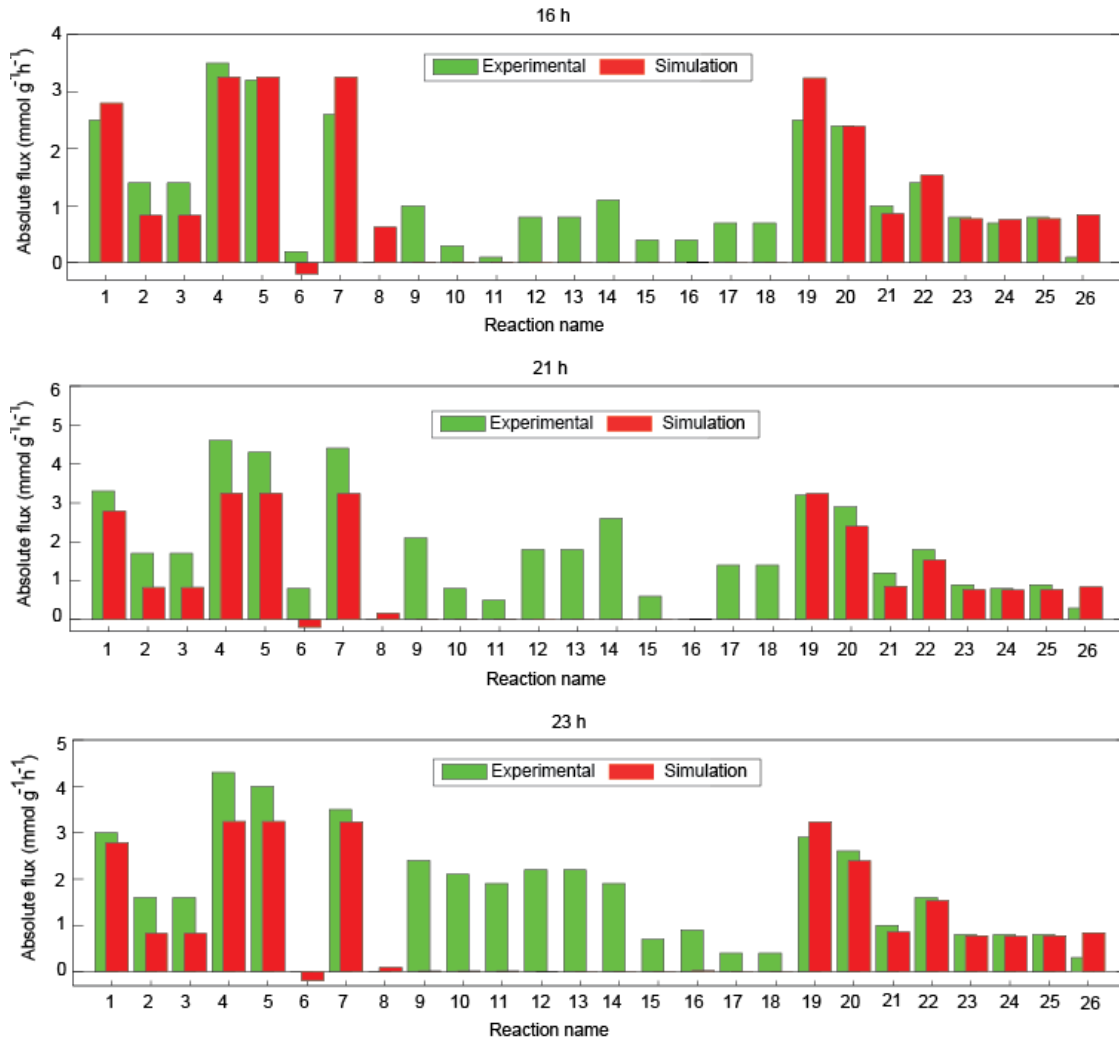


Figure S2: Comparison of the simulated flux with the experimental flux [1] for Δpgi at 16 h, 21h and 23h, respectively.

The indexes of the reaction names indicate 1: v_Pts4, 2: vE_Pfk-vE_Fbp, 3: vE_Fba, 4: vE_Gapdh, 5: vE_Gapdh, 6: vE_Pyk-vE_Pps, 7: vE_Pdh, 8: vE_Pta, 9: vE_Cs, 10: vE_Icdh, 11: vE_αkgdh, 12: vE_Sdh, 13: vE_Fum, 14: vE_Mdh, 15: vE_Mez, 16: vE_Ppc-vE_Pck, 17: vE_Icl, 18: vE_Ms, 19: vE_G6pdh, 20: vE_6Pgdh, 21: vE_R5pi, 22: vE_Ru5p, 23: vE_TktA, 24: vE_TktB, 25: vE_Tal, 26: vE_Edd.

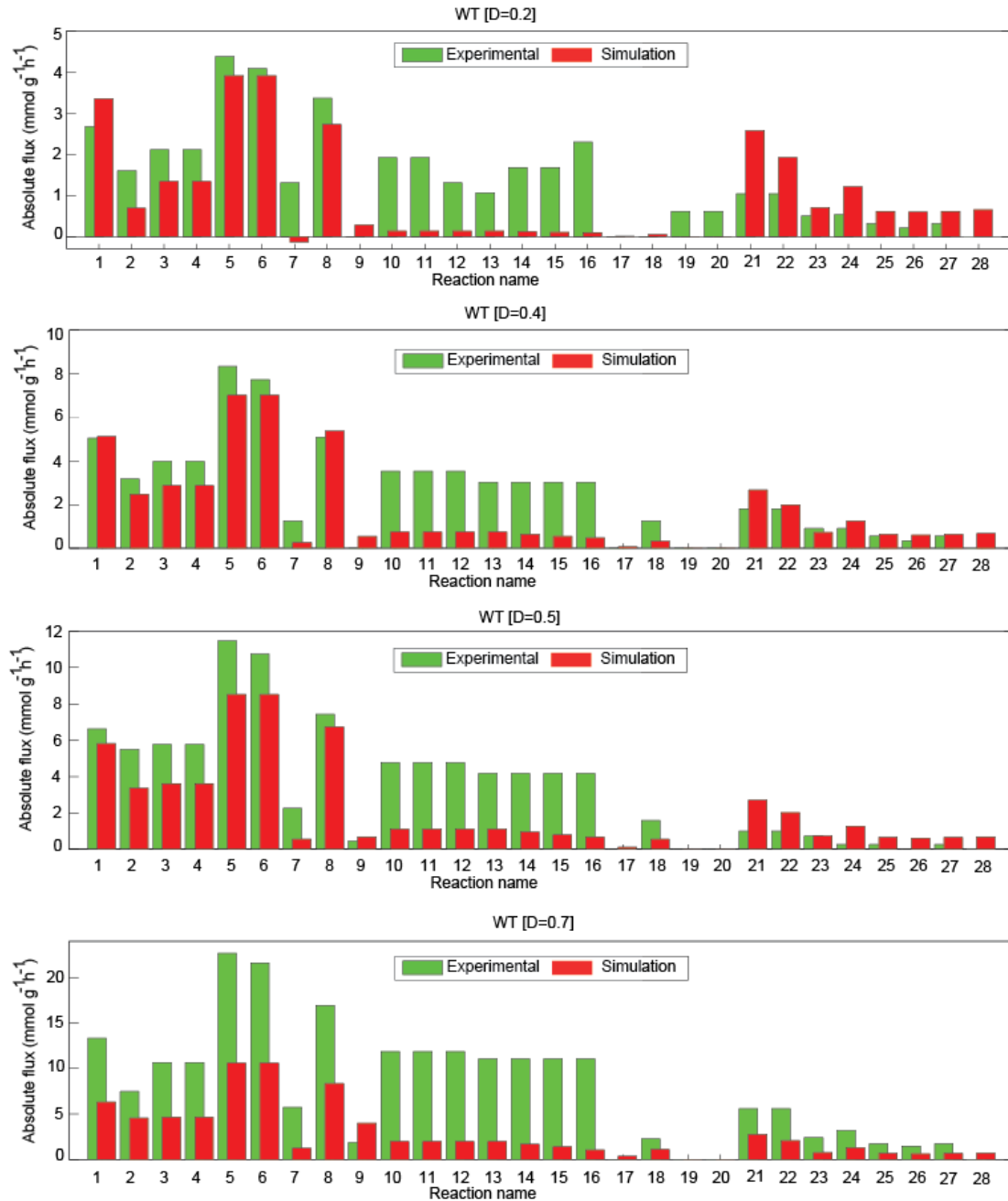
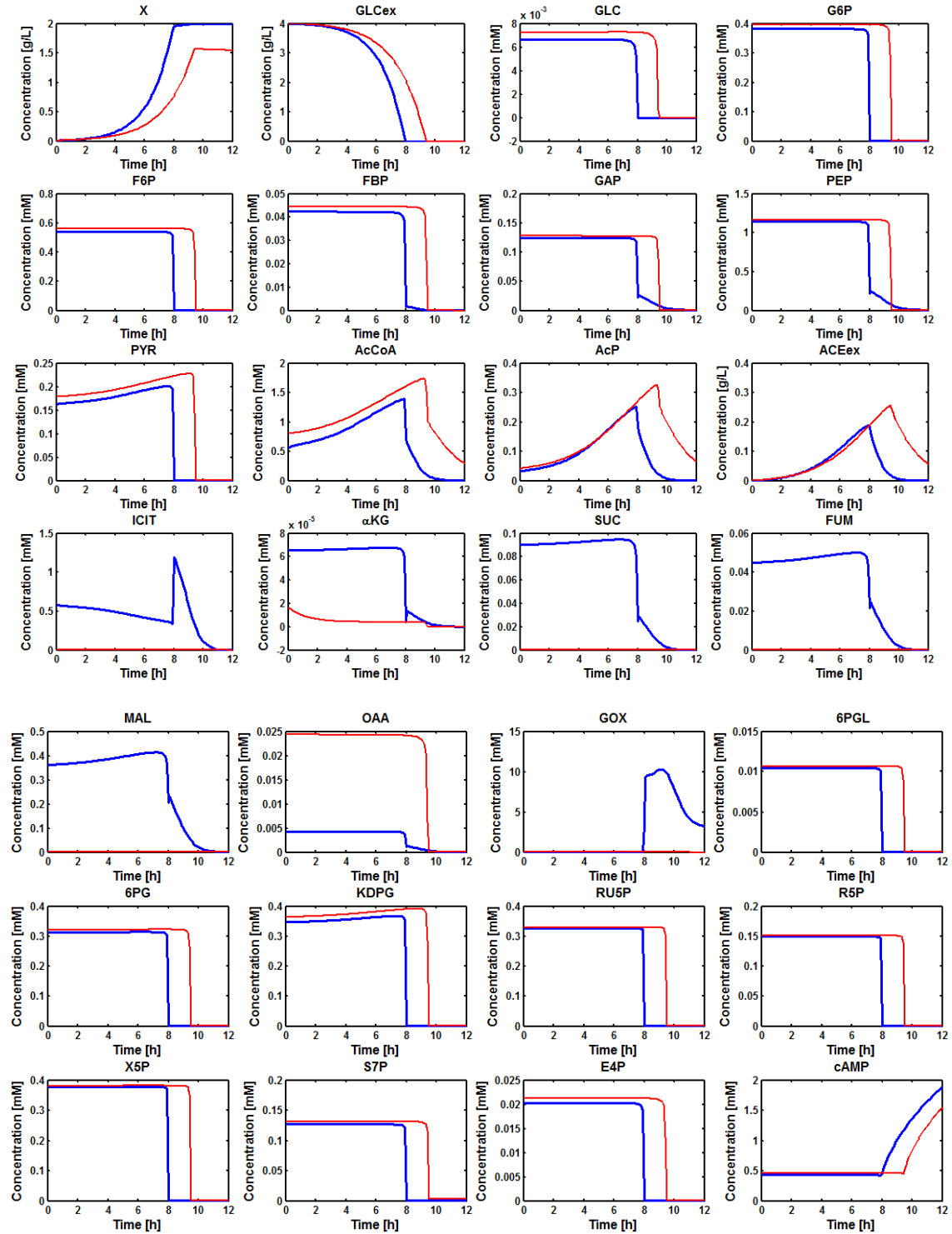


