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# Supplementary Materials

## 1. The spiral network

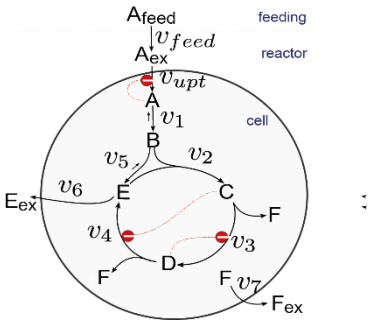


**Figure S1.** Network stoichiometry of the spiral network.

## 2. The PenG Network

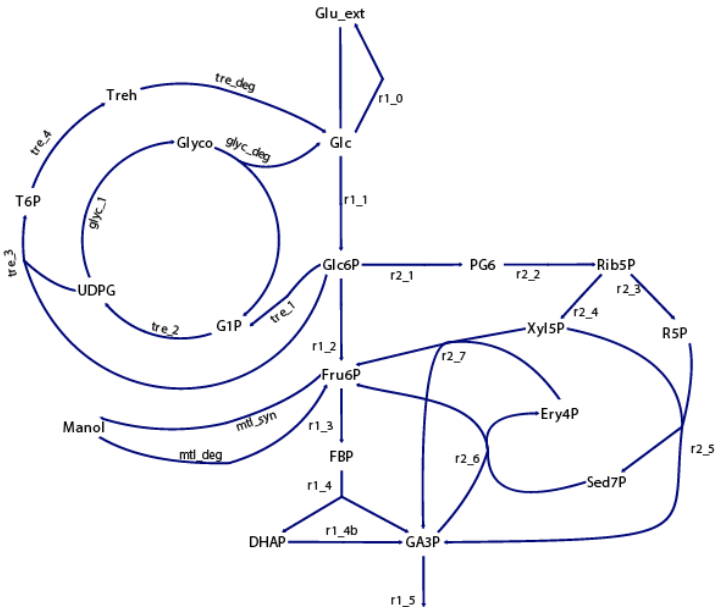


**Figure S2.** Network stoichiometry of the PenG network.

## 3. Estimated Flux Functions with Respective Concentration and c-Molar Isotopomer Simulations

It has to be noted that, for simplification, the weights for every series of observables have been set to 5% of the average of the respective series. Those weights are different to the ones of the previously published flux functions. Moreover, the previously published fit did not optimize a multi-objective objective function but constrained all right hand sides at the concentration breakpoints to the values of the best concentration fit and only optimized the enrichments. Therefore, the fits represent different points on the pareto frontier between the two sets of observables.

