Text S1

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Supplementary Text

Data controls

In what follows, we describe how we modified the ATP hydrolysis in the *in silico* organisms so that biomass production reflected nutrient catabolysis, and how we identified true biomass production from the results of FBA experiments.

ATP maintenance. Some of the *in silico* organisms were constructed to directly predict the *in vivo* growth rate, which is typically lower than the predicted biomass yield. The growth rate of an organism is related to the biomass yield, but it is a kinetic property that is affected by a variety of factors such as nutrient uptake, regulation of protein expression, and temperature. The biomass yield is dimensionless and reflects the efficiency with which the organism uses the nutrients available [1]. The authors of the *in silico* organisms model the growth rate by forcing the *in silico* organism to hydrolyze a fixed amount of extra ATP, known as ATP maintenance. The ATP maintenance is typically calculated by fitting growth rate data of the organism on a single medium [2]. As we are only modeling biomass yield, we remove ATP maintenance from the *in silico* organisms as follows.

There are two types of maintenance, growth-associated maintenance (GAM), and non-growth associated maintenance (NGAM). For NGAM, the hydrolysis of ATP is added as a separate reaction, and this merely changes the lower bound of nutrient uptake that is required for biomass production to begin (see section on b_{min} below). We turn off this reaction if it is present by constraining its flux to zero.

For GAM, the hydrolysis of ATP is incorporated into the biomass function, and this affects the overall growth rate of the *in silico* organism. However, the ATP hydrolysis in the biomass function accounts for both GAM and ATP needed to polymerize protein and DNA. The energetic costs of the polymerization of biomass components is important for biomass yield, and we therefore cannot remove the ATP hydrolysis from the biomass function entirely.

To solve this problem, we calculate the ATP needed for the polymerization of biomass components using the experimentally determined values published for *E. coli* [2, 3]. The published biomass function for each *in silico* organism contains the stoichiometry of the protein, DNA, and RNA, and it is straightforward to calculate the stoichimetric coefficient for ATP hydrolysis needed for polymerization costs alone. We replace the published coefficient for ATP hydrolysis with the calculated value. For *E. coli* and *S. cerevisiae*, this value of ATP needed for polymerization costs was already available [2, 4, 5].

Source of carbon. Consider a species s growing on nutrient i. By using FBA, we find the optimal biomass produced b_i^s. Often $b_i^s > 0$, but to decide whether it can be considered true biomass production, we have to take into account the following issues:

- *H. pylori* and *M. tuberculosis* present the unusual case of having nutrients in the minimal medium with which they can already produce biomass in the absence of any additional nutrients. This means that we will observe biomass production for any nutrient we test, even if the nutrient cannot be catabolized. We counter this by introducing a minimal biomass production, b^s_{min}. Any biomass production in excess of b^s_{min} is then attributable to the nutrient we are testing.
- In the latest reconstruction of *E. coli*, there are several nutrients for which Feist *et al.* considered the resulting biomass to be too small [2]. Additionally, when considering an organism that has $b^s_{min} > 0$, some nutrients such as pyrimidines will produce biomass above b^s_{min} even though they are not catabolized. The reason for this is that these nutrients are directly used in the biomass, i.e. these nutrients are not catabolized, and thereby save the organism carbon and energy, resulting in a larger biomass production. For these reasons, we estimated the minimal biomass production threshold b_{cat} beyond which biomass production is attributable to a nutrient being catabolized. We set $b_{cat} = 0.008$, and assume that nutrients for which $b^s_i - b^s_{min} < b_{cat}$ are not catabolized.

In building our model, our first concern is to determine whether a nutrient can be a source of carbon. Therefore, we reduce the biomass production b^s_i to a binary observation α^s_i such that:

$$\alpha^s_i = \begin{cases} NG & \text{if } b^s_i \leq b^s_{min} + b_{cat} \\ G & \text{if } b^s_i > b^s_{min} + b_{cat} \end{cases} \tag{1}$$

In the reconstructions of *E. coli* and *H. pylori*, there are five nutrients available that were added as sinks for metabolites that had been observed to accumulate *in silico* [2, 6]. We do not consider these nutrients in our analysis.

The biomass reaction for *S. aureus* was derived from the same source as *B. subtilis*, but it was designed so that its demand in the number of carbons is approximately 100-fold higher than that of *B. subtilis*. If we reduce the observation to a binary variable, this should not matter, even if the resulting biomass produced is 100-fold smaller. However, for some nutrients, FBA fails to reach a solution because the maximum nutrient uptake value of -1 is too small. We counter this by using a maximum nutrient uptake value of -100 in *S. aureus*.