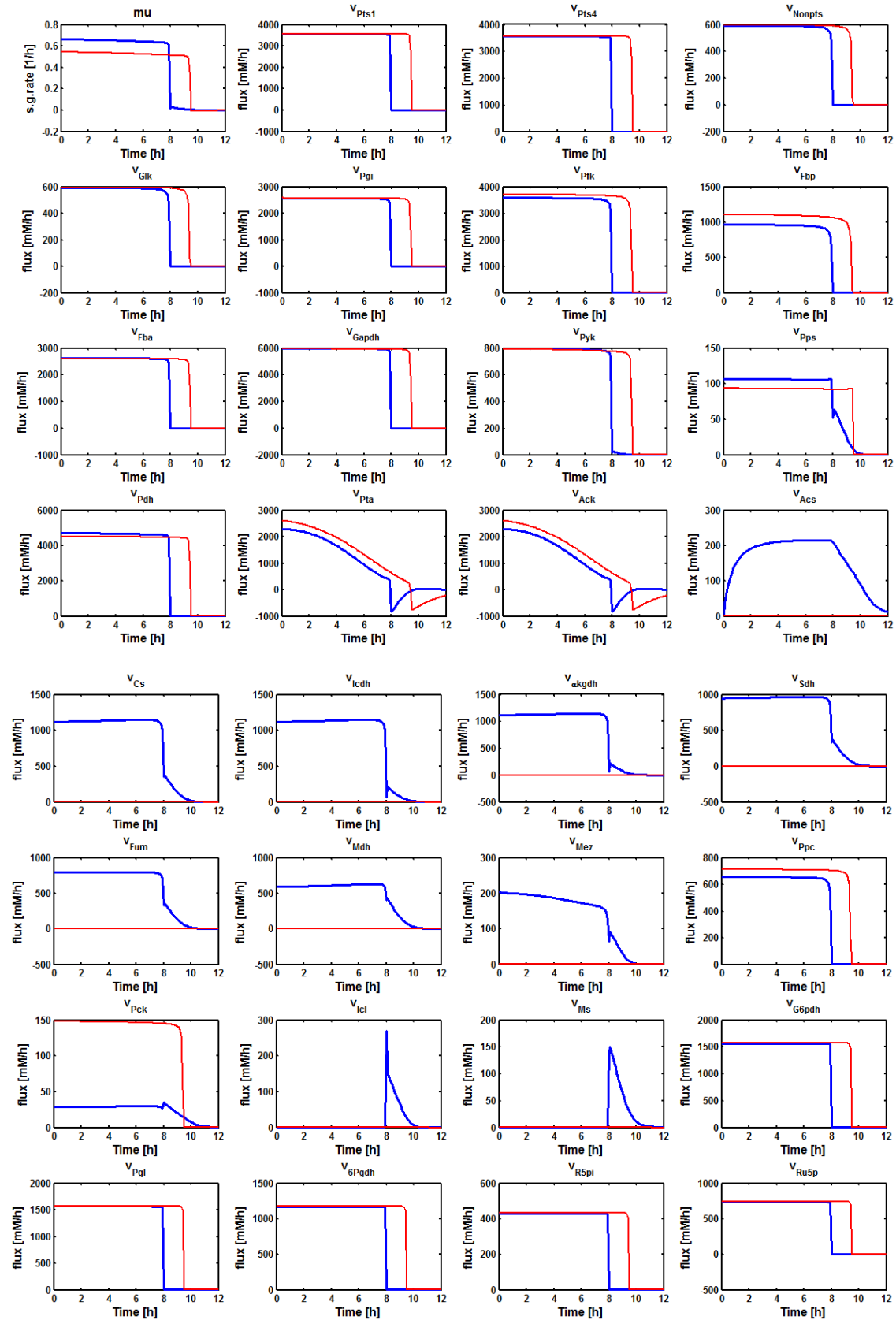
Figure S3: Comparison of the simulated flux with experimental flux [2] of WT at different dilution rates in a continuous culture.

The indexes of the reaction name indicate 1: v_Pts4, 2: vE_Pgi, 3: vE_Pfk - vE_Fbp, 4: vE_Fba, 5 : vE_Gapdh, 6: vE_Gapdh, 7: vE_Pyk - vE_Pps, 8: vE_Pdh, 9: vE_Ack - vE_Acs, 10: vE_Cs, 11: vE_Cs, 12: vE_Icdh, 13: vE_αkgdh, 14: vE_Sdh, 15: vE_Fum, 16: vE_Mdh, 17: vE_Mez, 18: vE_Ppc-vE_Pck, 19: vE_Icl, 20: vE_Ms, 21: vE_G6pdh, 22: vE_6Pgdh, 23: vE_R5pi, 24: vE_Ru5p, 25: vE_TktA, 26: vE_TktB, 27: vE_Tal, 28: vE_Edd.

A



B



B (continue...)

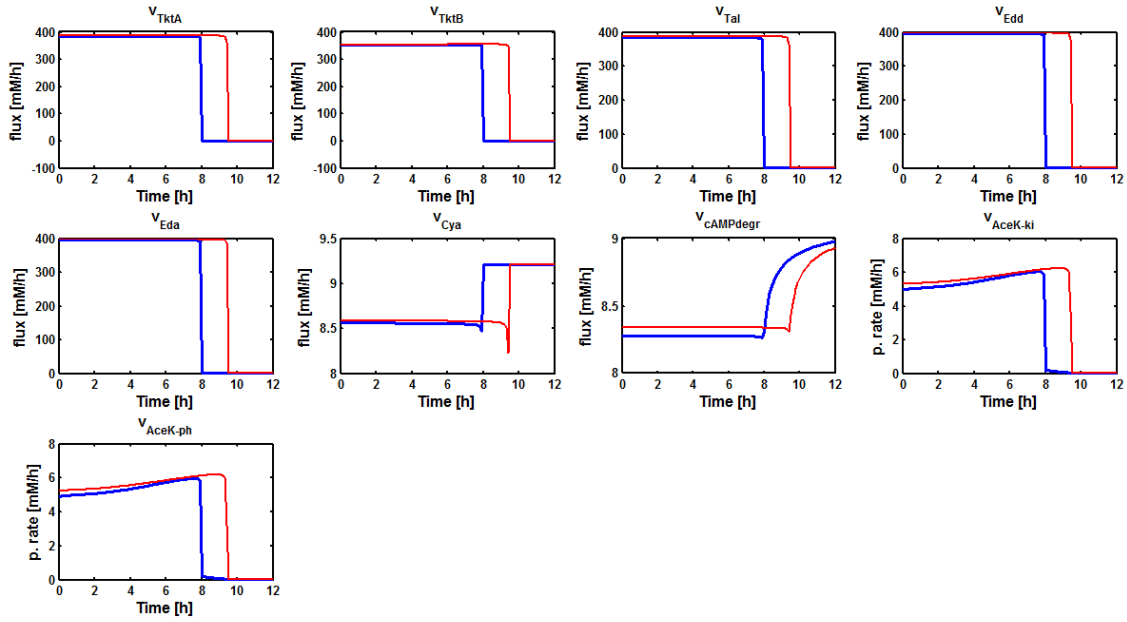
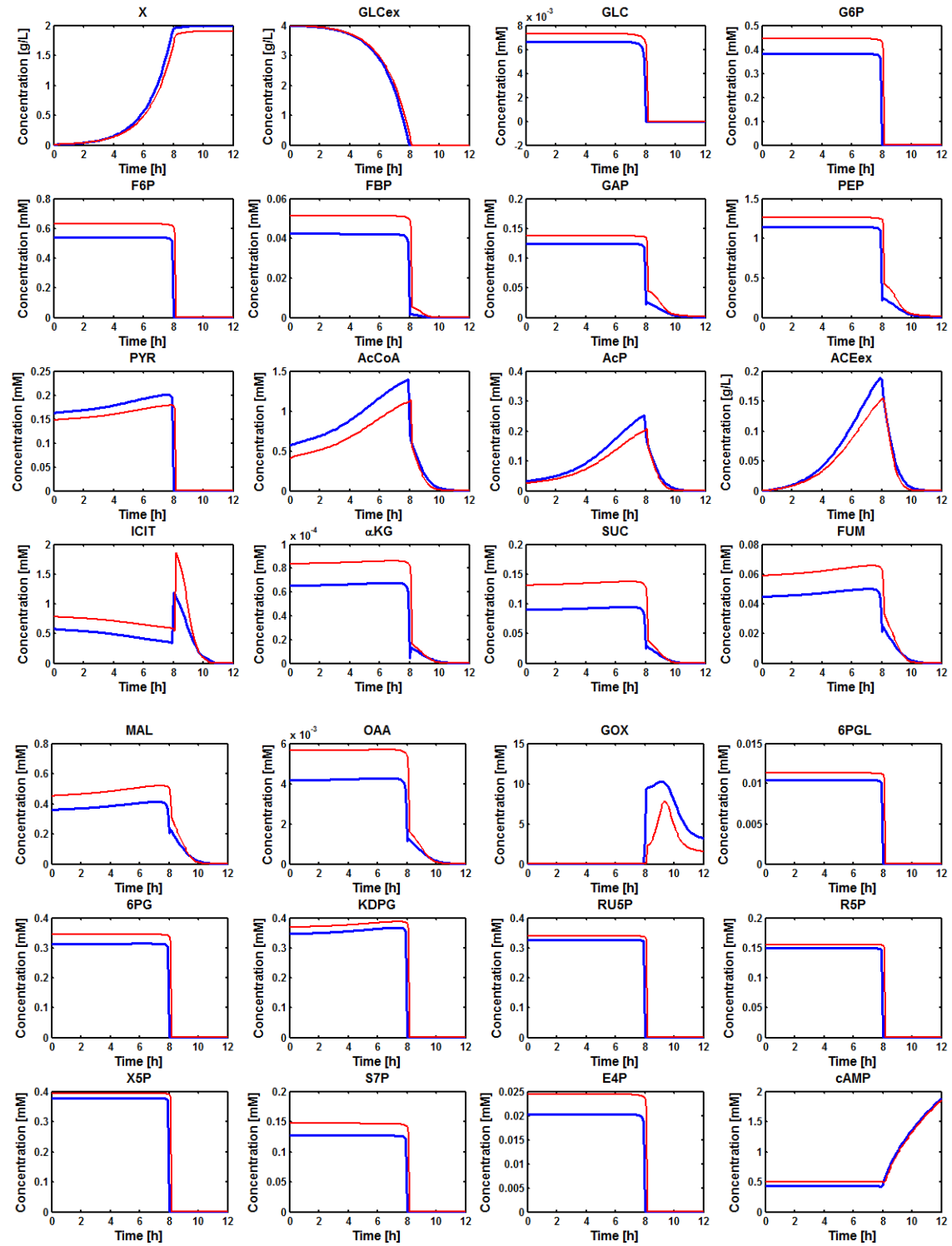


Figure S4: Effect of Crp regulation on dynamic behaviors.

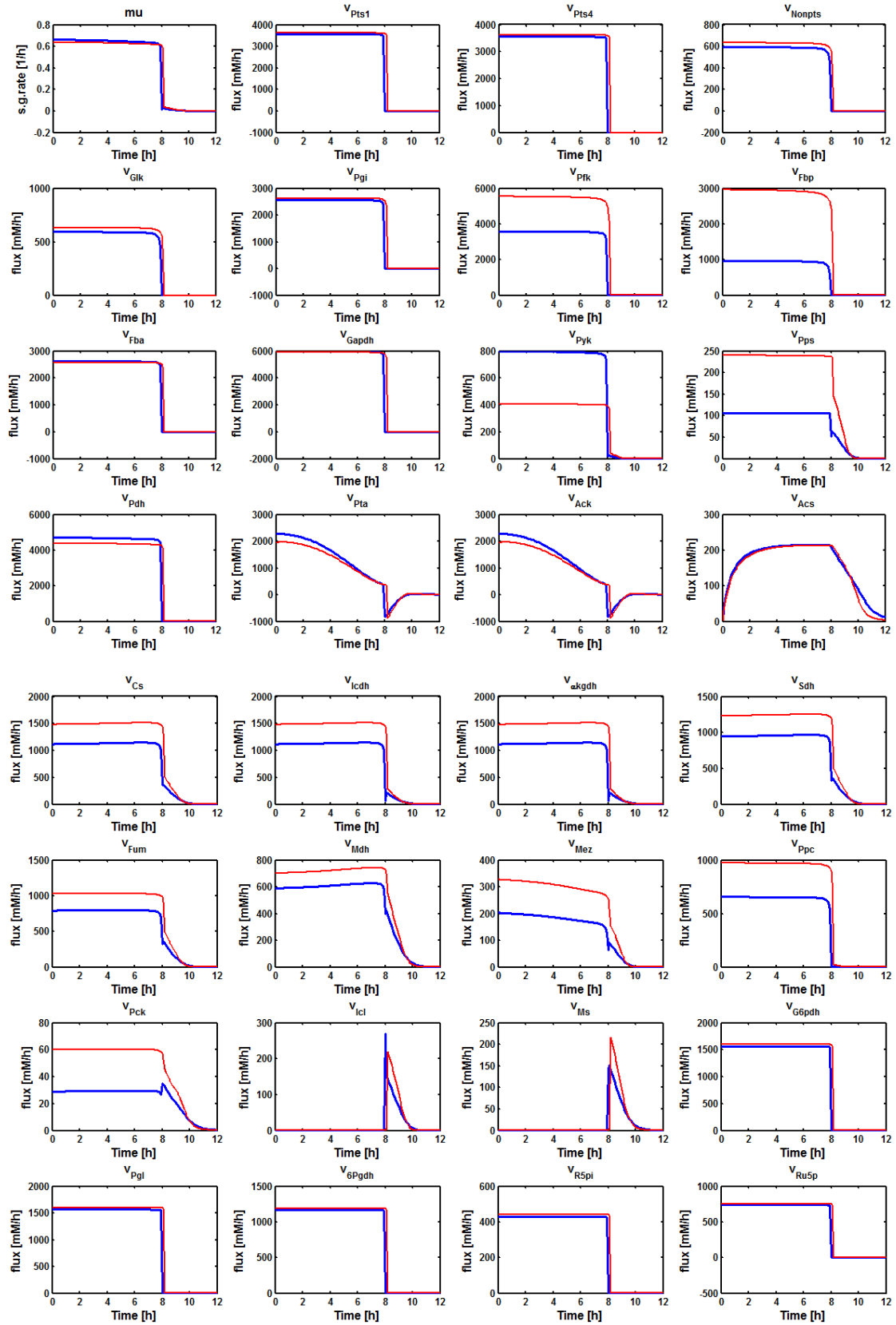
The blue and red lines indicate WT and the virtual mutant lacking a Crp-cAMP complex, respectively.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

A



B



B (continue...)