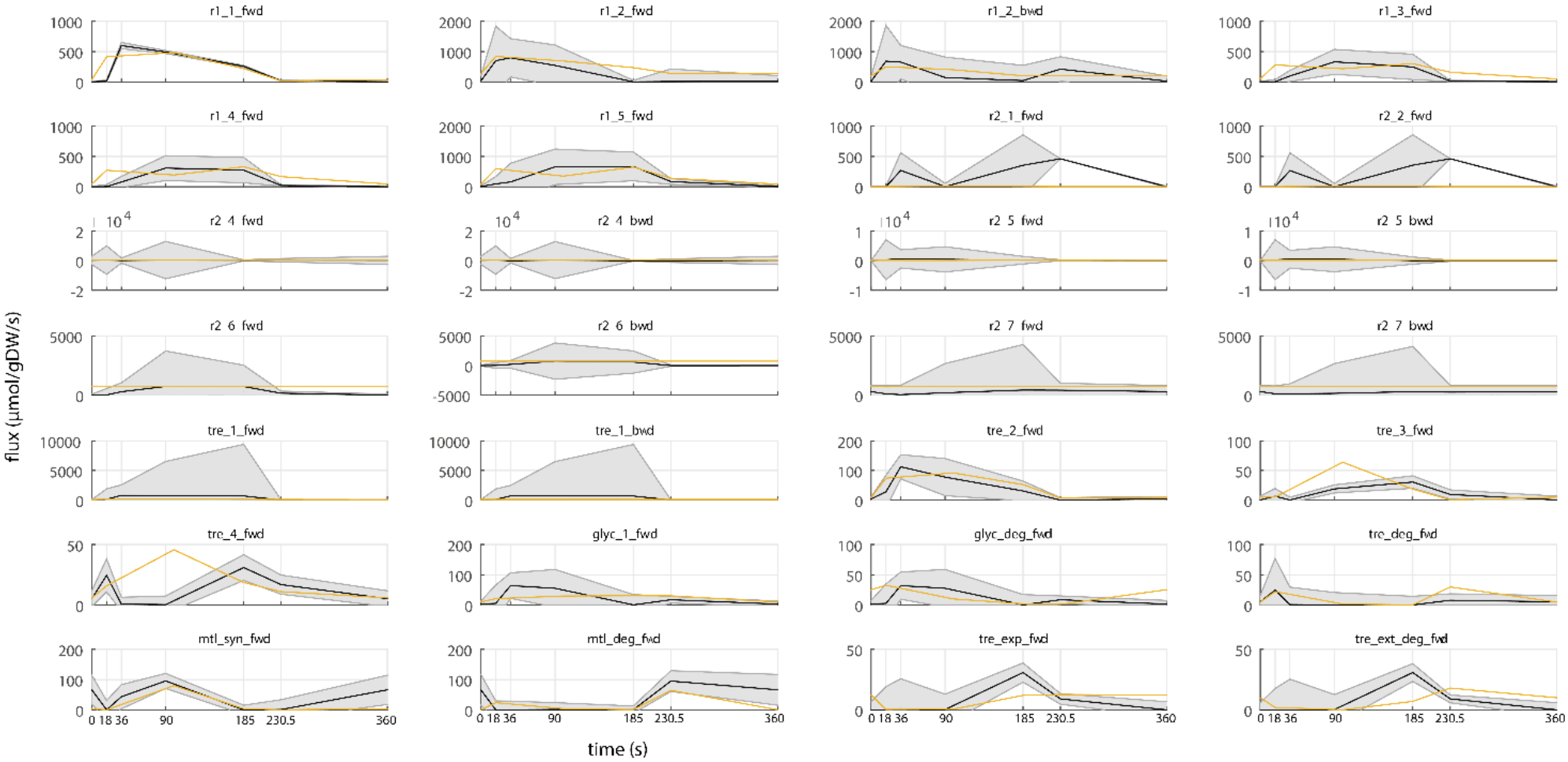


**Figure S3.** Estimated flux functions with asymptotic confidence intervals in comparison to the previously published best fit.