Supplementary Figures

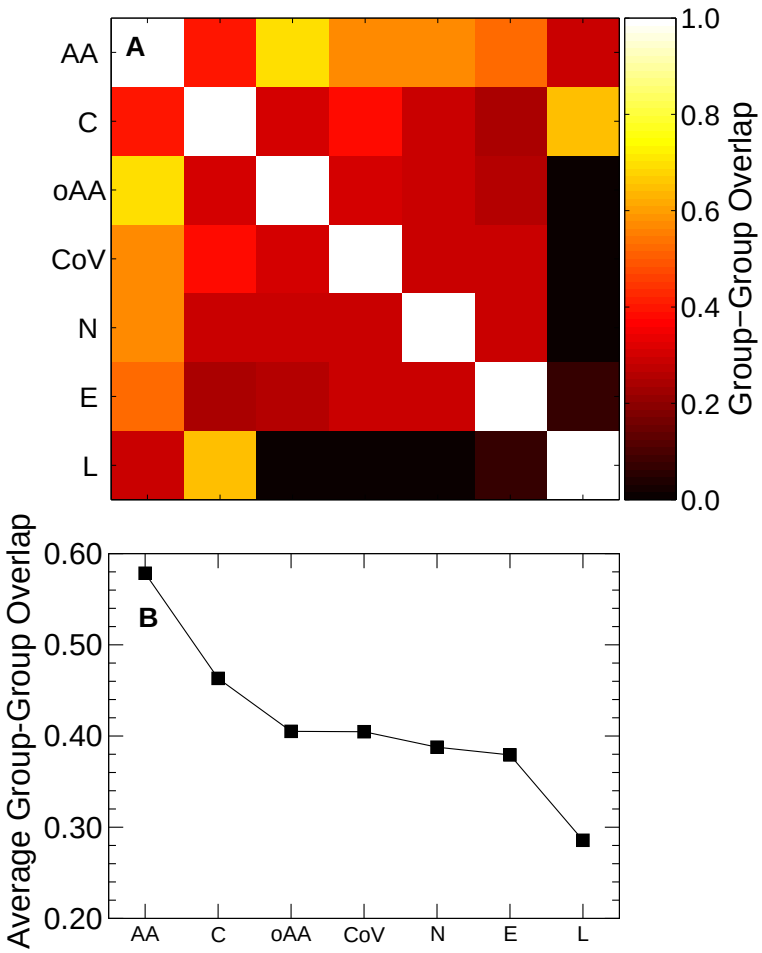

Figure S1. Redundancy of nutrient-pathway membership. A The overlap for pairs of groups. Many nutrients are found in more than one KEGG pathway, and also in more than one group of pathways. This redundancy is depicted here as group-group overlap. For each pair of groups, we count the number of nutrients that are members of pathways found in both groups, and normalize with the number of nutrients in the smaller group. We only perform this analysis on nutrients which are not classified as G or NG based on chemical structure and function (see main text). **B** Average overlap for individual groups. We find that Amino acid metabolism (AA) has the highest average overlap, sharing many nutrients with other groups. This finding is consistent with the notion that AA is central to metabolism. Key: AA=Amino acid metabolism; C=Carbohydrate metabolism; oAA=Metabolism of other amino acids; CoV=Metabolism of cofactors and vitamins; N=Nucleotide metabolism; E=Energy metabolism; L=Lipid metabolism.

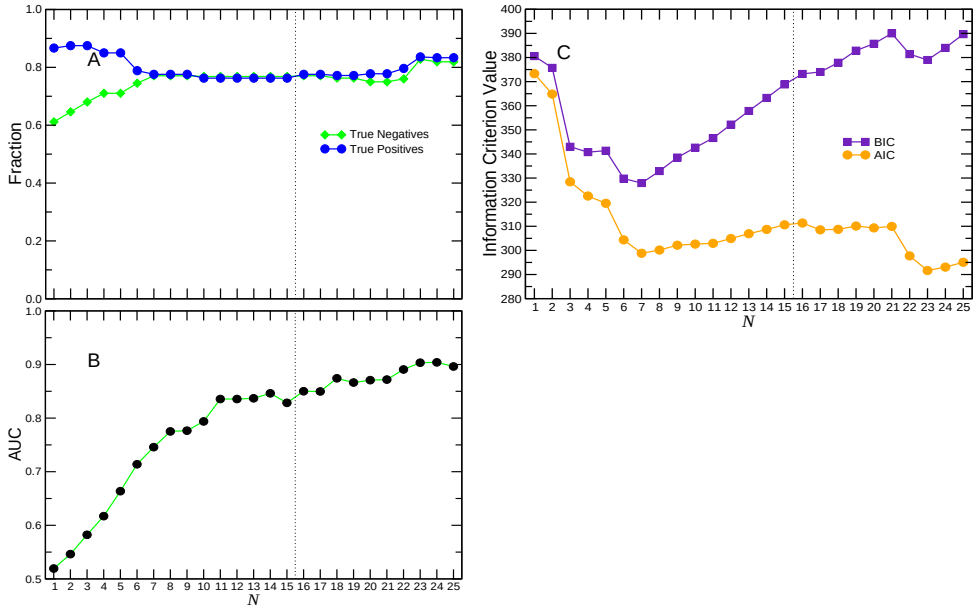

Figure S2. Model selection. We generate logistic models according to the pathways listed in supplemental table S6. We focus first on the G nutrients (15 pathways) and only then add the 11 pathways comprising mostly NG nutrients. Note how for $N > 7$ the values of the information criteria start increasing indicating that the model is overfitting the data.

Supplementary Tables

Supplemental Table S1: Minimal media for *in silico* organisms.

The presence of a symbol indicates that a species uptakes the nutrient in question. The symbol type indicates whether a nutrient's uptake is constrained: (
checkmark) a nutrient's uptake is unconstrained, (n) a nutrient's uptake is constrained by n. Such nutrients contain organic carbon and the value for n is taken from the biomass function.

In the case of cytosine in *S. aureus*, n is the sum of the CMP and dCMP requirements in the biomass. *M. barkeri* respires anaerobically, and thus does not have oxygen in its minimal media. In addition, *M. barkeri*'s source of sulfur is SO_3^{-2} and its terminal electron acceptor is H_2S.

Key: *Bs=B. subtilis*, *Ec=E. coli*, *Mb=M. barkeri*, *Sc=S. cerevisiae*, *Sa=S. aureus*, *Mt=M. tuberculosis*, *Hp=H. pylori*.

Table S1. Minimal media for *in silico* organisms.