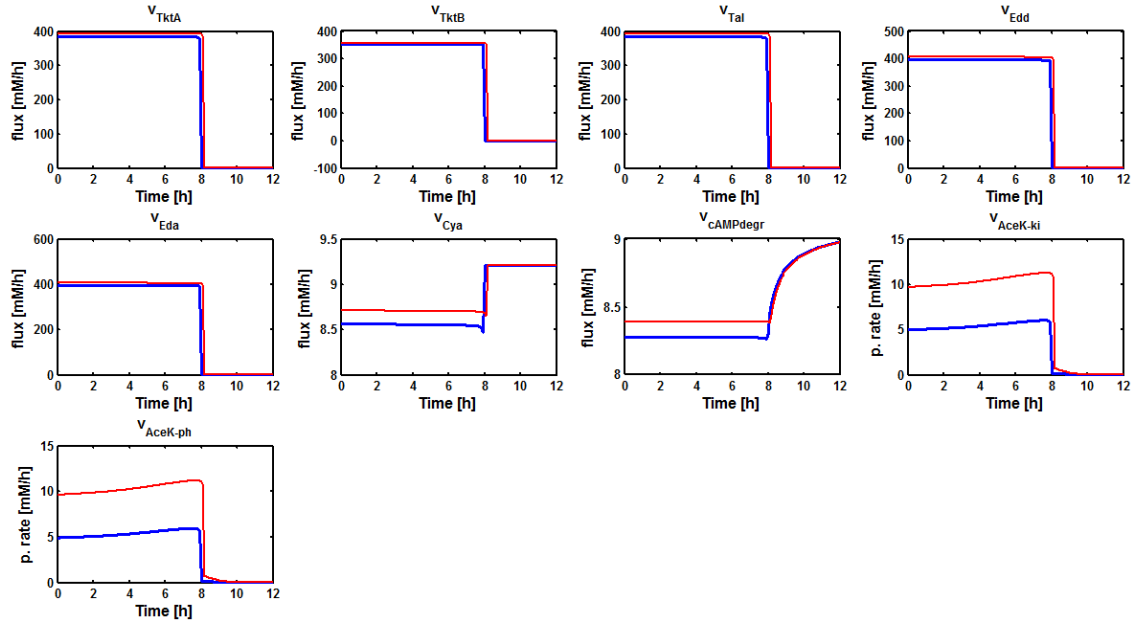
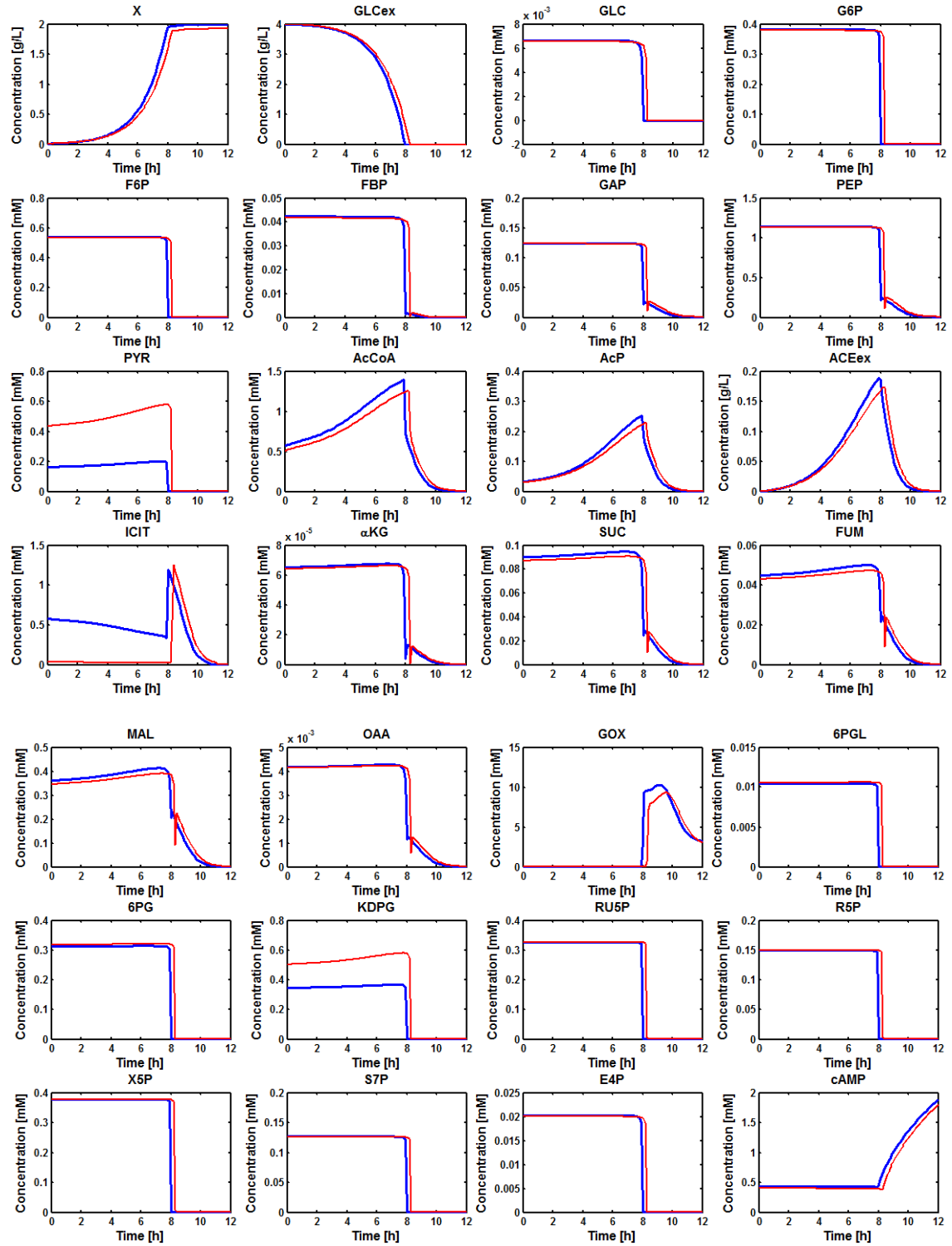


Figure S5: Effect of Cra regulation on dynamic behaviors.

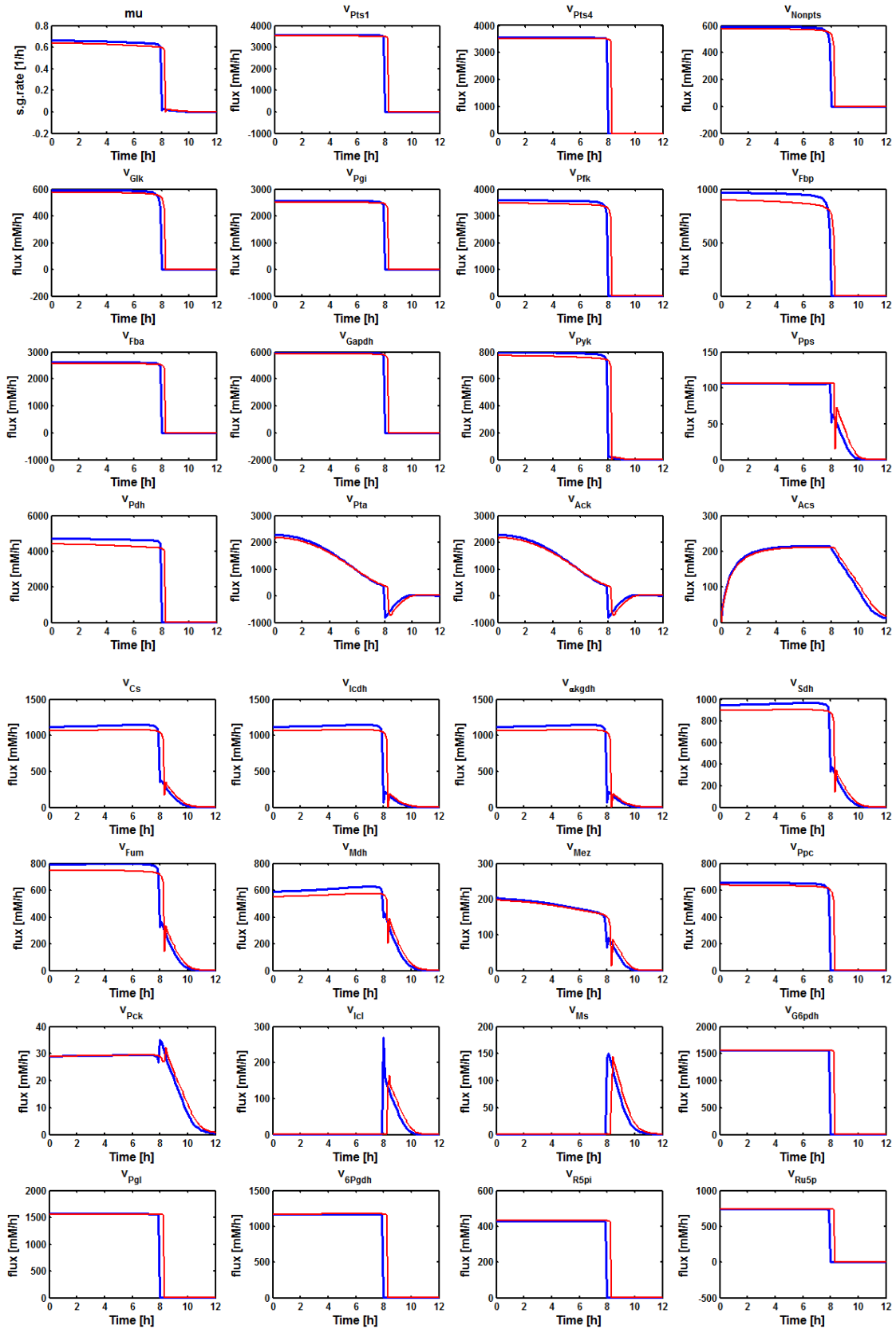
The blue and red lines indicate WT and the virtual mutant lacking of a Cra-FBP complex, respectively.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

A



B



B (continue...)

