Supplementary Information

A genome-scale metabolic model of *Saccharomyces cerevisiae* that integrates expression constraints and reaction thermodynamics

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Supplementary Notes

Implementing multiple expression systems

Since an important difference between bacterial and eukaryotic cells is the presence of multiple expression systems in the latter, we extended the original ETFL formulation to be able to consider multiple expression systems. Consider the following two constraints from the original formulation:

\[ \sum_{l} P_l = E_{\text{RNAP}} \]  \hspace{1cm} (1)

\[ \sum_{l} R_l = E_{\text{rib}} \]  \hspace{1cm} (2)

where \( R_l \) and \( P_l \) represent the amounts of ribosome and RNA polymerase that are allocated to transcribe and translate the gene \( l \), respectively. Equation (1) implies that the sum of the RNA polymerases allocated to transcribe different peptides must be equal to total available RNA polymerases, i.e., \( E_{\text{RNAP}} \). Similarly, Equation (2) implies that the sum of the ribosomes allocated to translate different peptides must be equal to total available ribosomes, i.e., \( E_{\text{rib}} \).

These constraints assume that all the genes are transcribed and translated by a single pool of RNA polymerase and ribosome, respectively. However, there are multiple types of RNA polymerase and ribosome in eukaryotes.

Without loss of generality and to make it clearer, we explain the extension for the case that there exist two types (pools) of RNA polymerase. Similar procedure can be applied to the cases that the number of RNA polymerases is different. Also, multiple types of ribosomes can be defined in the same way. Suppose that the cell has two RNA polymerases, \( \text{RNAP}_1 \) and \( \text{RNAP}_2 \).

Per each type of RNA polymerase, an enzymatic pool can be considered, which is represented as \( E_{\text{RNAP}}^i, i \in \{1,2\} \). The genes can be divided into at most three sets: (i) the genes transcribed by \( \text{RNAP}_1 \), represented by \( I_1 \), (ii) the genes transcribed by \( \text{RNAP}_2 \), represented by \( I_2 \) and (iii) the genes transcribed by both enzymes, represented by \( I_{1,2} \). Instead of Equation (1), the following constraints are applied:

\[ \sum_{l \in I_1} P_l \leq E_{\text{RNAP}}^1 \]  \hspace{1cm} (3)

\[ \sum_{l \in I_2} P_l \leq E_{\text{RNAP}}^2 \]  \hspace{1cm} (4)
The Equation (3) and Equation (4) ensure that, respectively, the sum of the allocated RNA polymerase to the genes in the set $I_1$ and $I_2$ cannot exceed the total available RNA polymerase in the pool. The equality in Equation (1) is converted to inequality in these equations to let part of the RNA polymerases be allocated to the genes in the set $I_{1,2}$. Then, the Equation (5) enforces the equality between the total allocated RNA polymerases and the available enzyme in the two pools. By maximizing growth rate subject to these constraints, the cheaper RNA polymerase, i.e., the one with the less metabolic demand, takes over all the genes from the shared set $(I_{1,2})$.

### Thermodynamic curation of the S. cerevisiae genome-scale model Yeast8

Including thermodynamic information in the S. cerevisiae GEM Yeast8 [1] allows us to constrain the reaction directionalities according to the second law of thermodynamics, that is, according to the Gibbs free energy of each reaction. Towards this end, we performed a thermodynamic curation of Yeast8. This curation was performed in two stages. In the first stage, we estimated the Gibbs free energy of formation of the compounds and the corresponding error for the estimation. First, we used MetaNetX (http://www.metanetx.org) [2] to annotate the compounds of Yeast8 with identifiers from public databases, such as KEGG [3], CHEBI [4], and SEED [5]. From these databases we obtained the structures of the compounds in the form of SMILES. For the compounds lacking SMILES, we manually derived them based on the structure and composition of the metabolites, including mainly lipids and phospholipids. We next used Marvin (version 18.1, 2018, ChemAxon http://www.chemaxon.com) to transform the SMILES into their major protonation state at pH 7 and to generate MDL Molfiles. These last ones were used in the Group Contribution Method (GCM) to estimate the standard Gibbs free energy of the formation of the compounds as well as the error of the estimation [6].

Following the described steps, we estimated the standard Gibbs free energy of formation for 1092 of 1326 total unique metabolites from Yeast8.