Name	*Bs*	*Ec*	*Mb*	*Sc*	*Sa*	*Mt*	*Hp*
H_2O	✓	✓	✓	✓	✓	✓	✓
O_2	✓	✓		✓	✓	✓	✓
CO_2	✓						
H^+	✓	✓	✓	✓	✓	✓	✓
$NH_4{}^+$	✓	✓	✓	✓	✓	✓	✓
$SO_4{}^{-2}$	✓	✓		✓	✓	✓	✓
$SO_3{}^{-2}$			✓				
H_2S			✓				
$HPO_4{}^{-2}$	✓	✓	✓	✓	✓	✓	✓
$MoO_4{}^{-2}$		✓					
K^+	✓	✓				✓	
Na^+	✓	✓	✓	✓		✓	
Ca^{+2}	✓	✓				✓	
Co^{+2}		✓	✓				
Cu^{+2}		✓				✓	
Fe^{+2}		✓		✓	✓		✓
Mg^{+2}	✓	✓					
Ni^{+2}			✓				
Zn^{+2}		✓					
Fe^{+3}	✓	✓				✓	✓
Mn^{+3}		✓					
Cl^-		✓				✓	
Cob(I)alamin		✓					
Cytosine					-2.73		
Glycine					-3.51		
L-Alanine							-0.488
L-Valine							-0.402
L-Leucine							-0.428
L-Isoleucine							-0.276
L-Arginine							-0.281
L-Methionine							-0.146
L-Histidine							-0.090
Pimelate							$-6e^{-6}$
Thiamin					-0.01		$-6e^{-6}$
Niacin			-0.0027		-0.01		
Glycerol						-0.0254	
4-Aminobenzoate			-0.0237				

Supplemental Table S2: Nutrient predictions.

The presence of a symbol indicates that a species uptakes the nutrient in question. The symbol type indicates whether the uptaken nutrient can be a source of carbon in the species in question: (✓) source of carbon, (x) not a source of carbon.

Table S2(a). Predictions for "Purines" & "Pyrimidines."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
Adenine			x	x
Cytosine		x		x
Uracil		x		
Xanthine		x	x	

Table S2(b). Predictions for "Fatty acids."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
Fatty acids	x	x	✓	x

Table S2(c). Predictions for "Cell boundary compounds."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
UDP-N-acetylglucosamine			x	
UDP-N-acetylgalactosamine			x	
Lipoprotein	x			
Phospholipid			x	
Teichoic acid		x		

Table S2(d). Predictions for "Cofactors."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
Acetly-CoA			x	
Biotin			x	
Ferrichome		x		
Glutathione			x	
Heme	x			
Hemin	x			
Sialic acid			x	
Pantothenate				x

Table S2(e). Predictions for "Sugar derivatives."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
D-Glucarate		✓		
GDP-Fucose			✓	
UDP-Galactose			✓	
Galactitol		✓		
Glucarate				✓
Sorbitol		✓		
Glutamine		✓		
Galacturonate	✓			
Mannitol		✓		
Xylitol		✓		
Glucose-6-phosphate				✓

Table S2(f). Predictions for "Sugars."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
1,3-β-D-Glucan	✓	✓		
Cellobiose		✓		
Fructose		✓		
Galactose			✓	
Glucose	✓	✓	✓	✓
Maltose		✓		
Mannose	✓	✓		
Sucrose			✓	
Trehalose	✓	✓		✓

Table S2(g). Predictions for "Inorganic compounds."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
Ca^{+2}	x	x	x	
SO_3^{-2}	x	x	x	
Al^{+3}			x	
NH_4^{+}	x	x	x	x
H_3O_3As	x	x	x	
Cd_2^{+}		x		
Cl^{-}	x	x	x	x
H_2O_4Cr	x			
Co^{+2}		x		
Cu^{+2}	x	x	x	x
Fe^{+3}	x	x		x
Pb	x		x	
Mg^{+2}	x	x	x	
Mn^{+3}	x	x	x	x
Hg_2^{+}		x		
MoO_4^{-2}	x	x		x
Ni^{+2}	x			x
NO_3^{-}	x			x
HPO_4^{-2}	x	x	x	x
K^{+}	x	x	x	x
H^{+}	x	x	x	x
Na^{+}	x	x	x	x
H_2O	x			
Zn^{+2}		x	x	

Table S2(h). Predictions for "Organic compounds."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
α-Ketoglutarate			✓	
3-Phenylpropionate	x			
Toluene	x		x	
Succinate	✓			
(S)-Lactate	✓			
Dracylic acid	x			
Glycine betaine	✓	✓		✓
L-Carnitine	x	x	x	
Bilineurine	✓	✓	✓	
Folate			x	
Formate	x	x	x	x
Fumarate			✓	
Glycerol		✓	✓	
Glycerol 3-phosphate	✓			
L-Malate			✓	
Malonate	x			
Muconate	x			
Oxalic acid	✓	✓	✓	✓
Oxaloacetate			✓	
Phosphoenolpyruvate			x	
1,4-Butanediamine	✓	✓		
Shikimate	x			
Acetamide	✓			
Spermidine	x	x		
Succinate			✓	
Taurine	x			
Citrate	✓			
Urea	x		x	

Table S2(i). Predictions for "Amino acids."

Name	*R. palustris*	*L. monocytogenes*	*D. dictysoideum*	*T. acidophilum*
Glycine	✓	✓	✓	✓
L-Alanine	✓	✓	✓	✓
D-Alanine	x	x	x	x
L-Serine	✓	✓	✓	✓
D-Serine	✓	✓	✓	✓
L-Threonine	✓	✓	✓	✓
L-Glutamate	✓	✓	✓	✓
D-Glutamate	x	x	x	x
L-Glutamine	✓	✓	✓	✓
L-Aspartate	✓	✓	✓	✓
L-Asparagine	✓	✓	✓	✓
L-Proline	✓	✓	✓	✓
L-Arginine	✓	✓	✓	✓
L-Cysteine	✓	✓	✓	✓
D-Cysteine	x	x	x	x
L-Methionine	x	x	x	x
D-Methionine	x	x	x	x
L-Leucine	x	x	x	x
L-Isoleucine	x	x	x	x
L-Valine	x	x	x	x
L-Lysine	x	x	x	x
L-Histidine	x	x	x	x
L-Phenylalanine	x	x	x	x
L-Tyrosine	x	x	x	x
L-Tryptophan	✓	✓	✓	✓

Supplemental Table S3: Reassignment of KEGG IDs and Pathways for nutrients in the *in silico* organisms.

Table S3(a). Simple compounds with reassigned KEGG IDs.

