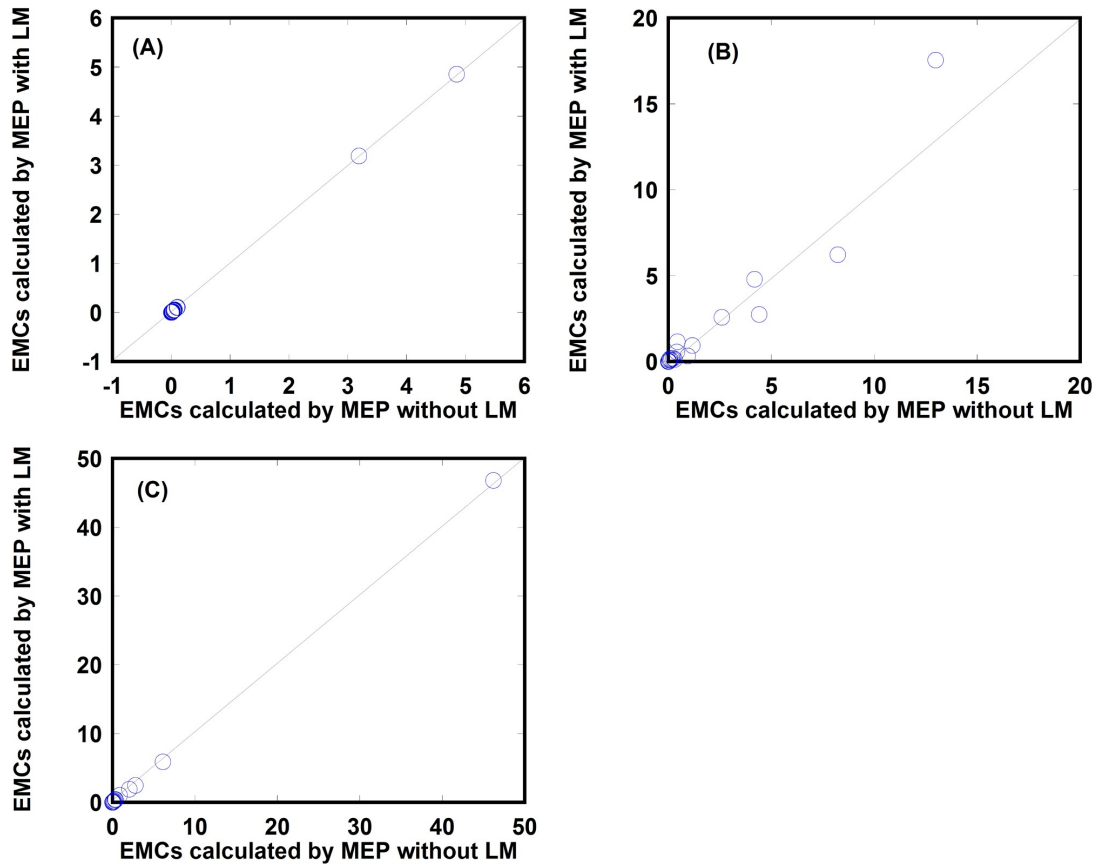
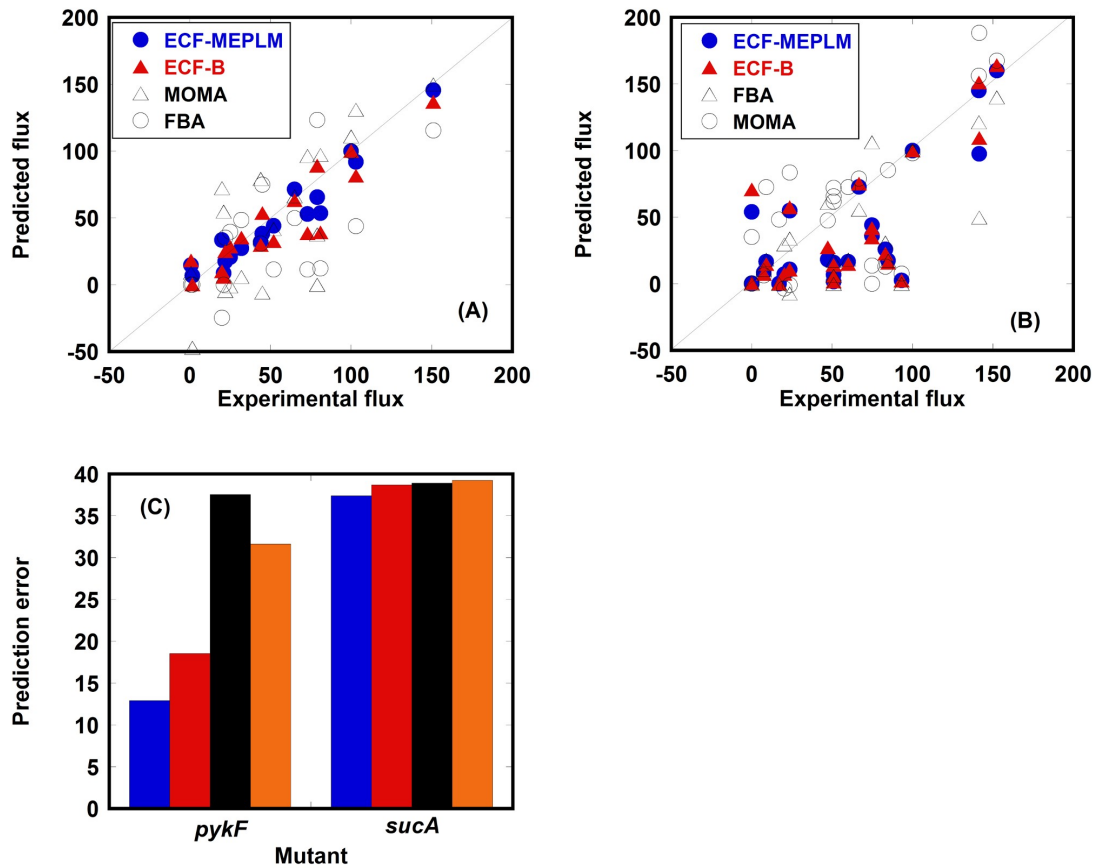


