### Table S1: List of minimal media considered as environmental conditions to study E. coli TRN. The 62 minimal media listed here are considered in aerobic conditions. The first 31 media shaded in grey are considered also in anaerobic conditions. Each carbon source is provided along with ammonia, sulphate, phosphate, proton, iron, potassium and sodium for uptake. Oxygen is provided in aerobic conditions. See supporting text (section on Treatment of external metabolites) for a discussion on how this list was compiled.

| Serial number | Carbon Source                         | Abbreviation of the carbon source |
|---------------|---------------------------------------|-----------------------------------|
| 1             | 2-Dehydro-3-deoxy-D-gluconate         | 2ddgln                           |
| 2             | N-acetyl-D-glucosamine                 | acgam                            |
| 3             | L-Arabinose                            | arab-L                           |
| 4             | Cytidine                               | cytd                             |
| 5             | D-Fructose                             | fru                              |
| 6             | L-Fucose                               | fuc-L                            |
| 7             | D-Glucose 6-phosphate                  | g6p                              |
| 8             | D-Galactose                            | gal                              |
| 9             | D-Galactarate                          | galct-D                          |
| 10            | D-Galactonate                          | galctl-D                         |
| 11            | Galactitol                             | galt                             |
| 12            | D-Glucosamine                          | gam                              |
| 13            | D-Glucose                              | glc-D                            |
| 14            | D-Glucarate                            | glcr                             |
| 15            | L-Iodonate                             | idon-L                           |
| 16            | Inosine                                | ins                              |
| 17            | Lactose                                | lcts                             |
| 18            | Maltose                                | malt                             |
| 19            | Maltohexaose                           | maltx                            |
| 20            | Maltoheptaose                          | maltpt                           |
| 21            | Maltohexaose                           | malttr                           |
| 22            | Maltooltriose                          | malttr                           |
| 23            | Maltooltriose                          | malttttr                         |
| 24            | MANNose                                | man                              |
| 25            | MELibiose                              | melib                            |
| 26            | D-Ribose                               | rib-D                            |
| 27            | L-Rhamnose                             | rmn                              |
| 28            | D-Sorbitol                             | sbt-D                            |
| 29            | Trehalose                              | tre                              |
| 30            | Xanthosine                             | xtsn                             |
| 31            | D-Xylose                               | xyl-D                            |
| 32            | 3-(3-hydroxy-phenyl)propionate         | 3hpppn                           |
| 33            | Acetate                                | ac                               |
| 34            | Acetoacetate                           | acac                             |
| 35            | D-Alanine                              | ala-D                            |
| 36            | L-Alanine                              | ala-L                            |
| 37            | L-Arginine                             | arg-L                            |
| 38            | L-Asparagine                           | asn-L                            |
| 39            | L-Aspartate                            | asp-L                            |
| 40            | Citrate                                | cit                              |
| 41            | Fumarate                               | fum                              |
| 42            | L-Glutamine                            | glu-L                            |
| 43            | L-Glutamate                            | glu-L                            |
| 44            | Glycine                                | gly                              |
| 45            | Glycerol                               | glyc                             |
| 46            | Glycolate                              | glyc                             |
| 47            | Hexadecanoate (n-C16:0)                | hdca                             |
|   | Chemical Name                      | Code  |
|---|-----------------------------------|-------|
| 48| D-Lactate                         | lac-D |
| 49| L-Lactate                         | lac-L |
| 50| L-Malate                          | mal-L |
| 51| D-Mannitol                        | mnl   |
| 52| Octadecanoate (n-C18:0)           | ocdca |
| 53| Phenylpropanoate                  | pppn  |
| 54| L-Proline                         | pro-L |
| 55| Pyruvate                          | pyr   |
| 56| D-Serine                          | ser-D |
| 57| L-Serine                          | ser-L |
| 58| Succinate                         | succ  |
| 59| L-Tartrate                        | tartr-L|
| 60| L-Threonine                       | thr-L |
| 61| L-Tryptophan                      | trp-L |
| 62| Tetradecanoate (n-C14:0)          | ttdca |
Table S2: List of 21 genes whose configuration can oscillate

| Gene   | bnumber |
|--------|---------|
| nagC   | b0676   |
| nagA   | b0677   |
| nagB   | b0678   |
| nagE   | b0679   |
| deoR   | b0840   |
| uxaB   | b1521   |
| kdgR   | b1827   |
| uxA    | b3091   |
| uxC    | b3092   |
| exuT   | b3093   |
| exuR   | b3094   |
| kdgK   | b3526   |
| glmU   | b3730   |
| kdgT   | b3909   |
| exuA   | b4322   |
| exuB   | b4323   |
| exuR   | b4324   |
| deoC   | b4381   |
| deoA   | b4382   |
| deoB   | b4383   |
| deoD   | b4384   |
Table S3: Comparison of growth rate obtained using pure (unconstrained) FBA with that obtained using constrained FBA for various minimal media (see main text, methods section). For each media, the amount of carbon source uptake was set to 10 mM per g-DCW per hr and the uptake rates of all other inorganics in the media was left unconstrained.