Name	Reassigned KEGG ID
2-Methyl-1-butanol	C00233
2-Methylbutyl acetate	C00233
2-Methylpropanal	C00233
3-Aminobutanoate	C00334
Butanesulfonate	C01412
Butanoate	C00246
Ethanesulfonate	C00084
Hexacosanoate	C08320
Hexadecenoate	C08362
Hexanoate	C01585
Isobutyl acetate	C00233
L-Methionine R-Oxide	C02989
L-Methionine-R-Sulfoxide	C00073
L-Methionine-S-Sulfoxide	C00073
Maltoheptaose	C01935
Maltopentaose	C01935
Monomethylamine	C00543
Octadecanoate	C01530
Octadecenoate	C00712
Octadecynoate	C01595
Tetradecenoate	C08322
γ-Butyro-betaine	C00487

Table S3(b). Simple compounds lacking a KEGG ID.

Name
MOPS
Hexanesulfonate
Arseno-betaine
α-Methyl-D-glucoside
β-Methylglucoside

Table S3(c). Simple compounds with reassigned KEGG Pathways.

Name	Reassigned KEGG Pathway
(R)-Propane-1,2-diol	C00583
2,3-Diaminopropionate	C00163
2-Methylbutanal	C00671
5-Dehydro-D-gluconate	C00618
Acetamide	C00033
Butyro-betaine	C00487
Crotono-betaine	C00487
D-Allose	C00085
D-Arabinose	C01112, C00309
D-Gulitol	C00794
D-Mannosamine	C00645
D-Methionine	C00073
D-O-Phosphoserine	C00740
D-Psicose	C00085
Glycerol 2-phosphate	C00116
Glycerophosphoglycerol	C00093
Glycogen	C01935
Hexanoate	C05270
L-Idonate	C00618
Maltohexaose	C01935
Maltotetraose	C01935
Maltotriose	C01935
Mercaptoacetate	C00155
Methanesulfonate	C00409
Methyl β-D-galactopyranoside	C01019
Palatinose	C00089
Phosphonotyrosine	C00082
S-Methyl-L-Methionine	C00019
Saligenin	C01451
Tetradecenoate	C06424
β-D-Galactose	C00124

Table S3(d). Simple compounds lacking a KEGG Pathway.

Name
Methyl sulfide
2-Deoxy-D-glucose 6-phosphate
Isopentyl alcohol
Isovaleraldehyde
Gentiobiose
L-Djenkolic acid
Proline betaine
Dimethyl sulfoxide
Isoamyl acetate
Phenethyl acetate
Isobutyl alcohol
Acetyl ester

Supplemental Table S4: Composition of complex nutrients.

The simple nutrients that compose each complex nutrients are listed here for all the species which take up the complex nutrient. The absence of a symbol indicates that the species does not take up the nutrient in question. x) The species takes up the nutrient but does not catabolize it; ∘) The species takes up the nutrient but does not catabolize all of the simple nutrients that compose it; ✓) The species takes up the nutrient and catabolizes all of its components.

Table S4(a). Composition of complex nutrients in the "Amino acids" class

Family	Name	*Ec*
Pyruvate, Indole	Tryptophan	

Table S4(b). Composition of complex nutrients in the "Fatty acid derivatives" class

Family	Name	*Ec*	*Sc*
Glycerol, myo-Inositol	1(Glycerol-3-Phospho)-myo-inositol	∘	x
Glycerol, Aminoethanol	Glycerophosphoethanolamine	✓	
Bilineurine, Glycerol	Glycerophosphocholine	∘	x
L-Serine, Glycerol	Glycerophosphoserine	✓	

Table S4(c). Composition of complex nutrients in the "Sugar derivatives" class

Family	Name	*Ec*	*Bs*	*Sa*
Acetate, D-GluA*	NAc-D-GluA*	✓	○	○
Pyruvate, Acetate, D-Mannose	N-Acetylneuraminic acid	✓	○	○
Uracil, D-Ribose, D-Galactose	UDP-galactose	○		
Acetate, D-Galactose	NAc-D-GalA** 1-phosphate	x		
D-Glucose, Acetate×2, D-Lactate, D-GluA*	NAc-D-GluA* w/ NAc-muramate	✓		
Acetate, Uracil, D-Ribose, D-GluA*	UDP-N-acetyl-D-GluA*mine	○		
L-Lysine, D-Fructose	Psicoselysine	○		
D-Glucose, Uracil, D-Ribose	UDP-D-glucose	○		
D-Glucose, Saligenin	Salicin		○	x
Uracil, D-Ribose, D-Glucuronate	UDP-glucuronate	○		
D-Glucose, 4-Hydroxyphenol	Arbutin		○	
Acetate, D-GluA*	NAc-D-GluA* 1-phosphate	✓		
Acetate, D-Galactose	2-Acetamido-2-deoxy-D-galactose	x		
Acetate, Uracil, D-Ribose, D-Galactose	UDP-N-acetyl-D-GalA**	○		
D-Glucose, Acetate, D-Lactate	N-Acetylmuramate	✓		
Acetate, D-Mannose	2-Acetamido-2-deoxy-D-mannose	✓	○	
D-Mannose, (R)-Glycerate	α-Mannosylglycerate	✓		
L-Lysine, D-Fructose	Fructoselysine	○		