In the second stage, we estimated the Gibbs free energy of the reactions that are part of the Yeast8. First, we integrated in the Yeast8 model the thermodynamic properties of the compartments present in the model, including pH, ionic strength, membrane potentials and generic compartment concentration ranges (Table S5 and Table S6). Then, the standard Gibbs free energies of formation are adjusted following the Debye-Hückel approximation to the
corresponding pH and ionic strength [7]. The corrected Gibbs free energies of formation were then used to compute Gibbs free energy of reactions. Considering a reaction with \( m \) components, its Gibbs free energy, \( \Delta_r G' \) is:

\[
\Delta_r G' = \sum_{j=1}^{m} n_j \Delta_f G_j^{\text{io}} + RT \ln \left( \prod_{j=1}^{m} x_j^{n_j} \right),
\]

where \( j = 1, ..., m \), \( n_j \) is the stoichiometric coefficient of compound \( j \); \( \Delta_f G_j^{\text{io}} \) is the standard Gibbs free energy of formation of compound \( j \); \( x_j \) is the concentration of the compound \( j \); \( R \) is the ideal gas constant, \( R = 8.31 \cdot 10^{-3} \text{ KJ} \text{K}^{-1} \text{mol}^{-1} \), and \( T \) is the temperature. In this case, \( T = 298 \text{ K} \).

In the case of transport reactions, the \( \Delta_r G' \) is corrected to account for the differences in pH and membrane potential between the compartments [7].

It is worth noting here, that these calculations and estimations of Gibbs free energies were performed for compounds and reactions under aqueous conditions. The Yeast8 model contains compounds that are part of membranes, and therefore they are no longer in an aqueous environment. We did not estimate \( \Delta_r G' \) for 1304 reactions that did not take place in aqueous environment, which resulted in a thermodynamic curation of 1880 out of 3991 reactions in the Yeast8 GEM.

In its current version, protons can freely circulate between the cytosol and the mitochondria in Yeast8. Seeking to have an improvement of the transport of protons across the mitochondrial membrane, we introduced in the Yeast8 GEM an additional compartment, to account for the mitochondrial inner-membrane space. This improvement allows to correctly capture the transport of protons in the electron transport chain (ETC) for the production of ATP by the enzyme ATP Synthase. Furthermore, this adjustment of proton transport will improve the estimation of the Gibbs free energy of the corresponding reactions as it will allow to account for the correct thermodynamic properties of the compartments involved (i.e., pH, ionic strength and membrane potential).

The thermodynamically curated Yeast8 model as well as the thermodynamic information (Gibbs free energy of formation for the compounds) are publicly available in Zenodo 10.5281/zenodo.4778047.
Comparing ETFL and the previous formulation of ME-models

In this section, we provide a general comparison between the ETFL [25] and the other ME-model formulations [23,24].

A key difference between the two formulations is that ETFL enables the integration of thermodynamic constraints and metabolomics data. Moreover, ETFL can account for multiple expression systems. On the other hand, the stable RNA splicing, and transcription initiation are only formulated in the other ME-model formulations. These functions can be also included in ETFL by expanding the formulation around the related processes. The transcription initiation is not completely neglected in ETFL but instead lumped in the other processes. This lumping is similar to the lumping used for translation initiation and elongation in all ME-models. Since it was shown that including such processes does not impact the predictions of the model in the protein limitation studies [24], and the transcription initiation is more complex in eukaryotic organisms, we did not model them at this stage. Also, in the other formulations of ME-models, the formation of metalloproteins is explicitly considered. In ETFL, the ionic requirements are lumped in the biomass reaction as it was done in the FBA models.

There were two formulations in the other ME-models regarding the enzyme mass balances. In the first formulation, presented in O'Brien et al. [23], the enzymes appeared as metabolites in the reactions, and to properly account for mass balances, two pseudometabolites per enzyme were added to the model. Consider this toy example, where the following reaction with flux \( v_1 \) is catalyzed by enzyme \( E \):

\[
v_1: \ a \xrightarrow{E} b
\]  