| Serial Number | Minimal Media | Oxygen Availability | Growth Rate with regulatory constraints (GRreg) | Growth Rate with no regulatory constraints (GRpure) | Ratio (GRreg/GRpure) |
|---------------|---------------|---------------------|-----------------------------------------------|-----------------------------------------------|---------------------|
| 1             | ac            | aerobic             | 0.234                                         | 0.234                                         | 0.998               |
| 2             | ala-D         | aerobic             | 0.416                                         | 0.423                                         | 0.985               |
| 3             | ala-L         | aerobic             | 0.416                                         | 0.423                                         | 0.985               |
| 4             | arab-L        | anaerobic           | 0.785                                         | 0.786                                         | 0.998               |
| 5             | arab-L        | aerobic             | 0.220                                         | 0.222                                         | 0.992               |
| 6             | arg-L         | aerobic             | 0.743                                         | 0.784                                         | 0.948               |
| 7             | asn-L         | aerobic             | 0.452                                         | 0.452                                         | 0.999               |
| 8             | asp-L         | aerobic             | 0.451                                         | 0.451                                         | 0.998               |
| 9             | cytd          | anaerobic           | 0.826                                         | 0.872                                         | 0.948               |
| 10            | cytd          | aerobic             | 0.282                                         | 0.394                                         | 0.716               |
| 11            | ddglcn        | anaerobic           | 0.830                                         | 0.831                                         | 0.998               |
| 12            | ddglcn        | aerobic             | 0.226                                         | 0.228                                         | 0.993               |
| 13            | fru           | anaerobic           | 0.955                                         | 0.957                                         | 0.998               |
| 14            | fru           | aerobic             | 0.297                                         | 0.299                                         | 0.992               |
| 15            | fuc-L         | aerobic             | 0.526                                         | 0.915                                         | 0.575               |
| 16            | fuc-L         | anaerobic           | 0.156                                         | 0.158                                         | 0.993               |
| 17            | fum           | aerobic             | 0.439                                         | 0.439                                         | 0.998               |
| 18            | g6p           | anaerobic           | 0.990                                         | 0.992                                         | 0.998               |
| 19            | g6p           | aerobic             | 0.377                                         | 0.380                                         | 0.992               |
| 20            | gal           | anaerobic           | 0.944                                         | 0.946                                         | 0.998               |
| 21            | gal           | aerobic             | 0.270                                         | 0.272                                         | 0.992               |
| 22            | galct-D       | anaerobic           | 0.663                                         | 0.664                                         | 0.998               |
| 23            | galct-D       | aerobic             | 0.209                                         | 0.210                                         | 0.993               |
| 24            | galctn-D      | anaerobic           | 0.830                                         | 0.831                                         | 0.998               |
| 25            | galctn-D      | aerobic             | 0.226                                         | 0.228                                         | 0.993               |
| 26            | galt          | anaerobic           | 1.007                                         | 1.009                                         | 0.998               |
| 27            | galt          | aerobic             | 0.253                                         | 0.255                                         | 0.993               |
| 28            | gam           | anaerobic           | 0.955                                         | 0.957                                         | 0.998               |
| 29            | gam           | aerobic             | 0.297                                         | 0.299                                         | 0.992               |
| 30            | glc-D         | anaerobic           | 0.955                                         | 0.957                                         | 0.998               |