NAc: N-Acetyl, $*$: D-Glucosamine, $**$: D-Galactosamine

Table S4(d). Composition of complex nutrients in the "Purines" class

Family	Name	*Ec*	*Bs*	*Sc*	*Hp*	*Sa*	*Mt*
D-Ribose, Adenine	Adenosine	✓	✓	○	○	x	
D-Ribose, Adenine	Deoxyadenosine	✓	✓	x	x		
D-Ribose, Adenine	ATP						x
D-Ribose, Adenine	dAMP	✓					
D-Ribose, Adenine	PAP			○			
D-Ribose, Adenine	3'-AMP	✓	✓				
D-Ribose, Adenine	5'-AMP	✓	✓				
D-Ribose, Adenine	2',3'-Cyclic AMP	✓					
D-Ribose, Guanine	Guanosine	✓	✓	○	○		
D-Ribose, Guanine	Deoxyguanosine	✓		x			
D-Ribose, Guanine	GTP	x					
D-Ribose, Guanine	GDP	x					
D-Ribose, Guanine	GMP	✓	✓				
D-Ribose, Guanine	dGMP	✓					
D-Ribose, Guanine	3'-GMP	✓	✓				
D-Ribose, Guanine	2',3'-Cyclic GMP	✓					
D-Ribose, Hypoxanthine	Inosine	✓	✓	○			
D-Ribose, Hypoxanthine	Deoxyinosine	✓		x			
D-Ribose, Hypoxanthine	IMP	✓					
D-Ribose, Hypoxanthine	dIMP	✓					
D-Ribose, Xanthine	Xanthosine	✓	✓	○			
D-Ribose, Xanthine	XMP	✓					

Table S4(e). Composition of complex nutrients in the "Pyrimidines" class

Family	Name	*Ec*	*Bs*	*Sc*	*Hp*	*Sa*	*Mt*
D-Ribose, Cytosine	Cytidine	○	○	○	x	x	x
D-Ribose, Cytosine	Deoxycytidine	○	○	x	x		
D-Ribose, Cytosine	CMP	○	○				
D-Ribose, Cytosine	dCMP	○					
D-Ribose, Cytosine	3'-CMP	○	○				
D-Ribose, Cytosine	2',3'-Cyclic CMP	○					
Uracil, D-Ribose	Uridine	○	○	○	x	x	
Uracil, D-Ribose	Deoxyuridine	○		x	x		
Uracil, D-Ribose	UMP	○	○				
Uracil, D-Ribose	dUMP	○					
Uracil, D-Ribose	3'-UMP	○	○				
Uracil, D-Ribose	2',3'-Cyclic UMP	○					
D-Ribose, Thymine	Deoxythymidine	○	○	x	x	x	
D-Ribose, Thymine	TMP	○	○				
D-Ribose, Thymine	dTTP			x			

Table S4(f). Composition of complex nutrients in the "Amino acid derivatives" class

Family	Name	*Ec*	*Bs*	*Sc*	*Mt*
Glycine×2	Peptide			x	
Glycine, L-Proline	Pro-Gly		x		
Glycine, L-Aspartate	Gly-Asp		x		
Glycine, L-Glutamine	Gly-Glu		x		
Glycine, L-Asparagine	Gly-Asn		x		
Glycine, L-Methionine	Gly-Met		x		
L-Glutamate, Glycine	Gly-Glu		x		
Glycine, L-Cysteine	Cys-Gly	✓	x		
Glycine, L-Proline	Pro-Gly	✓			
Glycine, L-Alanine	Ala-Gly		x		
L-Alanine, L-Threonine	Ala-Thr		x		
L-Alanine, L-Leucine	Ala-Leu		x		
L-Glutamate, L-Alanine	Ala-Glu		x		
L-Alanine, L-Glutamine	Ala-Gln		x		
L-Alanine, L-Histidine	Ala-His		x		
L-Alanine, L-Methionine	Met-Ala		x		
L-Alanine, L-Aspartate	Ala-Asp		x		
D-Alanine×2	D-Ala-D-Ala	✓	✓		
L-Glutamate, Glycine, L-Cysteine	Glutathione	✓	○	x	x
L-Glutamate×2, Glycine×2, L-Cysteine×2	Glutathione disulfide	x	○	x	
L-Alanine, L-Cysteine	Lanthionine		x		
L-Glutamate, L-Alanine, mdp†	LalaDglu-mdp†	○			
L-Glutamate, L-Alanine, D-Alanine, mdp†	LalaDglu-mdp†-Dala	○			
L-Cysteine, 2-Oxobutanoate	Cystathionine		x		
Indole, Ethanol	Indole-3-ethanol			x	
Ethanal, Indole	Indoleacetaldehyde			x	x
Acetate, L-Serine	O-Acetyl-L-serine	x			
Formate×2, L-Tyrosine×2	N,N-Bisformyl-dityrosine			x	

†: meso-2,6-diaminopimelate.

Supplemental Table S5: Nutrient classification.

The reconstruction for *B. subtilis* included two proteins that the organism excretes, and an antibiotic (puromycin); these were ignored.

Table S5(a). Nutrients classified as "Cofactors."

NADP+	Coenzyme A
S-Adenosyl-methionine	S-Adenosyl-homocysteine
Haem	Flavin mononucleotide
Thiamin diphosphate	Bilineurine
Coenzyme R	Vitamin PP
Cobamide (w/ Fe(III))	Niacin
Riboflavin	Thiamin
β-Nicotinamide ribonucleotide	Folate
4-Hydroxyphenol	Cob(II)alamin
Phosphorylcholine	Lipoate
Cob(I)alamin	Pantothenate
Choline sulfate	Thiamine monophosphate
myo-Inositol hexakisphosphate	Pimelate
S-Adenosyl-4-methylthio-2-oxobutanoate	Aerobactin
Cobinamide	Vitamin B12
Enterobactin (no Fe(III))	Ferrichrome (w/ Fe(III))
Fe(III) Dicitrate	Enterobactin (w/ Fe(III))
Ferroxamine (w/ Fe(III))	Fe(III)hydroxamate
Aerobactin (no Fe(III))	Coprogen (w/ Fe(III))
Coprogen (no Fe(III))	2,3-Dihydroxybenzoylserine (w/ Fe(III))
Fe(III) hydroxamate (no Fe(III))	Ferrichrome (no Fe(III))
Ferroxamine (no Fe(III))	Cob(I)alamin-HBI
Cob(I)alamin deg.	Riboflavin deg.
Acetyl-cystine bimane	Bimane
Citrate-Mg	

Table S5(b). Nutrients classified as "Purines."