To associate the enzyme abundance to the flux \( v_1 \), the following reactions were added:

\[
v_0: \text{enzyme} \xrightarrow{} \text{enzyme}_{\text{prime}} + \alpha \text{ coupling} \tag{7}
\]

\[
v_1: a + \text{enzyme}_{\text{prime}} \rightarrow b + \text{ enzyme} \tag{8}
\]

\[
v_2: \text{enzyme} + \text{coupling} \rightarrow \emptyset \tag{9}
\]

where coupling and \( \text{enzyme}_{\text{prime}} \) are pseudometabolites introduced to facilitate the addition of constraints and \( \alpha = \frac{\mu}{k_{\text{cat}}} \). While the mass balance constraint associated with \( \text{enzyme}_{\text{prime}} \) is an equality, the mass balance for coupling is an inequality. Writing the mass balances for the enzyme and the pseudometabolites, the following constraints can be derived:

\[
v_{\text{tmsl}} - v_{\text{deg}} - v_2 = 0 \tag{10}
\]

\[
v_1 - v_0 = 0 \tag{11}
\]

\[
v_2 \geq \alpha v_0 \tag{12}
\]
where \( v_{\text{tns}} \) and \( v_{\text{deg}} \) are respectively the rates of translation and degradation of the enzyme.

In the second formulation of ME-models, presented in Lloyd et al. [24], to simplify the solving process, the inequality constraint in Equation 12 was converted to an equality. This assumes that all the enzymes catalyze their reactions with the maximum possible rate at the optimal solution. This way, the two pseudometabolites and their corresponding reactions were removed.

In the ETFL formulation, no pseudometabolite is considered and the enzymes are not involved in the reactions as metabolites [25]. For the reaction presented by Equation 6, the following two constraints are imposed:

\[
\begin{align*}
v_{\text{tns}} - v_{\text{deg}} - v_{\text{dil}} &= v_{\text{tns}} - v_{\text{deg}} - \mu E = 0 \\
v_1 &\leq k_{\text{cat}} E
\end{align*}
\]  

(13)

(14)

where \( E \) is the total concentration of the enzyme and Equation 14 applies the generalized maximum flux (i.e., \( V_{\text{max}} = k_{\text{cat}} E \)). Although the constraints in Equations 13-14 differ from the ones in Equations 10-12 and the number of variables and constraints are different, it is straightforward to demonstrate that ETFL formulation and the formulation presented in O'Brien et al. are mathematically equivalent. That is, from Equation 10 and Equation 13, it follows that \( v_2 = \mu E \). Then, by replacing \( v_2 \) in Equation 12, we obtain Equation 14.

The equality assumption in Equation 12 presented in Lloyd et al. would be equivalently modeled in ETFL by converting the inequality in Equation 14 to an equality. This implies that at the optimal solution, all the enzymes perform under complete saturation, which might be an unrealistic assumption in some cases.
Supplementary Tables

Table S1: The scalar parameters used in yETFL

| Parameter                                      | Value and Unit   | Reference |
|-----------------------------------------------|------------------|-----------|
| GC ratio                                      | 38.3 %           | [8]       |
| Length of the chromosome                     | 12157105 bp      | [9]       |
| Median protein half-life                      | 8.8 h            | [10]      |
| Median mRNA half-life                         | 23 min           | [11]      |
| Median rRNA half-life                         | 5 days           | [12]      |
| Average mRNA length                          | 1250 nt          | [13]      |
| Median $k_{cat}$                              | 70.9 s$^{-1}$    | [14]      |
| Average translation rate                     | 10 (2-10) aa/s   | [15]      |
| Average transcription rate                   | 40 nt/s          | [16]      |
| Fraction of proteome allocated to metabolism and expression | 55 %             | [17]      |
| Ribosome occupancy ratio                      | 85 %             | [18]      |
| RNA polymerase occupancy ratio                | 25 %             | [19]      |
Table S2: The list of constraints in yETFL