**Table S1.** Best flux estimates found for the PenG model, all values in umol/gDW/h.

| | 0 s | 18 s | 36 s | 90 s | 185 s | 230.5 s | 360 s |
|---|---|---|---|---|---|---|---|
| **r1_1_fwd** | 0.691 | 11.581 | 600.000 | 493.116 | 257.404 | 18.137 | 0.691 |
| **r1_2_fwd** | 30.581 | 698.237 | 795.750 | 542.587 | 1.869 | 10.618 | 30.581 |
| **r1_2_bwd** | 22.753 | 682.819 | 652.364 | 143.461 | 40.008 | 421.277 | 22.753 |
| **r1_3_fwd** | 3.250 | 1.875 | 96.850 | 331.080 | 246.959 | 13.957 | 3.250 |
| **r1_4_fwd** | 0.166 | 1.875 | 77.915 | 307.633 | 274.415 | 21.002 | 0.166 |
| **r1_5_fwd** | 5.889 | 92.760 | 158.672 | 657.274 | 671.126 | 171.393 | 5.889 |
| **r2_1_fwd** | 0.177 | 0.661 | 268.952 | 2.105 | 354.458 | 461.993 | 0.177 |
| **r2_2_fwd** | 0.000 | 0.156 | 267.510 | 1.472 | 355.794 | 462.311 | 0.000 |
| **r2_4_fwd** | 251.235 | 451.182 | 124.624 | 446.247 | 251.394 | 331.438 | 251.235 |
| **r2_4_bwd** | 255.277 | 454.356 | 17.191 | 422.894 | 2.148 | 18.469 | 255.277 |
| **r2_5_fwd** | 3.111 | 352.153 | 629.308 | 471.102 | 175.334 | 164.837 | 3.111 |
| **r2_5_bwd** | 5.171 | 348.843 | 504.904 | 499.518 | 52.833 | 2.090 | 5.171 |
| **r2_6_fwd** | 8.390 | 23.220 | 295.129 | 743.652 | 736.643 | 168.366 | 8.390 |
| **r2_6_bwd** | 10.455 | 29.826 | 210.018 | 762.307 | 603.623 | 4.500 | 10.455 |
| **r2_7_fwd** | 305.267 | 114.414 | 47.250 | 208.708 | 436.804 | 424.321 | 305.267 |
| **r2_7_bwd** | 307.332 | 121.021 | 113.033 | 156.940 | 301.889 | 259.870 | 307.332 |
| **tre_1_fwd** | 10.100 | 143.243 | 796.548 | 750.272 | 701.161 | 8.956 | 10.100 |
| **tre_1_bwd** | 7.239 | 116.443 | 702.885 | 693.160 | 683.240 | 19.389 | 7.239 |
| **tre_2_fwd** | 4.053 | 28.071 | 112.468 | 77.594 | 30.886 | 0.109 | 4.053 |
| **tre_3_fwd** | 0.280 | 6.466 | 0.230 | 18.887 | 30.488 | 9.515 | 0.280 |
| **tre_4_fwd** | 5.185 | 24.505 | 0.691 | 0.292 | 30.943 | 16.851 | 5.185 |
| **glyc_1_fwd** | 2.975 | 5.332 | 64.066 | 55.156 | 0.398 | 17.235 | 2.975 |
| **glyc_deg_fwd** | 1.487 | 2.666 | 32.033 | 27.578 | 0.199 | 8.618 | 1.487 |
| **tre_deg_fwd** | 5.185 | 24.505 | 0.691 | 0.021 | 0.095 | 7.783 | 5.185 |
| **mtl_syn_fwd** | 66.168 | 0.169 | 43.371 | 95.695 | 0.000 | 0.911 | 66.168 |
| **mtl_deg_fwd** | 66.168 | 0.125 | 0.052 | 1.127 | 0.649 | 95.153 | 66.168 |
| **tre_exp_fwd** | 0.000 | 0.000 | 0.000 | 0.271 | 30.847 | 9.069 | 0.000 |
| **tre_ext_deg_fwd** | 0.000 | 0.000 | 0.000 | 0.271 | 30.847 | 9.069 | 0.000 |