ATP	5'-AMP	GDP
GTP	PAP	IMP
GMP	Adenine	Adenosine
Guanine	Hypoxanthine	Inosine
Deoxyguanosine	dAMP	dGMP
Urate	Xanthine	Guanosine
Deoxyadenosine	XMP	2'-AMP
3'-AMP	Xanthosine	2',3'-Cyclic AMP
Deoxyinosine	3'-GMP	2',3'-Cyclic GMP
dIMP		

Table S5(c). Nutrients classified as "Pyrimidines."

CMP	UMP	Uracil
Thymine	Deoxythymidine	dCMP
Orotate	Uridine	TMP
dUMP	Cytosine	dTTP
Cytidine	Deoxyuridine	Deoxycytidine
3'-UMP	2',3'-Cyclic CMP	2',3'-Cyclic UMP
2'-UMP	2'-CMP	3'-CMP

Table S5(d). Nutrients classified as "Fatty acids."

Hexadecanoate	Decanoate	Dodecanoate
Octanoate	Tetradecanoate	Octadecanoate
Hexadecenoate	Hexacosanoate	Octadecenoate
Octadecynoate	Tetradecenoate	Butanoate
Hexanoate		

Table S5(e). Nutrients classified as "Fatty acids related."

Glycerol 3-phosphate	Glycerol	Glycerophosphocholine
1(Glycerol-3-Phospho)-myo-inositol	Glycerophosphoethanolamine	Glycerol 2-phosphate
Glycerophosphoglycerol	Glucosyl-glycerol	Glycerophosphoserine

Table S5(f). Nutrients classified as "Cell boundary."

Bile acid	Ergosterol
Lanosterol	Fecosterol
Zymosterol	KDO(2)-lipid IV(A)
KDO2-lipid (A)	Episterol
Phosphatidylcholine	Phosphatidyl-myo-inositol
4-Amino-4-dLarab modified core oligosaccharide lipid A	Core oligosaccharide lipid A
(EC antigen)x4 core oligosaccharide lipid A	Phosphoethanolamine KDO(2)-lipid A
Hepta-acylated core oligosaccharide lipid A	Hepta-acylated KDO(s)-lipid(A)
Cold-adapted KDO(2)-lipid A	(O16 antigen)x4 core oligosaccharide lipid A
Phthiocerol dimycoserate A	Phenol palmitic acid
Phenol phthiocerol dimycoserate A	Episterol ester
Ergosterol ester	Fecosterol ester
Lanosterol ester	Zymosterol ester

Table S5(g). Nutrients classified as "Sugars."

D-Glucose	Sucrose	D-Fructose
D-Ribose	D-Galactose	D-Mannose
Xylose	Glycogen	Cellobiose
Maltose	D-Arabinose	Lactose
L-Sorbose	L-Arabinose	L-Xylulose
Melitose	L-Rhamnose	β-D-Galactose
L-Fucose	Trehalose	D-Allose
L-Lyxose	Chitobiose	Palatinose
2'-Deoxyribose	Maltotriose	Maltohexaose
Maltotetraose	Melibiose	D-Psicose
Gentiobiose	Dextrin	Pectin
Starch	Amylose	1,3-β-D-Glucan
Arabinan	5'-Deoxyribose	Maltoheptaose
Maltopentaose		

Table S5(h). Nutrients classified as "Sugars related."

UDP-D-glucose	UDP-N-acetyl-D-glucosamine
UDP-galactose	L-Ascorbate
D-Fructose 6-phosphate	D-Glucose 6-phosphate
D-Glucose 1-phosphate	α-D-Ribose 5-phosphate
myo-Inositol	N-Acetyl-D-glucosamine
UDP-glucuronate	D-Glucuronate
UDP-N-acetyl-D-galactosamine	2-Dehydro-3-deoxy-D-gluconate
D-Gluconate	N-Acetylneuraminic acid
D-Mannose 6-phosphate	D-Glucosamine
D-Galacturonic acid	6-Phospho-D-gluconate
D-Glucosamine 6-phosphate	Xylitol
D-Mannitol	α-D-Galactopyranose 1-phosphate
L-Arabitol	D-Mannose 1-phosphate
2-Acetamido-2-deoxy-D-mannose	L-Idonate
L-Gulitol	D-Glucaric acid
D-Galactarate	D-Galactonic acid
D-Fructuronate	L-Gulono-1,4-lactone
5-Dehydro-D-gluconate	2-Acetamido-2-deoxy-D-galactose
Salicin	D-Galactitol
D-Gulitol	N-Acetylmuramate
Methylthio-D-ribose	D-Mannosamine
Methyl β-D-galactopyranoside	N-Acetyl-D-glucosamine 1-phosphate
D-Glucuronate 1-phosphate	Arbutin
2-Deoxy-D-glucose 6-phosphate	Amygdalin
α-Mannosylglycerate	L-Galactonate
N-Acetyl-D-galactosamine 1-phosphate	N-Acetyl-D-glucosamine w/ N-Acetylmuramate
Fructoselysine	Psicoselysine
α-Methyl-D-glucoside	β-Methylglucoside

Table S5(i). Nutrients classified as "Inorganic."

H_2O	O_2	HPO_4^{-2}
CO_2	$H_2O_7P_2^{-2}$	NH_4^+
H_2O_2	Mn^{+3}	Zn^{+2}
SO_4^{-2}	Cu^{+2}	Ca^{+2}
H^+	S	NO_2^-
SO_3^{-2}	Cl^-	Co^{+2}
CHN	CO	K^+
NO_3^-	H_2S	CHO_3^-
Ni^{+2}	Mg^{+2}	$O_3S_2^{-2}$
NO	$HO_{10}P_3$-4	N_2
Hg_2^+	$O_2.^-$	HN_2O
Na^+	Cd_2^+	CNO^-
HO_4As^{-2}	CNS	$O_9P_3^{-3}$
Pb	H_3O_3As	O_3P^{-3}
Ag	O_2S	Fe^{+2}
Fe^{+3}	MoO_4^{-2}	H_2O_4Cr
Sb	H_2	O_4W^{-2}

Table S5(j). Nutrients classified as "Amino acids."