| Constraints                                                                 | Description                                      |
|---------------------------------------------------------------------------|--------------------------------------------------|
| $\sum_j s_{ij} (v^f_j - v^b_j) = 0, \forall i \in \text{Met}$             | Mass balances for the metabolites                |
| $v^\text{asm}_k - k^{\text{deg}}_k E_k - \mu E_k = 0, \forall k \in \text{Enz}$ | Mass balances for the enzymes                    |
| $v^\text{tnl}_l - \sum_j \eta^l_j v^\text{asm}_j = 0, \forall l \in \text{Pep}$ | Mass balances for the peptides                   |
| $v^{\text{tcp}}_l - k^{\text{deg}}_l F_l - \mu F_l = 0, \forall l \in \text{mRNA}$ | Mass balances for the mRNAs                     |
| $v^{\text{charging}}_l + \sum_{aa_i} \eta^l_{aa_i} v^{\text{tnl}}_{aa_i} - \mu T^e_{aa_i} = 0, \forall aa_i \in \text{AA}$ | Mass balances for the charged tRNAs             |
| $-v^{\text{charging}}_l + \sum_{aa_i} \eta^l_{aa_i} v^{\text{tnl}}_{aa_i} - \mu T^u_{aa_i} = 0, \forall aa_i \in \text{AA}$ | Mass balances for the uncharged tRNAs           |
| $v^{\text{tcp}}_{\text{rRNA}_i} - k^{\text{deg}}_{\text{rRNA}_i} F_{\text{rRNA}_i} - \mu F_{\text{rRNA}_i} - \eta^\text{Rib}_{\text{rRNA}_i} v^{\text{asm}}_{\text{Rib}} = 0, \forall \text{rRNA}_i \in \text{rRNA}$ | Mass balances for the rRNAs                     |
| $v^f_j \leq \sum_{k \in \text{Enz}_j} k^f_{\text{cat},k} E_k, \forall j \in \text{Rxn}$ | Forward catalytic efficiency                     |
| $v^b_j \leq \sum_{k \in \text{Enz}_j} k^b_{\text{cat},k} E_k, \forall j \in \text{Rxn}$ | Backward catalytic efficiency                    |
| $v^{\text{tnl}}_l \leq k_{\text{cat}}^{\text{Rib}} \eta^l_{aa_i} R_l, \forall l \in \text{Pep}$ | Translation catalytic efficiency                 |
| $v^{\text{tcp}}_l \leq k_{\text{cat}}^{\text{ENAP}} L^l_{\text{t}} - P_l, \forall l \in \text{mRNA}$ | Transcription catalytic efficiency               |
| $R_l \leq \frac{L^l_{\text{t}}}{L_{\text{Rib}}} F_l, \forall l \in \text{Pep}$ | Translation coupling                             |
| $P_l \leq \frac{L^l_{\text{t}}}{L_{\text{ENAP}}} n_l \text{DNA}, \forall l \in \text{mRNA}$ | Translation coupling                             |
| $\sum_l P_l = E_{\text{ENAP}}$ | RNA polymerase total capacity                   |
\[
\sum_{i \in L_A} R_i \leq E_{Rib}^A \quad \text{Ribosome A capacity}
\]
\[
\sum_{i \in L_B} R_i \leq E_{Rib}^B \quad \text{Ribosome B capacity}
\]
\[
\sum_{i \in (L_A \cup L_B \cup L_{A,B})} R_i = E_{Rib}^A + E_{Rib}^B \quad \text{Ribosome total capacity}
\]
\[
\sum_{j \neq \text{dummy protein}} \text{MW}_j E_j = \varphi \cdot P^m \quad \text{ME-enzyme allocation}
\]

### Thermodynamic Constraints

\[
-\Delta_r G_j' + RT \sum_{i=1}^m s_{ij} C_i + \Delta_r G_j^c = 0 \quad \forall j \in \text{Rxn}_G
\]
Calculation of the free Gibbs energy

\[
\Delta_r G_j' \leq M(1 - b_j^f) \quad \forall j \in \text{Rxn}_G
\]
Forward Gibbs energy coupling

\[
-\Delta_r G_j' \leq M(1 - b_j^b) \quad \forall j \in \text{Rxn}_G
\]
Backward Gibbs energy coupling

\[
0 \leq v_j^f \leq M b_j^f \quad \forall j \in \text{Rxn}
\]
Forward directionality coupling

\[
0 \leq v_j^b \leq M b_j^b \quad \forall j \in \text{Rxn}
\]
Backward directionality coupling

\[
b_j^f + b_j^b \leq 1 \quad \forall j \in \text{Rxn}
\]
Simultaneous use of directionalities

### Constant Biomass Constraints

\[
\sum_j \text{MW}_j E_j = P^m
\]
Total protein allocation

\[
\sum_l \text{MW}_l F_l = R^m
\]
Total RNA allocation

### Variable Biomass Constraints

\[
\sum_j \text{MW}_j E_j = \sum_u \lambda_u P_u^m
\]
Total protein allocation

\[
\sum_l \text{MW}_l F_l = \sum_u \lambda_u R_u^m
\]
Total RNA allocation
\[ MW_{\text{DNA}} = \sum_{u} \lambda_{u} D_{u}^{m} \]

\[ \eta_{\text{biomass}} = \frac{\chi_{u,bb_{i}}^{m}}{\chi_{\text{ref},bb_{i}}^{m}} \mu - \eta_{\text{pool}} u_{\text{pool}} = 0, \quad \forall bb_{i} \in \text{BBB} \]