| 31            | glc-D         | aerobic             | 0.297                                         | 0.299                                         | 0.992               |
| 32            | glcn          | anaerobic           | 0.876                                         | 0.877                                         | 0.998               |
| 33            | glcn          | aerobic             | 0.241                                         | 0.243                                         | 0.990               |
| 34            | glcr          | anaerobic           | 0.663                                         | 0.664                                         | 0.998               |
| 35            | glcr          | aerobic             | 0.209                                         | 0.210                                         | 0.993               |
| 36            | gin-L         | aerobic             | 0.644                                         | 0.644                                         | 0.999               |
| 37            | glu-L         | aerobic             | 0.670                                         | 0.674                                         | 0.994               |
| 38            | glyc          | aerobic             | 0.555                                         | 0.555                                         | 0.998               |
| 39            | glyclt        | aerobic             | 0.177                                         | 0.177                                         | 0.998               |
| 40            | hpppn         | aerobic             | 1.124                                         | 1.125                                         | 0.999               |
| 41            | idon-L        | anaerobic           | 0.866                                         | 0.867                                         | 0.998               |
| 42            | idon-L        | aerobic             | 0.207                                         | 0.208                                         | 0.992               |
| 43            | ins           | anaerobic           | 0.888                                         | 0.889                                         | 0.998               |
| 44            | ins           | aerobic             | 0.350                                         | 0.352                                         | 0.995               |
| 45            | lac-D         | aerobic             | 0.410                                         | 0.413                                         | 0.992               |
| 46            | lac-L         | aerobic             | 0.372                                         | 0.375                                         | 0.992               |
|   |   | Anaerobic | Aerobic |   |
|---|---|-----------|---------|---|
| 47 | lcts | 1.900 | 1.903 | 0.998 |
| 48 | lcts | 0.566 | 0.571 | 0.992 |
| 49 | malt-L | 0.427 | 0.439 | 0.971 |
| 50 | malt | 1.911 | 1.914 | 0.998 |
| 51 | malt | 0.593 | 0.598 | 0.992 |
| 52 | malt-hx | 5.826 | 5.835 | 0.998 |
| 53 | malt-hx | 1.995 | 2.010 | 0.992 |
| 54 | maltpt | 4.824 | 4.832 | 0.998 |
| 55 | maltpt | 1.591 | 1.603 | 0.992 |
| 56 | malt-tr | 2.867 | 2.871 | 0.998 |
| 57 | malt-tr | 0.890 | 0.897 | 0.992 |
| 58 | malt-trr | 3.822 | 3.828 | 0.998 |
| 59 | malt-trr | 1.186 | 1.195 | 0.992 |
| 60 | man | 0.955 | 0.957 | 0.998 |
| 61 | man | 0.297 | 0.299 | 0.992 |
| 62 | melib | 1.900 | 1.903 | 0.998 |
| 63 | melib | 0.566 | 0.571 | 0.992 |
| 64 | mnl | 1.020 | 1.025 | 0.995 |
| 65 | pro-L | 0.754 | 0.762 | 0.990 |
| 66 | pyr | 0.346 | 0.348 | 0.992 |
| 67 | rib-D | 0.750 | 0.751 | 0.998 |
| 68 | rib-D | 0.139 | 0.140 | 0.992 |
| 69 | rmn | 0.526 | 0.915 | 0.575 |
| 70 | rmn | 0.156 | 0.158 | 0.993 |
| 71 | sbt-D | 1.020 | 1.025 | 0.995 |
| 72 | sbt-D | 0.256 | 0.258 | 0.992 |
| 73 | ser-D | 0.346 | 0.348 | 0.992 |
| 74 | ser-L | 0.354 | 0.356 | 0.994 |
| 75 | succ | 0.469 | 0.469 | 0.998 |
| 76 | tre | 1.911 | 1.914 | 0.998 |
| 77 | tre | 0.593 | 0.598 | 0.992 |
| 78 | xtsn | 0.857 | 0.859 | 0.998 |
| 79 | xtsn | 0.346 | 0.348 | 0.995 |
| 80 | xyl-D | 0.785 | 0.786 | 0.998 |
| 81 | xyl-D | 0.220 | 0.222 | 0.992 |
Table S4: Abbreviations used to label nodes corresponding to conditions and stimuli in Fig. 4 and their corresponding names

| Abbreviation | Name              |
|--------------|-------------------|
| C1           | CRP noGLC         |
| C2           | Surplus FDP       |
| C3           | Surplus PYR       |
| C4           | NRI_low           |
| C5           | NRI_hi            |
| C6           | Growth            |
| C7           | pH                |
| S1           | Dipyridyl         |
| S2           | High NAD          |
| S3           | Heat shock        |
| S4           | Stress            |
| S5           | Oxidative stress  |
| S6           | LBMedia           |
| S7           | High osmolarity   |
| S8           | Salicylate        |
**Table S5:** The table shows the number of genes in *E. coli* TRN with K regulatory inputs

| Number of regulatory inputs $K$ | Number of Genes |
|-------------------------------|-----------------|
| 1                             | 259             |
| 2                             | 189             |
| 3                             | 68              |
| 4                             | 39              |
| 5                             | 10              |
| 6                             | 4               |
| 8                             | 2               |