L-Glutamate	Glycine	L-Alanine
L-Lysine	L-Aspartate	L-Arginine
L-Glutamine	L-Serine	L-Methionine
L-Tryptophan	L-Phenylalanine	L-Tyrosine
L-Cysteine	L-Leucine	D-Alanine
L-Histidine	L-Proline	L-Asparagine
L-Valine	L-Threonine	D-Glutamate
L-Isoleucine	D-Serine	D-Cysteine
D-Methionine		

Table S5(k). Nutrients classified as "Amino acids related."

Glutathione	L-Ornithine
Glutathione disulfide	1,4-Butanediamine
Agmatine	Chorismic acid
L-homoserine	Spermidine
L-Carnitine	L-Citrulline
Indole	Tyramine
L-Cystine	Shikimate
L-Cysteate	Cystathionine
PACT	Trimethylamine
Phenylacetaldehyde	Indoleacetaldehyde
4-Hydroxyphenylacetate	(3S)-3-Methyl-2-oxopentanoate
meso-2,6-Diaminoheptanedioate	Glycine betaine
Spermine	Indoleacetate
Indole-3-ethanol	O-Acetyl-L-serine
D-Ala-D-Ala	3-Phosphoserine
Trimethylamine N-oxide	Cys-Gly
Cadaverine	L-Pyroglutamic acid
D-O-Phosphoserine	L-Methionine S-Oxide
S-Methyl-L-Methionine	3,4-Dihydroxyphenethylamine
4-Hydroxyphenylacetaldehyde	3,4-Dihydroxyphenylacetaldehyde
Phenylethylamine	Phenylpropanoate
Phenylethyl alcohol	Phosphoarginine
Ectoine	Phosphonotyrosine
L-Djenkolic acid	Proline betaine
Dihydro-3-coumaric acid	L-Threonine O-3-phosphate
3-Hydroxycinnamic acid	MOPS
L-Methionine R-Oxide	Lanthionine
Gly-Glu	Gly-Asn
Ala-Thr	Ala-Leu
Ala-His	Ala-Gly
Ala-Glu	Ala-Gln
Pro-Gly	Gly-Asp
Met-Ala	Gly-Met
Gly-Glu	Ala-Asp
Arseno-betaine	Peptide
LalaDglu-meso-2,6-diaminoheptanedioate	LalaDglu-meso-2,6-diaminoheptanedioate-Dala
γ-Butyro-betaine	4-hydroxy-5-methyl-3-2H-furanone
L-Methionine-R-Sulfoxide	L-Methionine-S-Sulfoxide
Pro-Gly	N,N-Bisformyl-dityrosine

Table S5(l). Nutrients classified as "Organic compounds."

Pyruvate	α-Ketoglutarate	Acetate
Oxaloacetate	Succinate	Glyoxylate
Formate	Formalin	Phosphoenolpyruvate
Ethanal	Urea	3-Aminopropionate
Fumarate	Methyl alcohol	L-Malate
Citrate	Glycolate	Propionate
Acetoacetate	Carbamoyl-phosphate	Glycerone
(S)-Lactate	Aminoethanol	3-Phospho-DL-glycerate
Taurine	D-Lactate	(R)-Glycerate
Glycolaldehyde	Isocitrate	4-Aminobutyrate
O-Phosphorylethanolamine	Methanethiol	5-Aminolevulinate
(R)-Dimethylketol	Ethanol	Propionaldehyde
(R)-Malate	Allantoic acid	(CH3)2NH
meso-Tartarate	4-Aminobenzoate	D-Glyceraldehyde
Methyl sulfide	(S)-Propane-1,2-diol	2-Phospho-D-glycerate
2,3-Butanedione	D-Tartrate	(S)-2-Hydroxy-2-methyl-3-oxobutanoate
Phosphoglycolate	7-8-Diaminononanoate	8-Amino-7-oxononanoate
4-Trimethylammoniobutanoate	Methane	Oxamate
Allantoin	2-Propenamide	Mercaptoacetate
2-Methylbutanal	Saligenin	3-Carboxy-3-hydroxyisocaproate
(R)-Propane-1,2-diol	(R,R)-2,3-Butanediol	2-Hydroxyethanesulfonate
2-Hydroxybutyrate	Acetamide	2,3-Diaminopropionate
Aminoacetaldehyde	Isopentyl alcohol	Isovaleraldehyde
Dimethyl sulfoxide	Methanesulfonate	Crotono-betaine
Butyro-betaine	Isoamyl acetate	Phenethyl acetate
Sulfoacetic acid	Isobutyl alcohol	Hexanesulfonate
Ethanesulfonate	Butanesulfonate	3-Aminobutanoate
Acetyl ester	4-hydroxybenzyl alcohol	Monomethylamine
2-Methylbutyl acetate	2-Methyl-1-butanol	2-Methylpropanal
Isobutyl acetate		

Supplemental Table S6: Uptake of Sugars, Sugar derivatives, Fatty acids, and Bases.

The presence of a symbol indicates that a species uptakes the nutrient in question. The symbol type indicates whether the uptaken nutrient can be a source of carbon in the species in question: (✓) source of carbon, (x) not a source of carbon.

Table S6(a). Purines.

Name	*Bs*	*Ec*	*Mb*	*Sc*
Adenine	✓	✓		x
Guanine	✓	✓		x
Xanthine	✓	✓		x
Hypoxanthine	✓	✓		x
Urate	✓			

Table S6(b). Pyrimidines.

Name	*B. subtilis*	*E. coli*	*M barkeri*	*S. cerevisiae*
Uracil	x	x		x
Cytosine	x	x		x
Thymine	x	x		x
Orotate		x		

Table S6(c). Fatty acids.