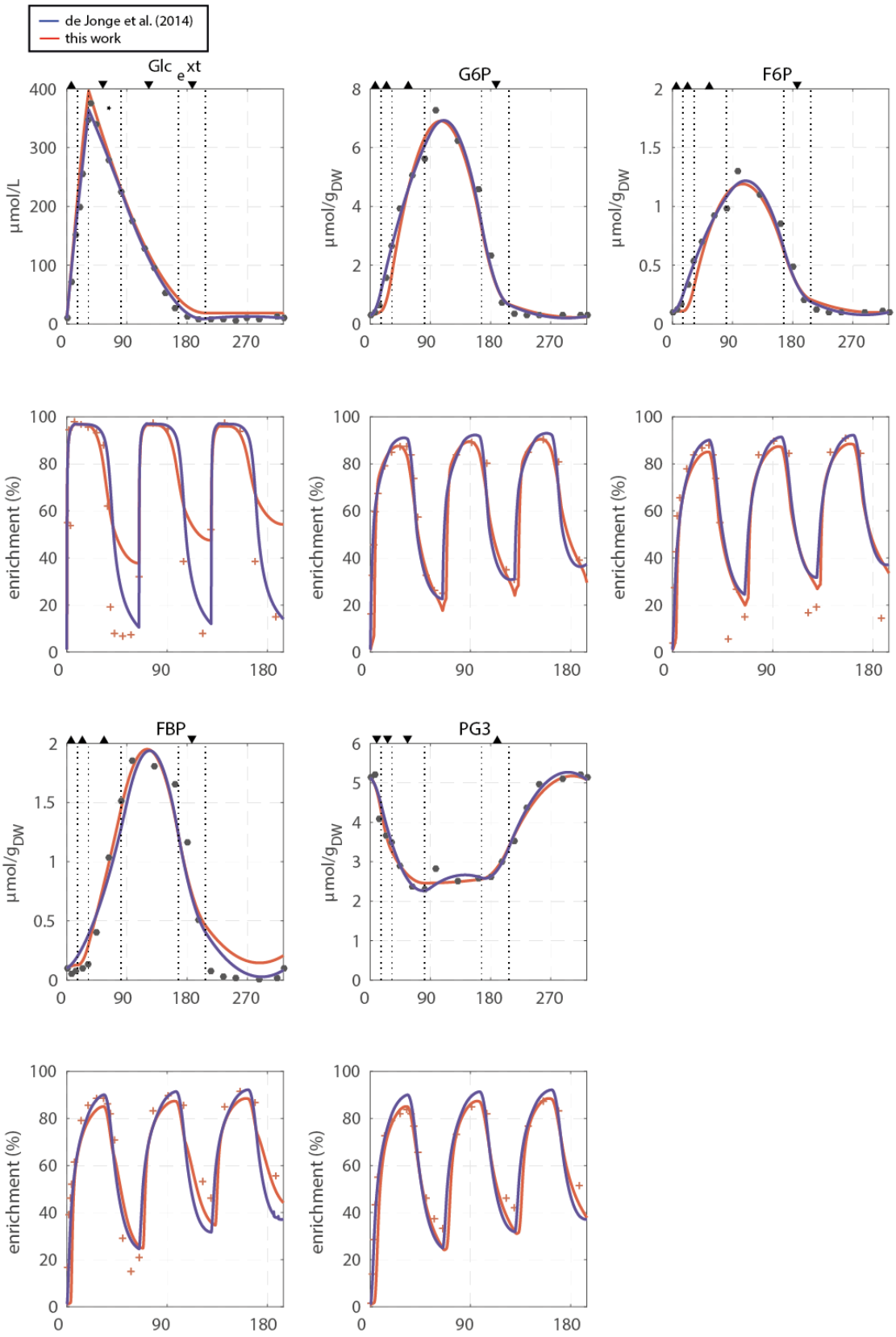


**Figure S4.** Comparison of previously published (**blue**) and best parameters found using the implicit filtering algorithm. Triangles on the top indicate the introduced shape constraint; monotonous increase (**upwards pointing triangle**) and monotonous decrease (**downwards pointing triangle**), no convexity constraints have been introduced.