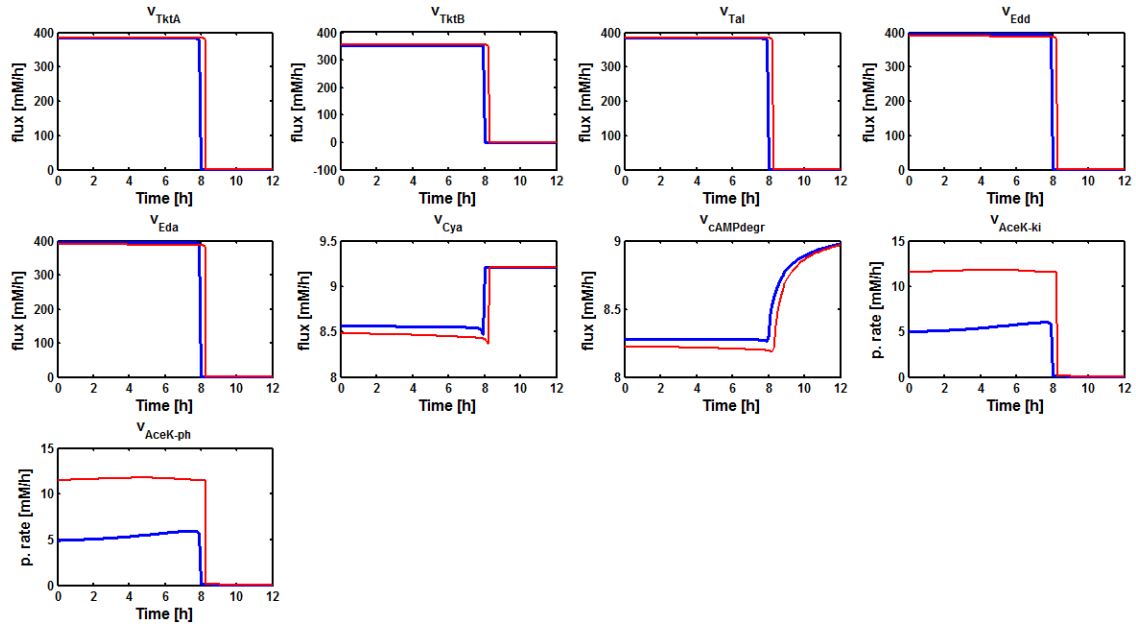
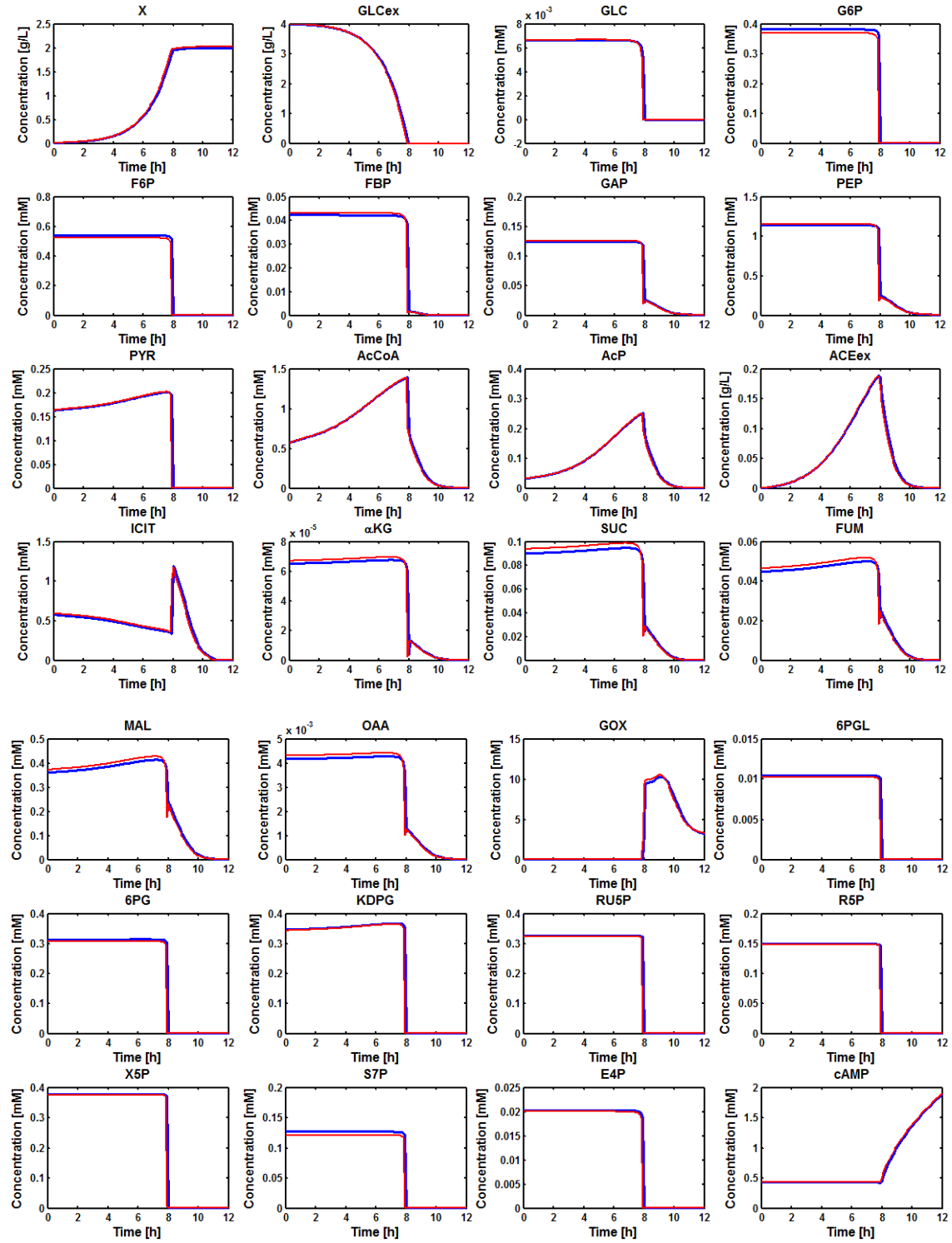


Figure S6: Effect of PdhR regulation on dynamic behaviors.

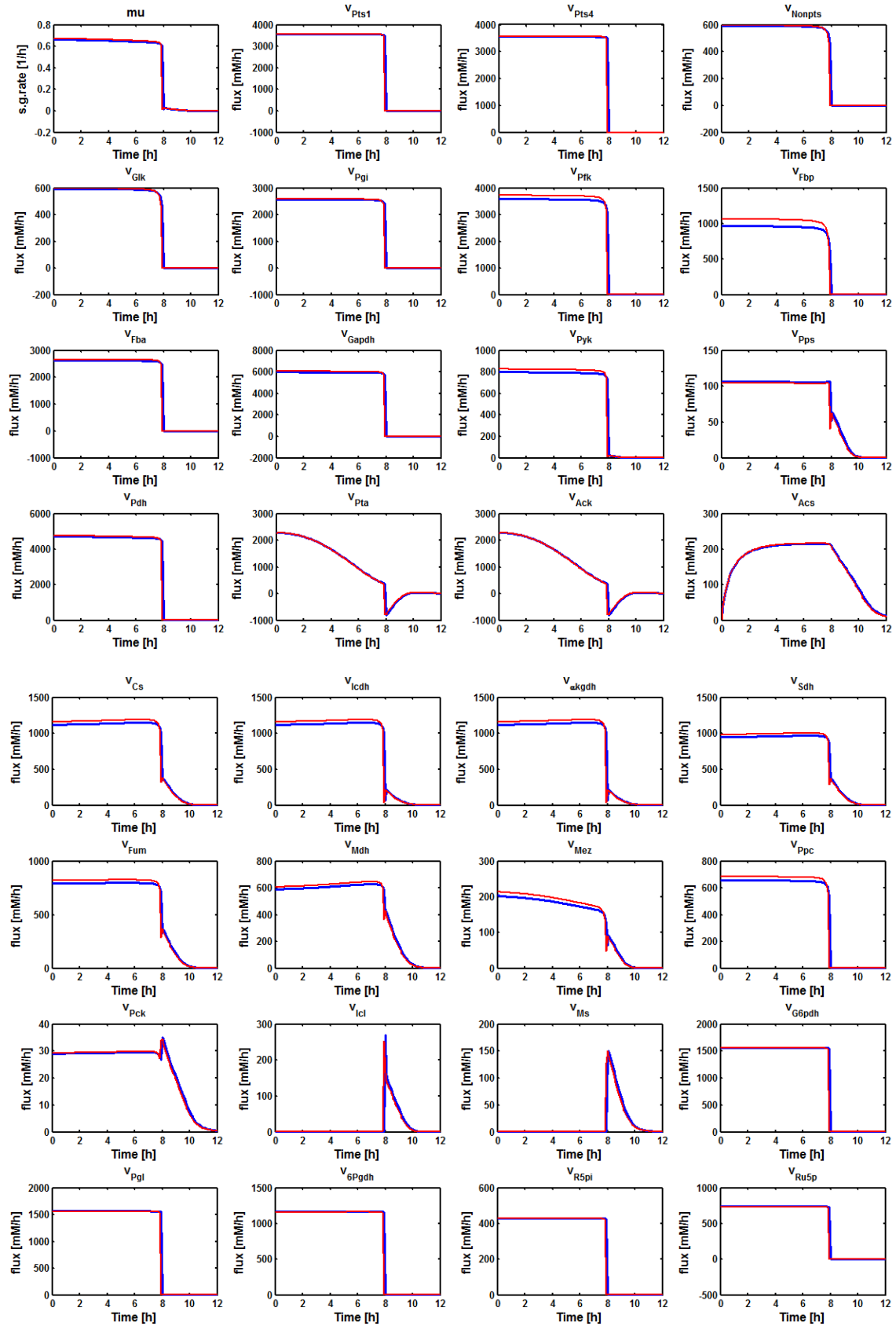
The blue and red lines indicate WT and the virtual mutant lacking a PdhR-PYR complex, respectively.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

A



B



B (continue...)

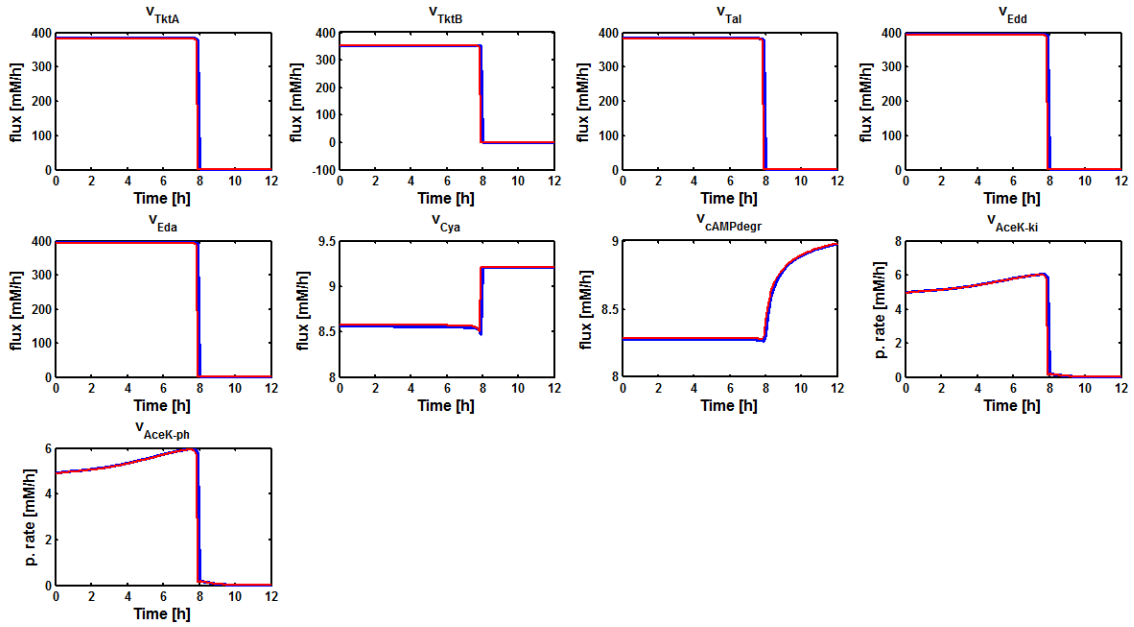
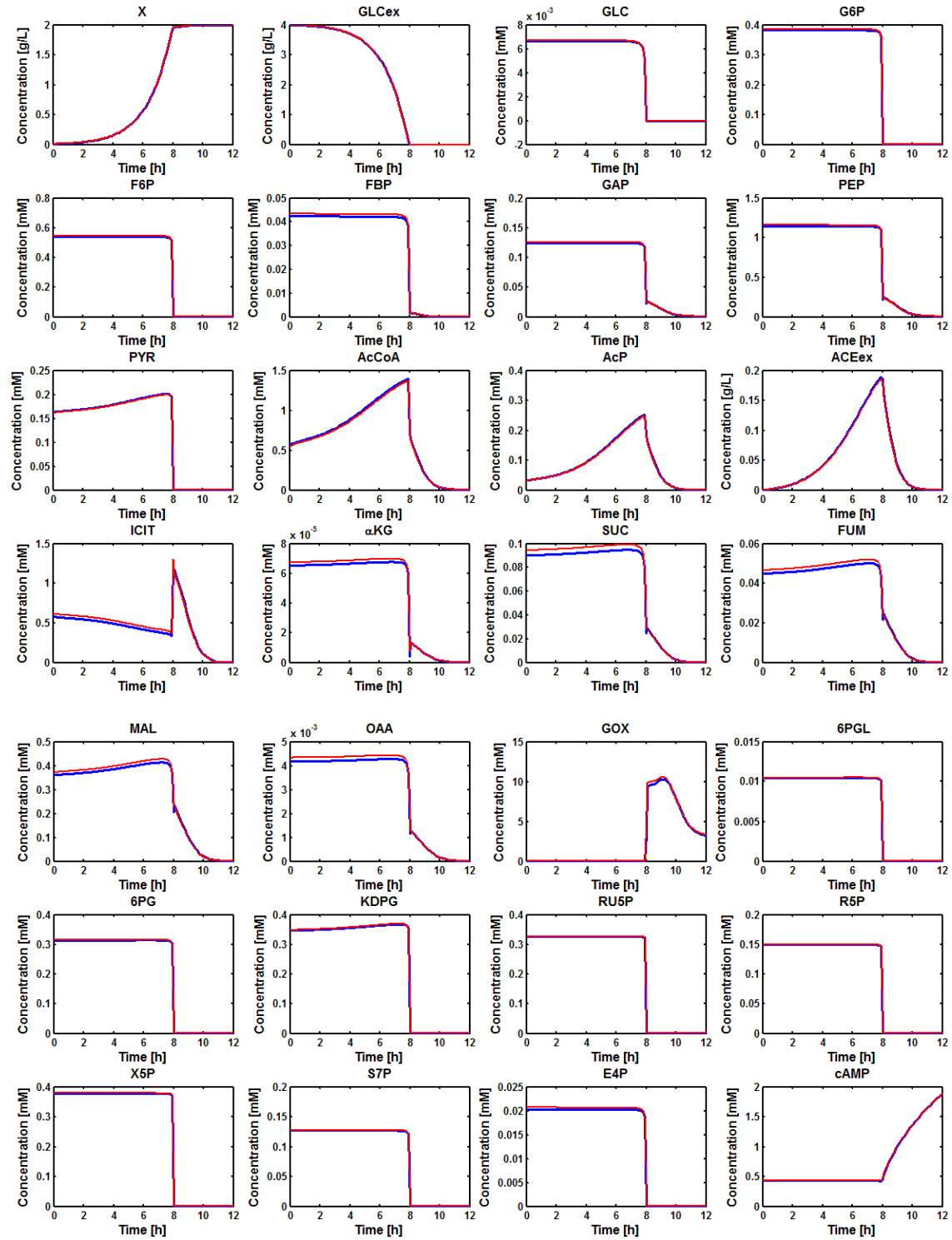