DNA allocation

Mass balances for the other biomass building blocks
Table S3: definition of the variables, parameters and sets used in Table S2.

| Symbol       | Definition                                                                 |
|--------------|---------------------------------------------------------------------------|
| $\mu$        | Specific growth rate                                                      |
| $v_j^f$      | Flux of the reaction $j$ in forward direction                            |
| $v_j^b$      | Flux of the reaction $j$ in backward direction                           |
| $v_k^{asm}$  | Flux of the assembly of the enzyme complex $k$                            |
| $v_l^{tcp}$  | Flux of the transcription of the mRNA $l$                                |
| $v_l^{btl}$  | Flux of the translation of the peptide $l$                              |
| $v_{aai}^{charging}$ | Flux of charging the tRNAs with the amino acid $aa_i$                 |
| $F_l$        | Concentration of mRNA $l$                                                |
| $E_k$        | Concentration of enzyme $k$                                              |
| DNA          | Concentration of DNA                                                     |
| $p_l$        | RNA polymerase concentration allocated to transcription of the mRNA $l$ |
| $R_l$        | Ribosome concentration allocated to translation of the peptide $l$      |
| $\tau_{aai}^c$ | Concentration of tRNAs charged with amino acid $aa_i$              |
| $\tau_{aai}^u$ | Concentration of tRNAs uncharged with amino acid $aa_i$              |
| $C_i$        | Concentration of metabolite $i$                                          |
| $\Delta_rG_j'$ | Free Gibbs energy of the reaction $j$                                  |
| $\Delta_rG_j^*$ | Standard free Gibbs energy of the reaction $j$                        |
| $b_j^f$      | Binary variable to represent if the forward direction is active for reaction $j$ |
| Variable | Description |
|----------|-------------|
| $b_j^b$ | Binary variable to represent if the backward direction is active for reaction $j$ |
| $\lambda_{\mu}$ | Binary variables to determine which growth bin is active |
| $k_{\text{cat},k}^f$ | Turnover number of the enzyme $k$ in the forward direction |
| $k_{\text{cat},k}^b$ | Turnover number of the enzyme $k$ in the backward direction |
| $k_*^\text{deg}$ | Degradation constant of the macromolecule * |
| $k_{\text{cat}}^{\text{Rib}}$ | Ribosomal elongation rate |
| $k_{\text{cat}}^{\text{RNAP}}$ | RNA polymerase elongation rate |
| $p^m$ | Fraction of the cell that is protein |
| $R^m$ | Fraction of the cell that is RNA |
| $D^m$ | Fraction of the cell that is DNA |
| $\varphi$ | Fraction of the proteome that is metabolism and expression enzymes |
| MW, | Molecular weight of the macromolecule * |
| $R$ | Universal gas constant |
| $T$ | Temperature |
| $M$ | An arbitrarily large number |
| $L_l^\text{nt}$ | Length of the mRNA $l$ |
| $L_l^{\alpha\alpha}$ | Length of the peptide $l$ |
| $L_{\text{Rib}}$ | Ribosomal footprint |
| $L_{\text{RNAP}}$ | RNA polymerase footprint |
| Met | Set of all metabolites |
| Rxn | Set of all reactions |
| Rxn$_G$ | Set of reactions with defined Gibbs energy |
| Enz | Set of all enzymes |
| Symbol | Description                                |
|--------|--------------------------------------------|
| Pep    | Set of all peptides                        |
| mRNA   | Set of all mRNAs                           |
| rRNA   | Set of all rRNAs                           |
| AA     | Set of all amino acids                     |
| BBB    | Set of all biomass building blocks         |
Table S4: Different amino acid ratios in *Saccharomyces cerevisiae* [20]

| Amino acid | Fraction (%) |
|------------|--------------|
| Ala        | 9.77         |
| Arg        | 3.86         |
| Asx        | 9.28         |
| Cys        | 0.14         |
| Glx        | 15.48        |
| Gly        | 8.89         |
| His        | 1.93         |
| Ile        | 5.89         |
| Leu        | 8.01         |
| Lys        | 6.57         |
| Ala        | 9.77         |
| Arg        | 3.86         |
| Met        | 1.14         |
| Phe        | 3.76         |
| Pro        | 4.22         |
| Ser        | 5.33         |
| Thr        | 5.57         |
| Trp        | 0.65         |
| Tyr        | 1.96         |
| Val        | 7.33         |
Table S5: Biomass composition of *Saccharomyces cerevisiae* at different growth rates [20-22]