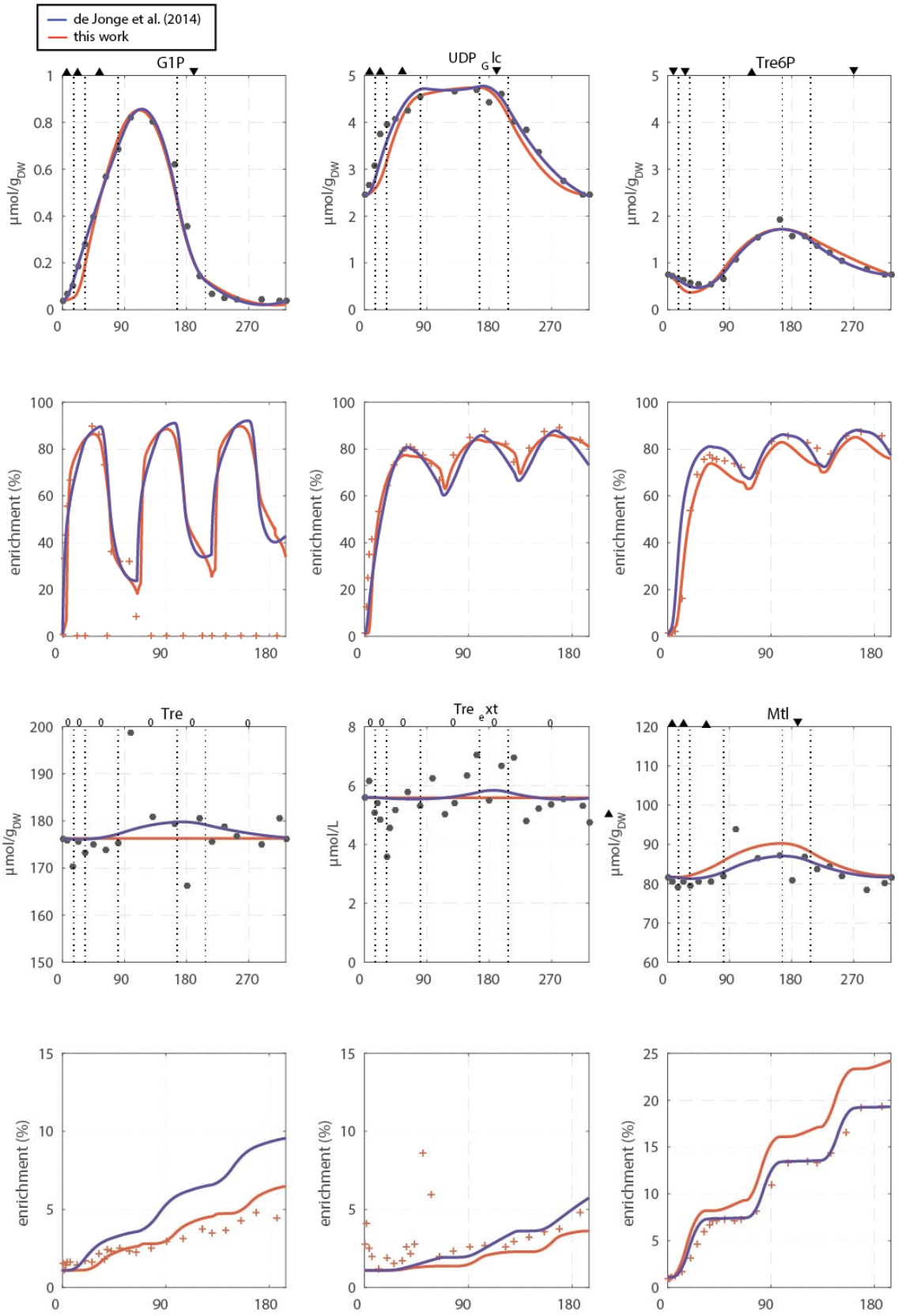


**Figure S5.** Comparison of previously published (**blue**) and best parameters found using the implicit filtering algorithm. Triangles on the top indicate the introduced shape constraint; monotonous increase (**upwards pointing triangle**) and monotonous decrease (**downwards pointing triangle**), no convexity constraints have been introduced.