Figure S7: Effect of allosteric regulation of Pfk on dynamic behaviors.

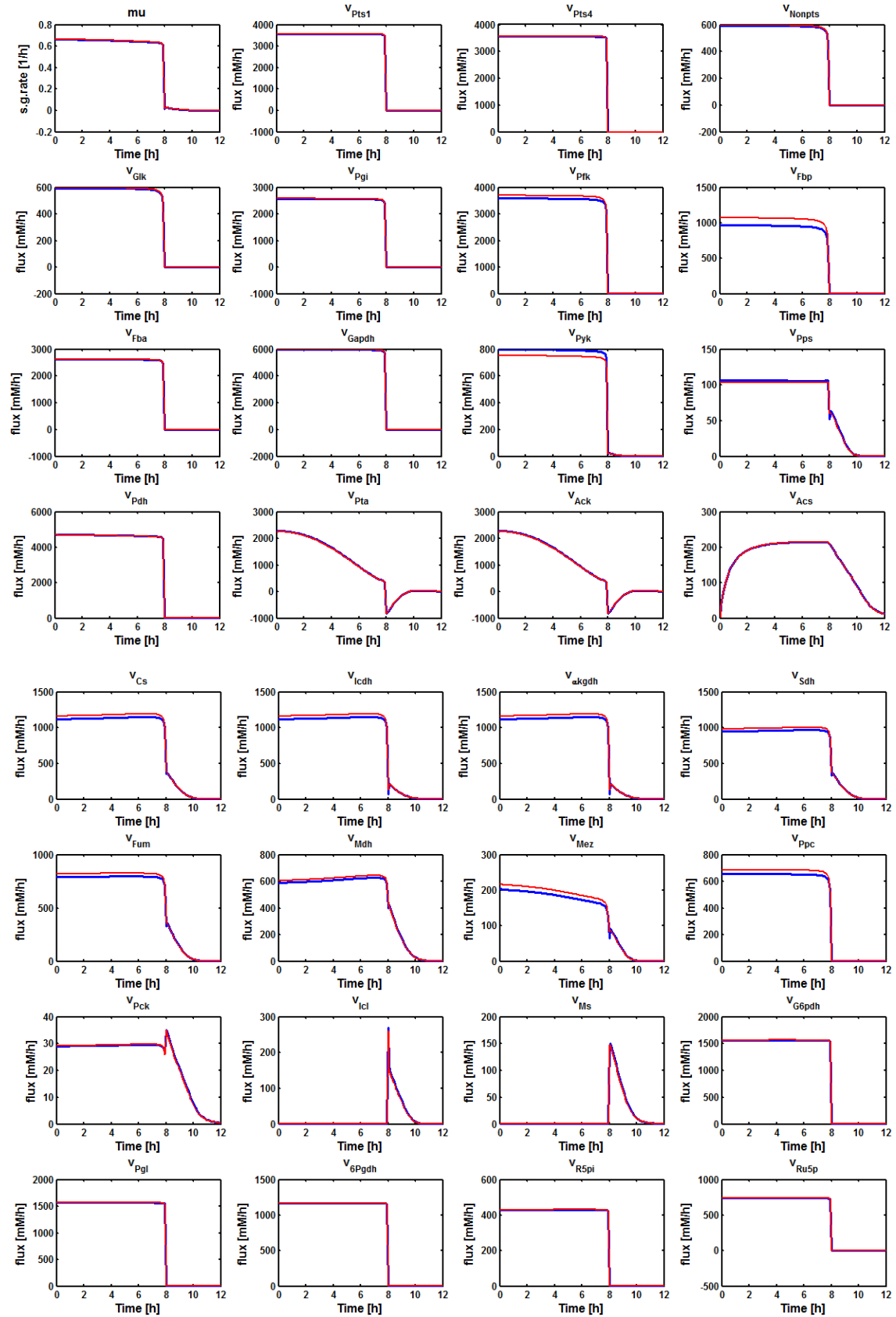
The blue and red lines indicates WT and the virtual mutant lacking the allosteric regulations via Pfk, respectively.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

A



B



B (continue...)

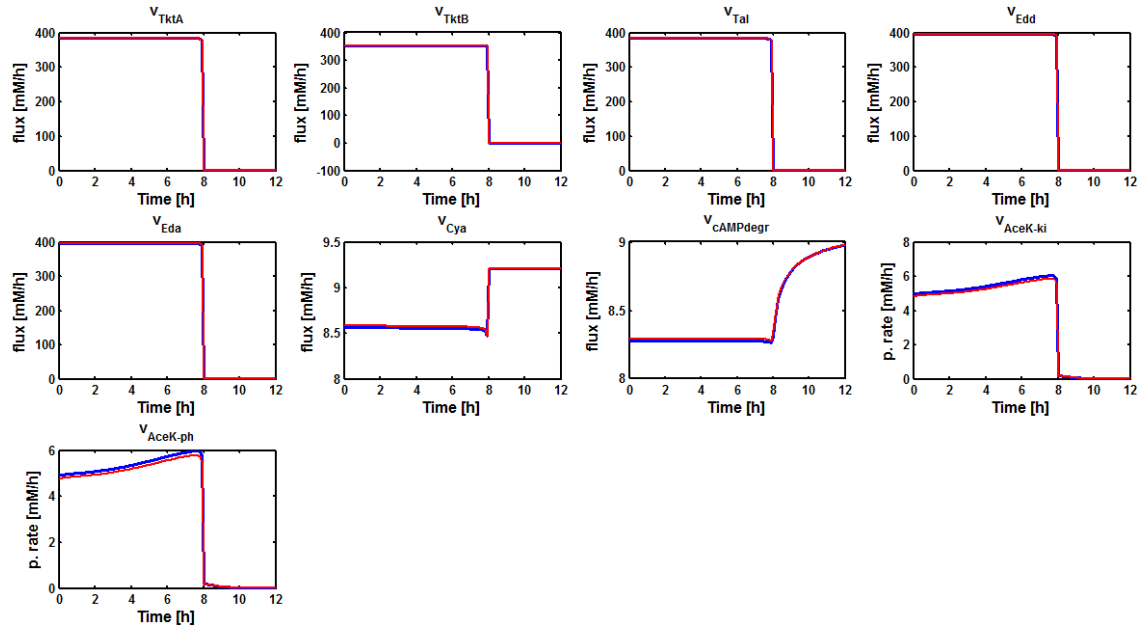
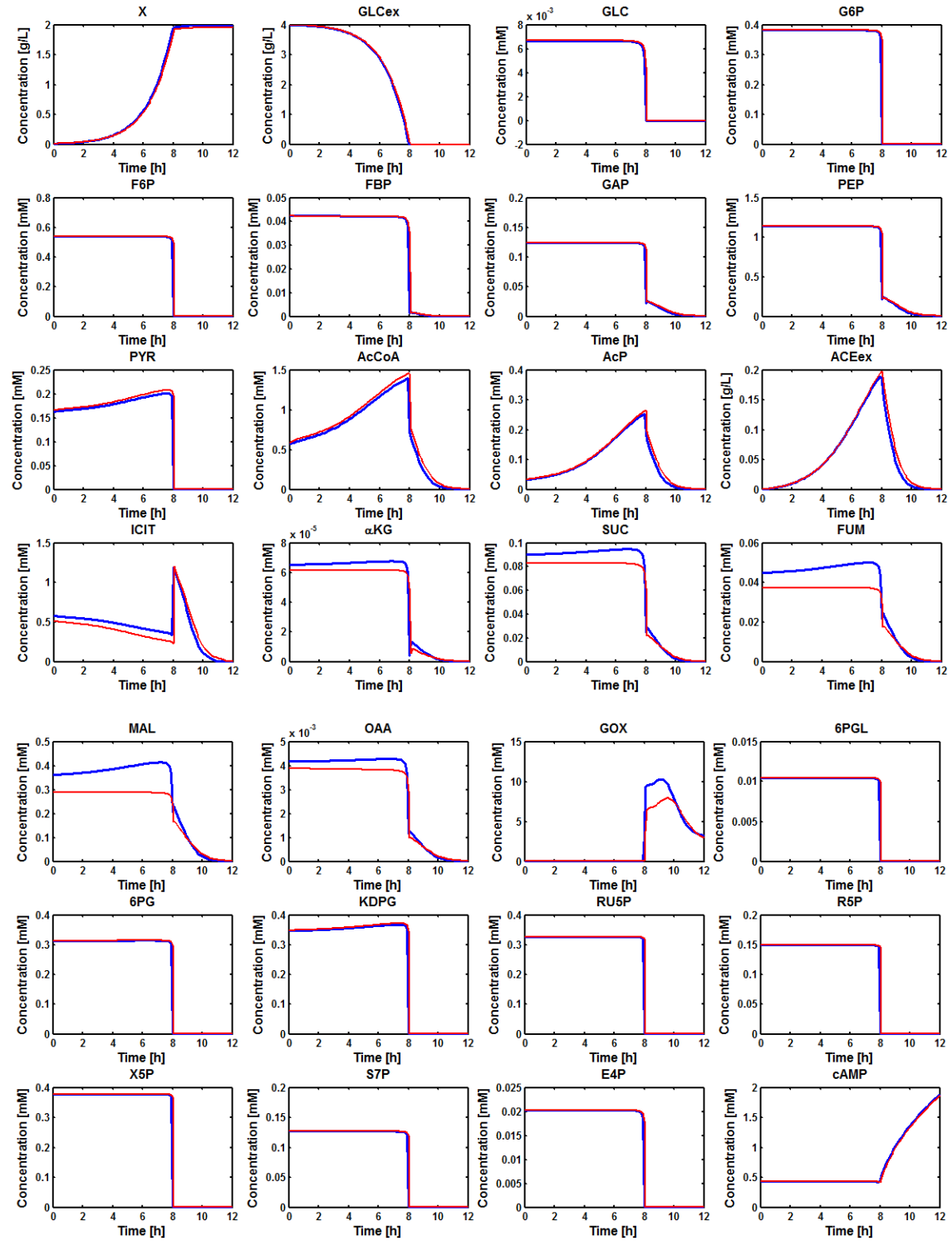


Figure S8: Effect of allosteric regulation of Pyk on dynamic behaviors.