| mu    | Protein | RNA | Carbohydrate | Lipid | DNA | Ion | Water | Pi |
|-------|---------|-----|--------------|-------|-----|-----|-------|----|
| 0.022 | 34.5    | 3.8 | 44.9         | 8     | 0.4 | 3   | 4.1   | 1.4|
| 0.052 | 38.5    | 4.6 | 40.9         | 7.8   | 0.4 | 2.7 | 3.9   | 1.2|
| 0.087 | 39.7    | 5.4 | 40.6         | 6.2   | 0.4 | 3   | 3.7   | 1.1|
| 0.107 | 40.7    | 6.6 | 38.7         | 6.1   | 0.3 | 2.7 | 4.1   | 0.8|
| 0.126 | 40.1    | 5.7 | 38.8         | 7     | 0.4 | 2.7 | 4.4   | 1  |
| 0.158 | 42.2    | 5.9 | 35.9         | 7     | 0.4 | 2.9 | 4.8   | 0.9|
| 0.211 | 43.8    | 6.6 | 34.4         | 6.7   | 0.4 | 2.9 | 4.4   | 0.7|
| 0.3   | 48      | 9.4 | 30.1         | 7     | 0.4 | 2.9 | 1.5   | 0.7|
| 0.35  | 51.9    | 10.2| 27.7         | 7     | 0.4 | 2.9 | 0     | 0  |
| 0.4   | 52.4    | 11  | 25.4         | 7     | 0.4 | 2.9 | 0.2   | 0.7|
Table S6: Corrected physicochemical specification of different compartments in Yeast8

| Compartment Name                  | Compartment Symbol | pH   | Ionic Strength | Concentration Range (M) |
|-----------------------------------|--------------------|------|----------------|-------------------------|
| cytoplasm                         | c                  | 7.0000 | 0.25          | 10⁻⁶ - 5x10⁻²         |
| mitochondrion                     | m                  | 7.5000 | 0.25          | 10⁻⁶ - 5x10⁻²         |
| mitochondrial membrane            | mm                 | 7.5000 | 0.25          | 10⁻⁶ - 5x10⁻²         |
| vacuole                           | v                  | 6.1700 | 0             | 10⁻⁶ - 5x10⁻²         |
| vacuolar membrane                 | vm                 | 6.1700 | 0             | 10⁻⁶ - 5x10⁻²         |
| peroxisome                        | p                  | 8.2000 | 0             | 10⁻⁶ - 5x10⁻²         |
| extracellular                     | e                  | 5.0000 | 0             | 10⁻⁸ - 10⁻¹           |
| Golgi                             | g                  | 6.3500 | 0             | 10⁻⁶ - 5x10⁻²         |
| Golgi membrane                    | gm                 | 6.3500 | 0             | 10⁻⁶ - 5x10⁻²         |
| endoplasmic reticulum             | er                 | 7.2000 | 0             | 10⁻⁶ - 5x10⁻²         |
| endoplasmic reticulum membrane    | erm                | 7.2000 | 0             | 10⁻⁶ - 5x10⁻²         |
| nucleus                           | n                  | 7.0000 | 0             | 10⁻⁶ - 5x10⁻²         |
| lipid particle                    | lp                 | 7.0000 | 0.25          | 10⁻⁶ - 5x10⁻²         |
| cell envelope                     | ce                 | 7.0000 | 0             | 10⁻⁶ - 5x10⁻²         |
| inter-membrane mitochondrion      | im                 | 7.0000 | 0             | 10⁻⁶ - 5x10⁻²         |
Table S7: membrane potentials for different compartments in Yeast8 (compartment symbols are used from Table S5)

|   | c   | m   | mm  | v   | vm  | p   | e   | g   | gm  | er  | erm | n   | lp  | ce  | im  |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| c | 0   | -180| -180| 0   | 0   | 60  | 0   | 0   | 0   | 0   | 0   | -15 | 0   | 0   | 0   |
| m | 180 | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| mm| 180 | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| v | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| vm| 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| p | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| e | -60 | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| g | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| gm| 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| er| 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| erm| 0  | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| n | 15  | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| lp| 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| ce| 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
| im| 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   |
Supplementary References

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