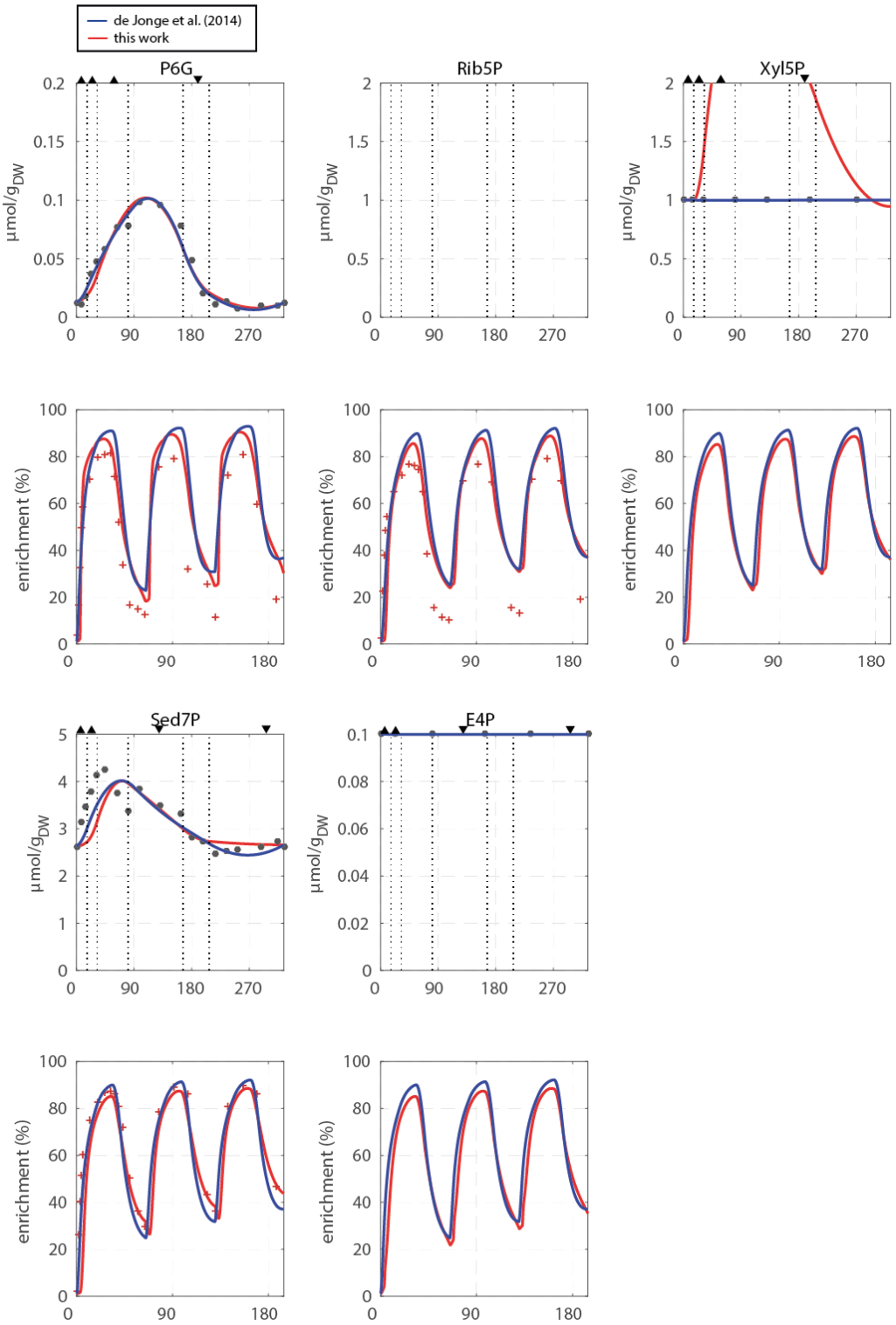


**Figure S6.** Comparison of previously published (**blue**) and best parameters found using the implicit filtering algorithm. Triangles on the top indicate the introduced shape constraint; monotonous increase (**upwards pointing triangle**) and monotonous decrease (**downwards pointing triangle**), no convexity constraints have been introduced.