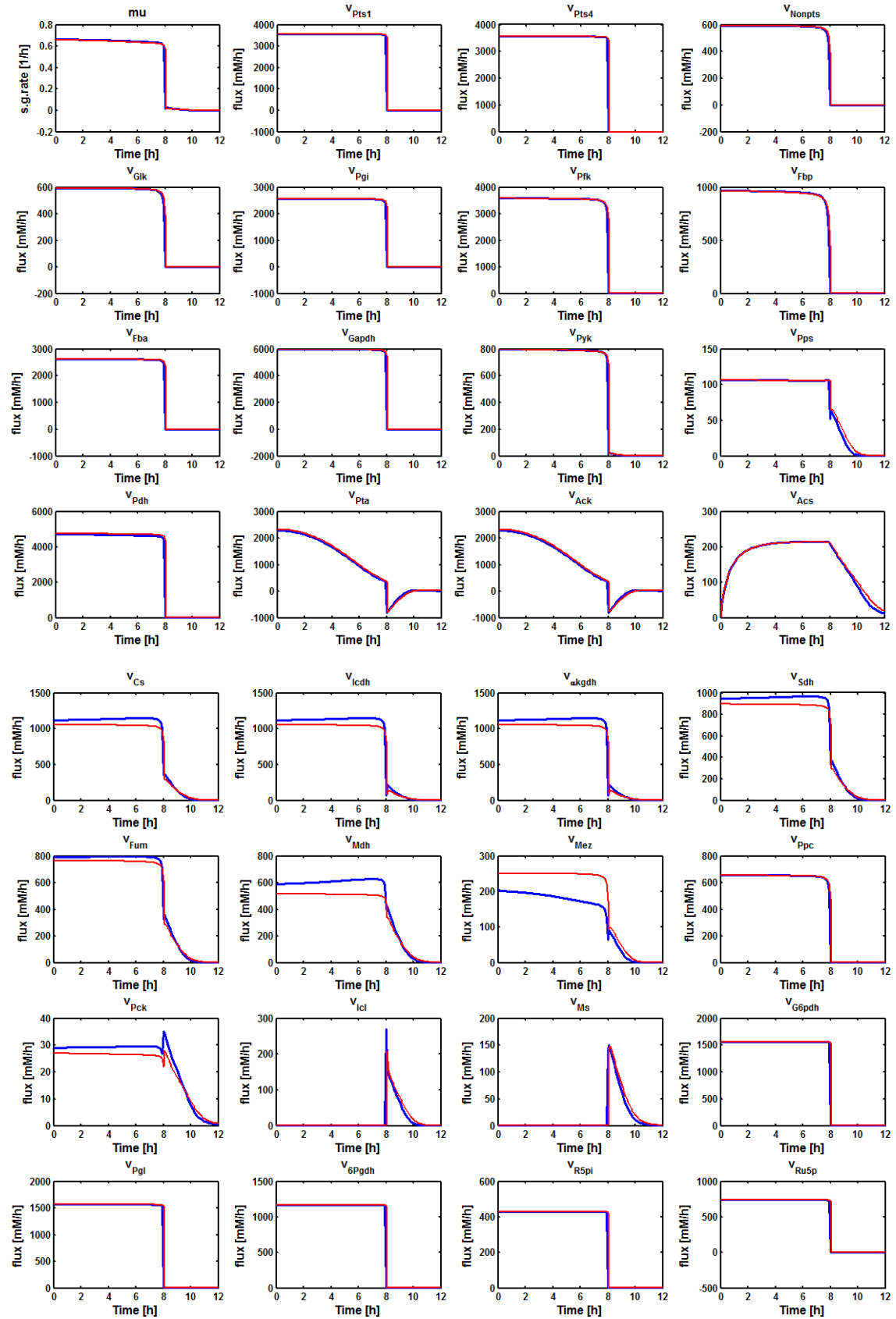
The blue and red lines indicate WT and the virtual mutant lacking the allosteric regulation of Pyk.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

A



B



B (continue...)

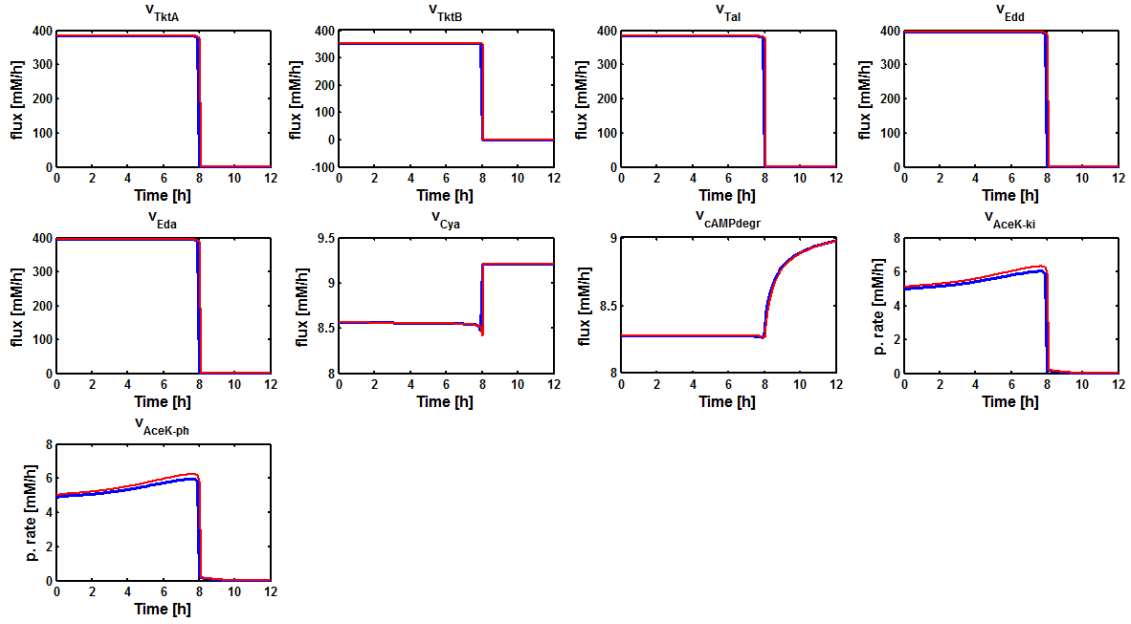
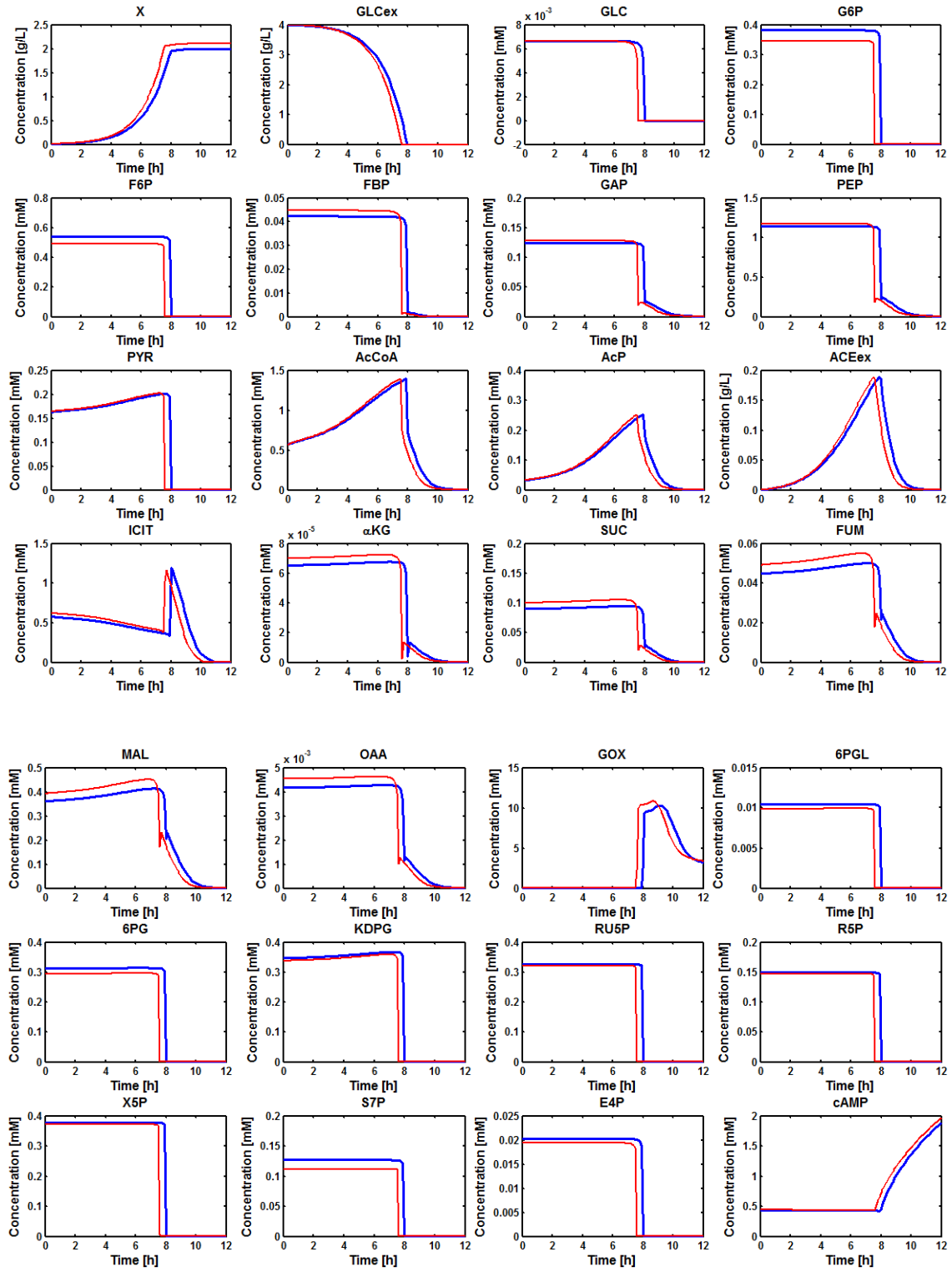


Figure S9: Effect of allosteric regulation of Mez on dynamic behaviors.

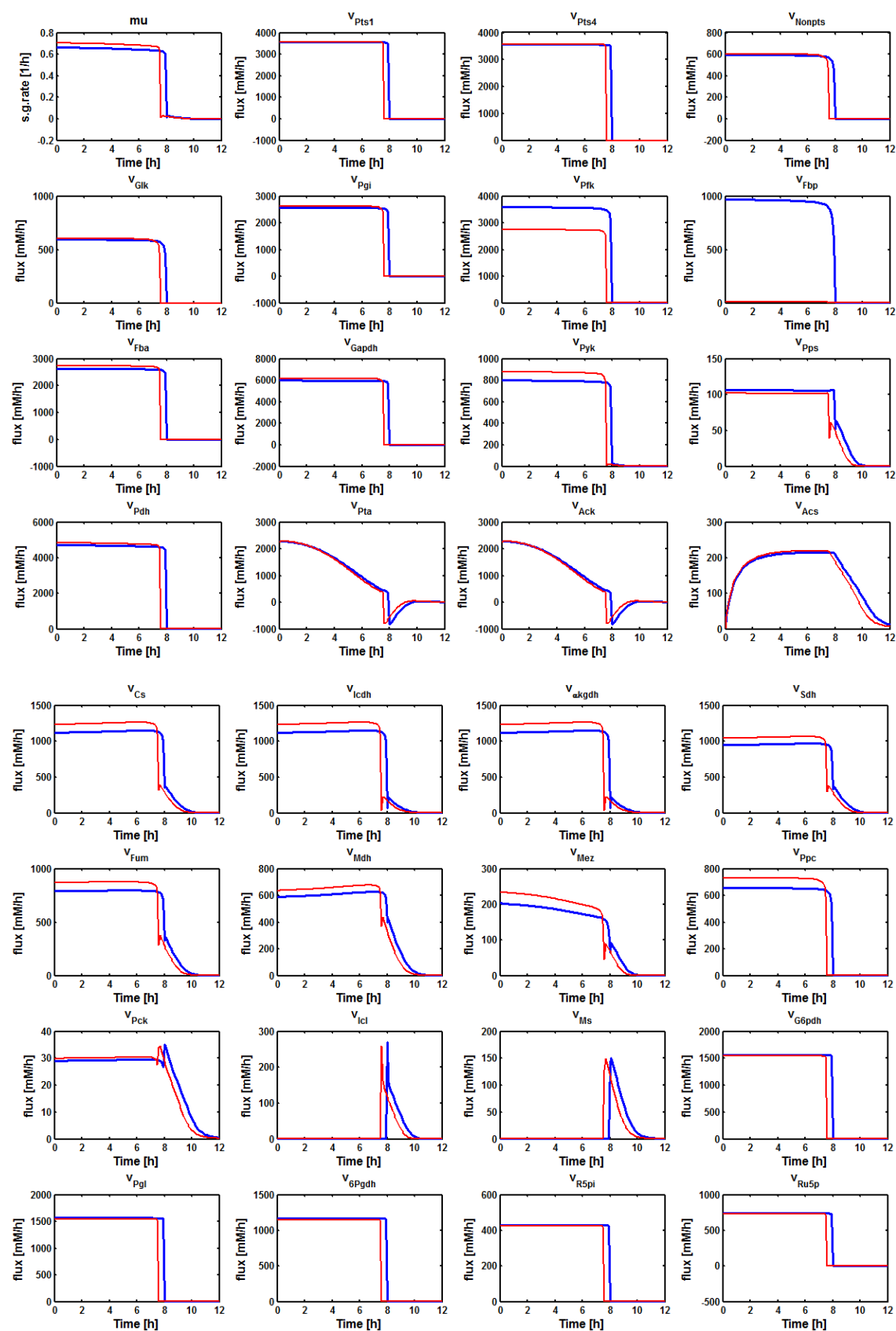
The blue and red lines indicate WT and the virtual mutant lacking the allosteric regulation of Mez.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

A



B



B (continue...)