**Figure S3** Flux distributions predicted by MEPLM and by MEP without LMs in *S. cerevisiae* under three conditions: The specific growth rate is 0.15 h<sup>-1</sup>(A), 0.30 h<sup>-1</sup> (B) and 0.40 h<sup>-1</sup>(C). The metabolic network model is shown in the previous work in which there are 62 EMs (9).



**Figure S4** EMCs predicted by MEPLM and by MEP without LMs in *S. cerevisiae* under three conditions: The specific growth rate is  $0.15 \text{ h}^{-1}$ (A),  $0.30 \text{ h}^{-1}$  (B) and  $0.40 \text{ h}^{-1}$ (C). The metabolic network model is shown in the previous work (9).



**Figure S5** Flux prediction error for *E. coli* gene deletion mutants by ECF-MEPLM

Upper panel (A, B): The flux distributions are predicted by ECF-MEPLM, ECF-B, FBA and MOMA under aerobic conditions for the two gene deletion mutants in *E. coli*: (A) *pykF*; (B) *sucA*. Model **I** shown in **Table 1** was used and the predicted flux distributions were compared with 20 (A) and 24 (B) experimental fluxes. Thirteen (A) and eighteen (B) relative enzyme activity data of mutants to wild type were used for the calculation by ECF-MEPLM.

Lower panel (C): Prediction errors for ECF-MEPLM (blue column), ECF-B (red column), FBA (black column) and MOMA (orange column) for *pykF* and *sucA* mutants.