Name	*B. subtilis*	*E. coli*	*M barkeri*	*S. cerevisiae*
Butanoate		✓		
Hexanoate		✓		
Octanoate		✓		
Decanoate		✓		x
Dodecanoate		✓		x
Tetradecanoate		✓		x
Tetradecenoate		✓		
Hexadecanoate		✓		x
Hexadecenoate		✓		x
Octadecanoate		✓		x
Octadecenoate		✓		x
Octadecynoate				x
Hexacosanoate				x

Table S6(d). Sugars.

Name	*B. subtilis*	*E. coli*	*M barkeri*	*S. cerevisiae*
D-Glucose	✓	✓		✓
D-Mannose	✓	✓		✓
D-Fructose	✓	✓		✓
D-Arabinose	✓			x
D-Galactose	✓	✓		✓
D-Allose		✓		
β-D-Galactose		✓		
D-Ribose	✓	✓		✓
2'-Deoxyribose	✓			
5'-Deoxyribose				
L-Fucose		✓		
L-Xylulose		✓		
L-Lyxose		✓		
L-Rhamnose	✓	✓		
L-Sorbose	✓			x
L-Arabinose	✓	✓		x
Sucrose	✓	✓		✓
Lactose	✓	✓		
Maltose	✓	✓		✓
Melibiose	✓	✓		✓
Trehalose	✓	✓		✓
Cellobiose	✓			
Palatinose	✓			
Chitobiose	x			
Glycogen	✓			
Melitose	✓			
Starch	✓			
Dextrin	✓			
Arabinan	✓			
Xylose	✓	✓		✓
Maltotriose	✓	✓		
Maltotetraose		✓		
Maltopentaose		✓		
Maltohexaose		✓		
Amylose		✓		
1,3-β-D-Glucan				✓
Pectin				x

Table S6(e). Sugar derivatives.

Name	*B. subtilis*	*E. coli*	*M barkeri*	*S. cerevisiae*
Xylitol				✓
L-Arabitol	✓			x
L-Gulitol	✓	✓		✓
D-Gulitol				x
D-Mannitol	✓	✓		
D-Galactitol	✓	✓		
α-D-Ribose 5-phosphate		✓		
D-Fructose 6-phosphate		✓		
D-Glucose 6-phosphate	✓	✓		
D-Glucose 1-phosphate	✓	✓		
D-Glucuronate 1-phosphate		✓		
D-Mannose 1-phosphate	✓			
D-Mannose 6-phosphate	✓	✓		
D-Glucosamine 6-phosphate	✓	✓		✓
α-D-Galactopyranose 1-phosphate		✓		
6-Phospho-D-gluconate	✓			
5-Dehydro-D-gluconate		✓		
2-Dehydro-3-deoxy-D-gluconate	✓	✓		
D-Gluconate	✓	✓	x	
D-Glucuronate	✓	✓		
D-Glucaric acid	✓	✓		
D-Glucosamine	✓	✓		
D-Fructuronate		✓		
D-Galactarate	✓	✓		
D-Galacturonic acid	✓	✓		x
D-Galactonic acid		✓		
L-Galactonate		✓		
L-Idonate		✓		
L-Ascorbate		✓		
myo-Inositol	✓	x		x
Methylthio-D-ribose	x			
α-Methyl-D-glucoside	✓			
β-Methylglucoside	✓			

Supplemental Table S7: G and NG nutrients in pathways considered for the logistic model.

The data in this table complements Figure S2.

Table S7. G and NG nutrients in candidate pathways.

Model	Pathway	G	NG	G^*	NG^*
1	Glyoxylate and dicarboxylate metabolism	13	2	13	2
2	Glycerolipid metabolism	10	1	8	1
3	Alanine, aspartate and glutamate metabolism	11	1	7	1
4	Glycolysis / Gluconeogenesis	9	2	6	2
5	Arginine and proline metabolism	14	5	7	4
6	Glycine, serine and threonine metabolism	12	5	7	5
7	Propanoate metabolism	6	2	4	2
8	Methane metabolism	6	5	3	4
9	Phenylalanine metabolism	7	9	3	8
10	Purine metabolism	5	1	2	0
11	Vitamin B6 metabolism	4	1	2	0
12	Butanoate metabolism	9	5	2	4
13	Pyruvate metabolism	9	4	1	1
14	Porphyrin and chlorophyll metabolism	4	1	1	0
15	Cysteine and methionine metabolism	7	12	1	10
16	Valine, leucine and isoleucine biosynthesis	2	11	0	8
17	Lysine degradation	1	5	0	5
18	Tyrosine metabolism	4	7	0	4
19	Taurine and hypotaurine metabolism	4	4	0	3
20	Phenylalanine, tyrosine and tryptophan biosynthesis	1	7	0	3
21	Biotin metabolism	0	3	0	2
22	Folate biosynthesis	0	4	0	1
23	beta-Alanine metabolism	2	5	0	1
24	Tryptophan metabolism	0	3	0	1
25	Glycerophospholipid metabolism	3	2	0	1

G^* and NG^* are the numbers of G and NG nutrients respectively that are not included in the previous pathways. For example, Cysteine and methionine metabolism only has one G nutrient out of seven that are not included in the previous 14 pathways.

Table S8. Coefficients for the logistic model.

Pathway	β
Constant (β_0)	−1.46
Alanine, aspartate and glutamate metabolism	3.84
Arginine and proline metabolism	1.78
Folate biosynthesis	−16.43
Glycerolipid metabolism	2.85
Glycine, serine and threonine metabolism	1.92
Glycolysis / Gluconeogenesis	1.78
Glyoxylate and dicarboxylate metabolism	2.49
Propanoate metabolism	3.18
Interaction	γ
Arginine and proline metabolism:β-Alanine metabolism	−3.15
Propanoate metabolism:Pantothenate and CoA biosynthesis	−3.33

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