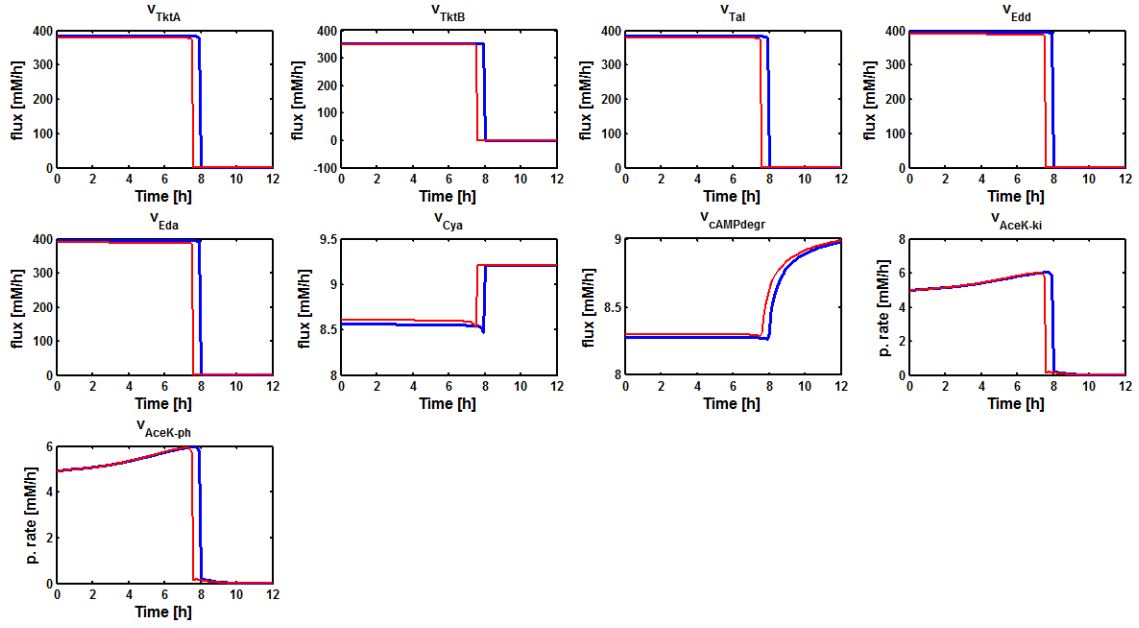
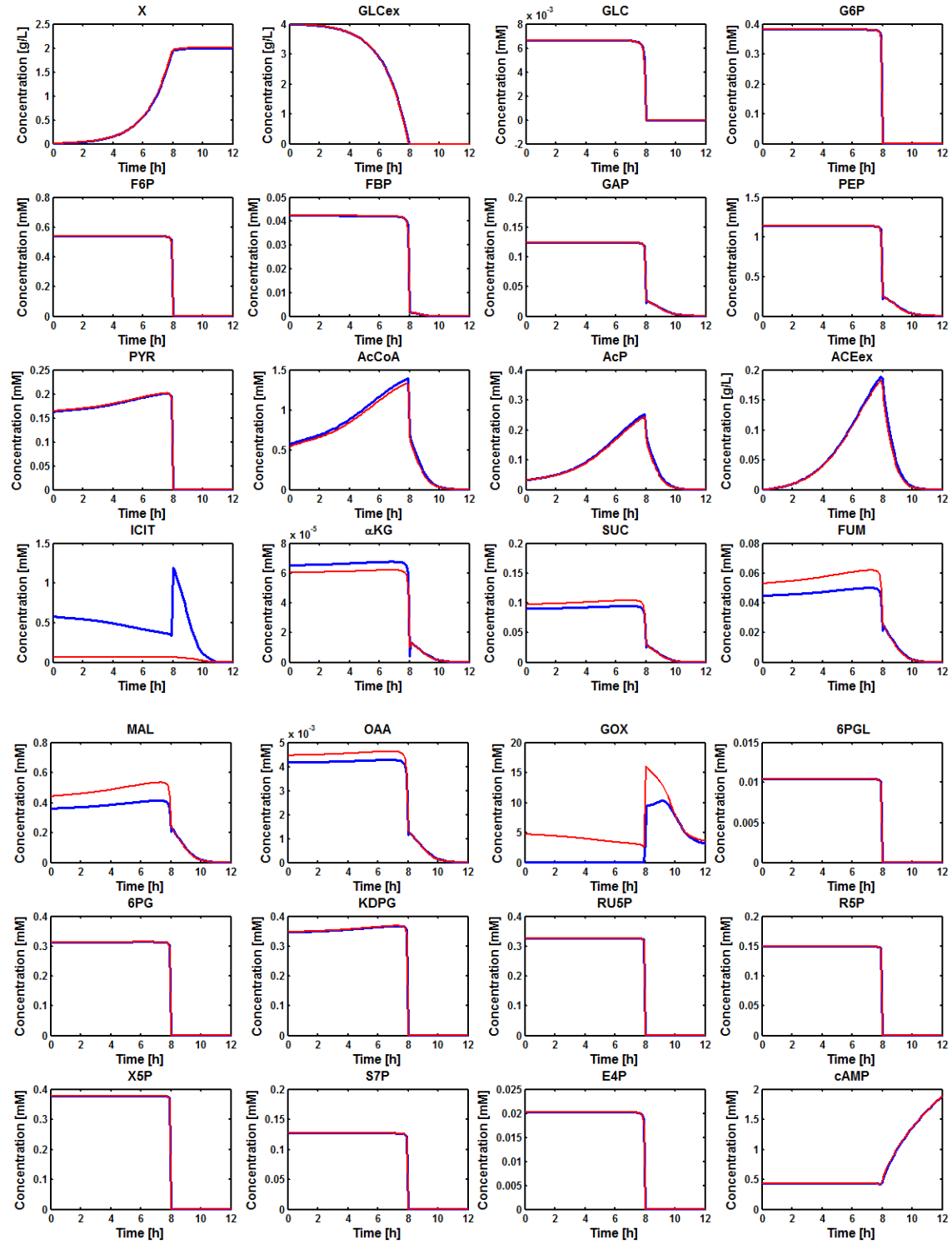


Figure S10: Effect of allosteric regulation of Fbp on dynamic behaviors.

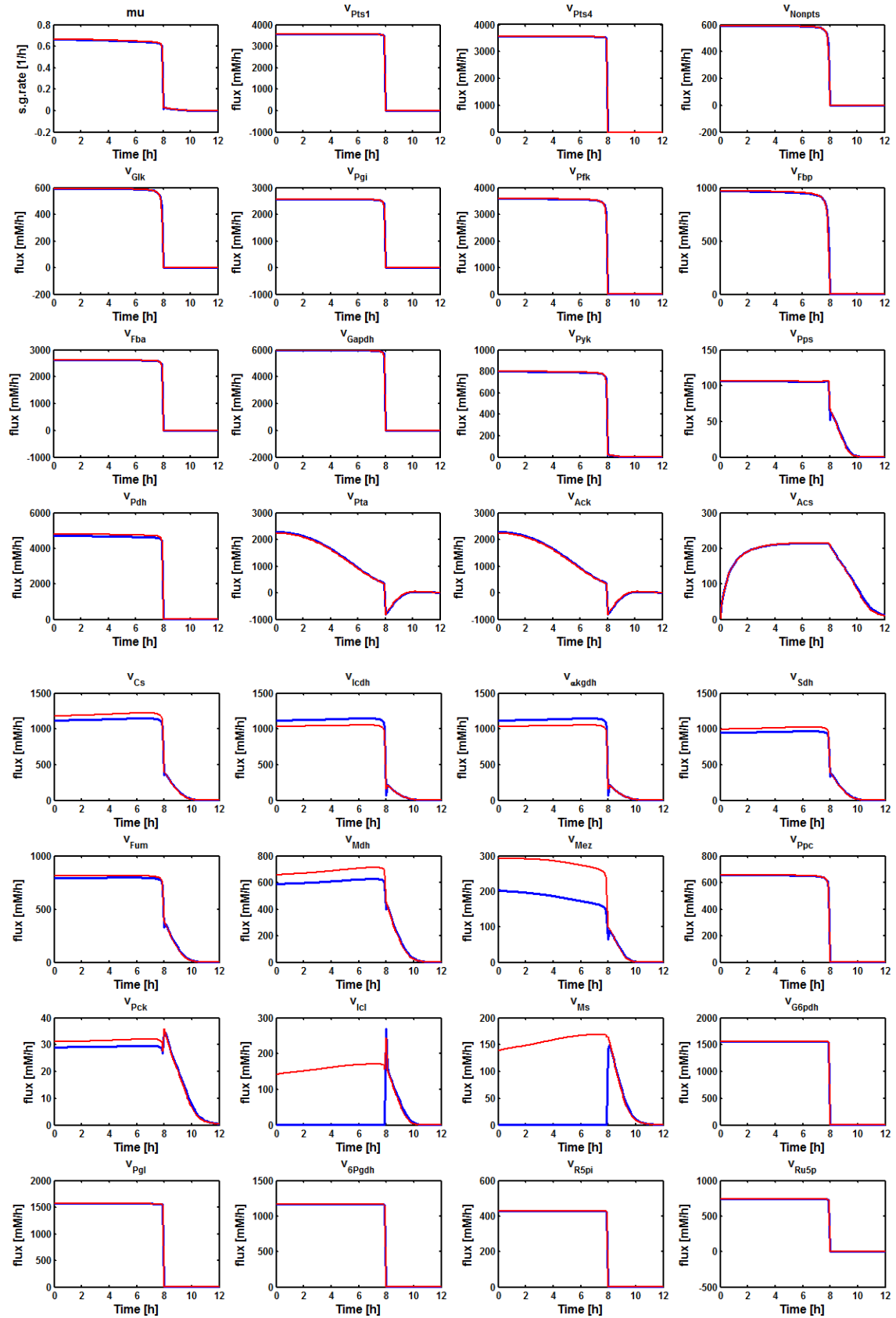
The blue and red lines indicate WT and the virtual mutant lacking the allosteric regulation of Fbp.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

A



B



B (continue...)

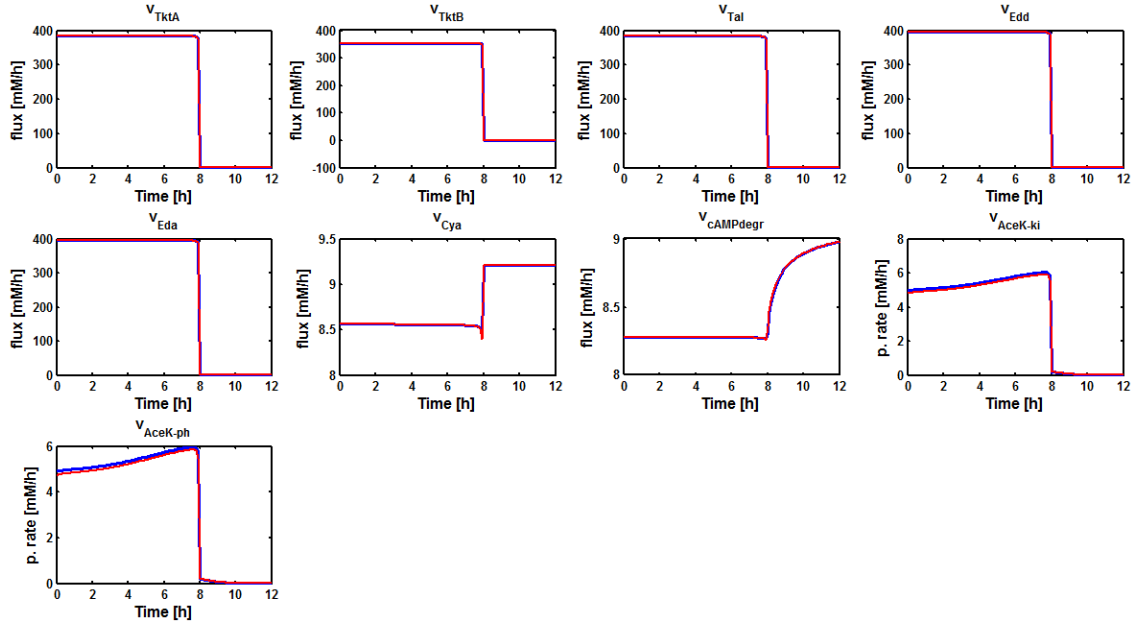
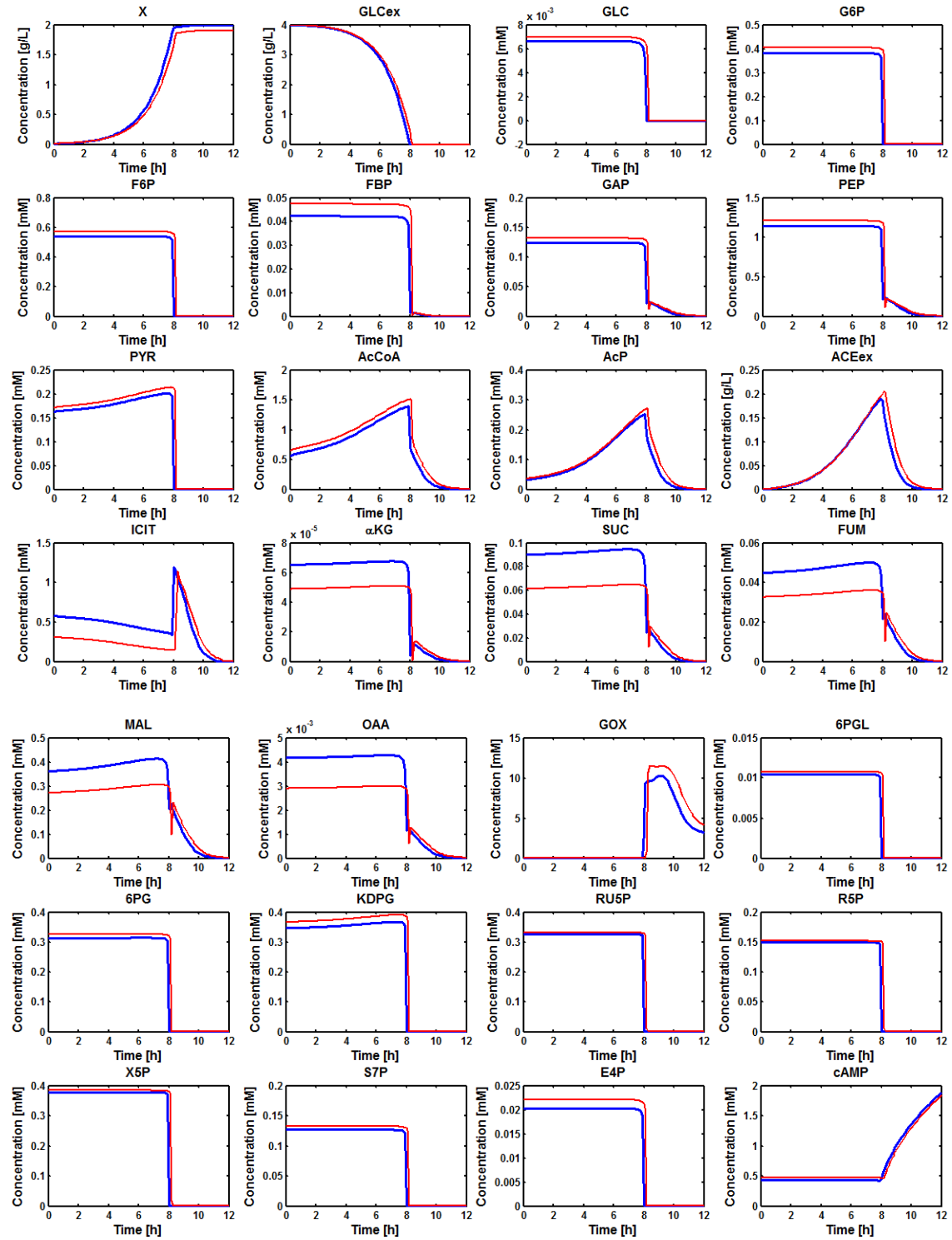


Figure S11: Effect of allosteric regulation of Icl on dynamic behaviors.

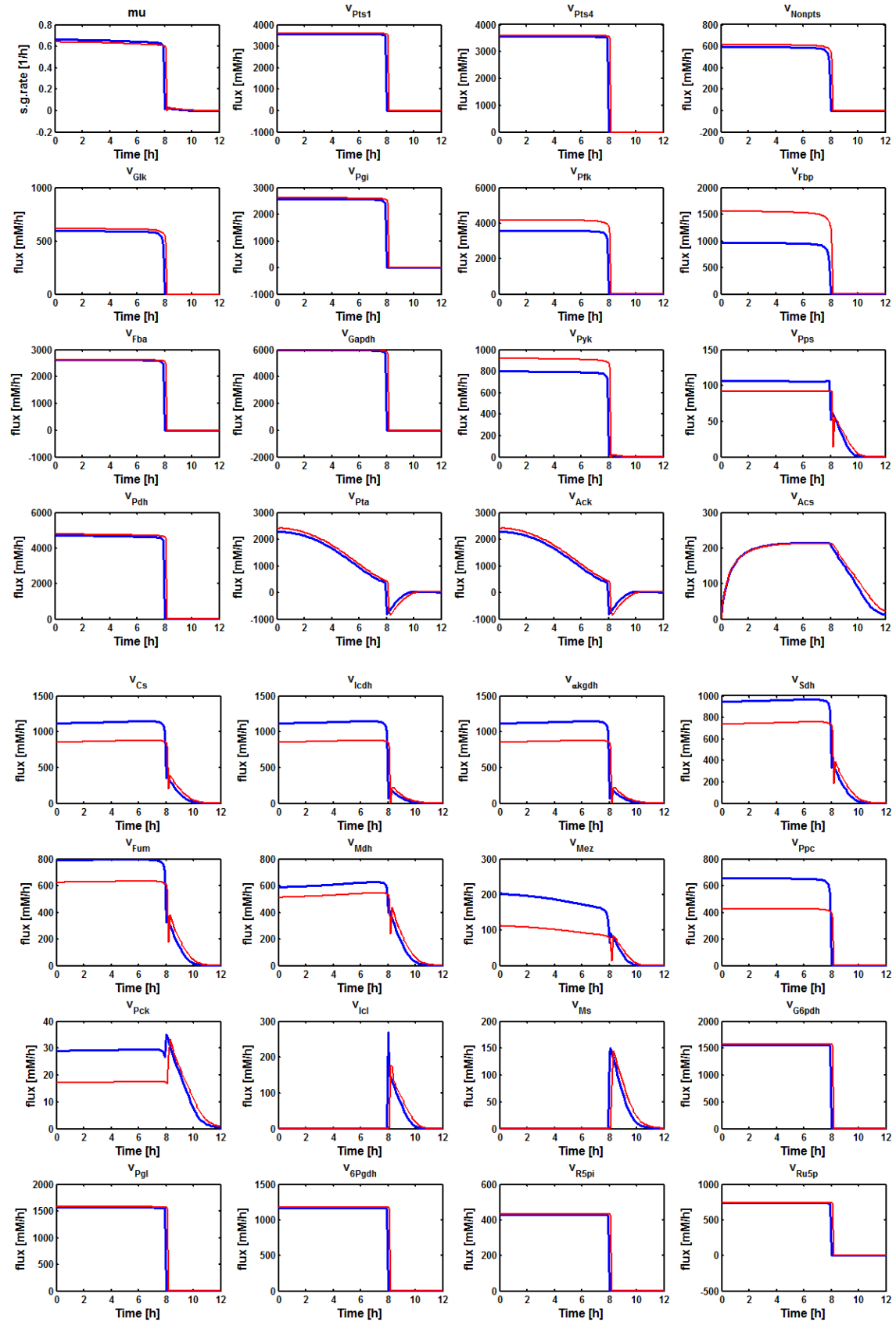
The blue and red lines indicate WT and the virtual mutant lacking the allosteric regulation of Icl.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

A



B



B (continue...)

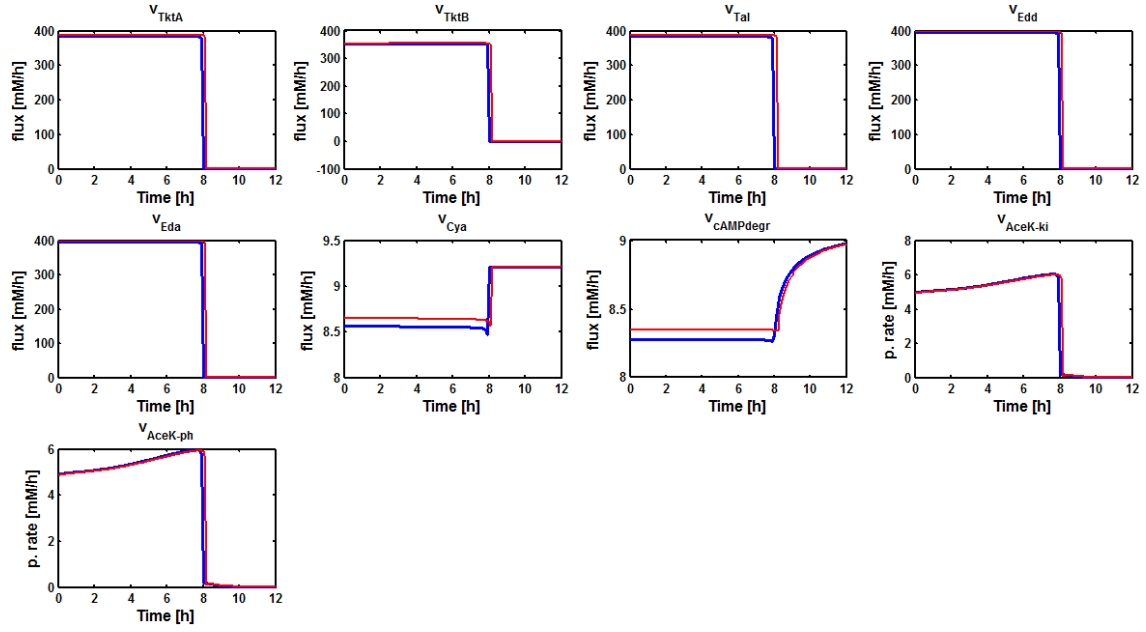


Figure S12: Effect of allosteric regulation of Ppc on dynamic behaviors.

The blue and red lines indicate WT and the virtual mutant lacking the allosteric regulation of Ppc.

A. Metabolite concentrations; **B.** Rates (Specific growth rate [s.g.rate]; flux; phosphorylation rate [p.rate]).

References

1. Toya Y, Ishii N, Nakahigashi K, Hirasawa T, Soga T, Tomita M, Shimizu K: **¹³C-metabolic flux analysis for batch culture of *Escherichia coli* and its *Pyk* and *Pgi* gene knockout mutants based on mass isotopomer distribution of intracellular metabolites.** *Biotechnol Prog* 2010, **26**:975-992.
2. Ishii N, Nakahigashi K, Baba T, Robert M, Soga T, Kanai A, Hirasawa T, Naba M, Hirai K, Hoque A, et al: **Multiple high-throughput analyses monitor the response of *E. coli* to perturbations.** *Science* 2007, **316**:593-597.