Embden-Meyerhof glycolytic pathway and Gluconeogenesis

Group of Subsystems:

Subsystem: Embden-Meyerhof and Gluconeogenesis

Subsystem: Embden-Meyerhof and Gluconeogenesis in Archaea

Svetlana Gerdes and Ross Overbeek
Fellowship for Interpretation of Genomes

Introduction

Glycolysis (Embden-Meyerhof-Parnas pathway) is the most common sequence of reactions for the conversion of glucose-6-P into pyruvate in all domains of life. It generates ATP, reduced equivalents, and precursor metabolites for a multitude of essential cellular processes. During growth on substrates other then hexoses, essential glycolytic intermediates are synthesized via glyconeogenesis, reversion of EMP. While Glycolysis and glyconeogenesis are well-conserved in bacteria and eukaryotes, Archaea have developed unique variants of these pathways, presented in a separate subsystem. Striking examples of unique features of glycolytic pathways in archaea include: zero or very low ATP yields; reduction of ferredoxin rather than NADH; many unusual glycolytic enzymes, including ADP-dependent gluco- and phosphofructo- kinases, non-orthologous PGMs, FBAs, non-phosphorylating GAP dehydrogenases, etc. Notably, less variation is observed in glyconeogenic than in glycolytic enzymes. This may reflect the independent evolution of catabolic branches in bacteria and archaea diverging from originally glyconeogenic EMP pathway (refs. 2, 5) . Since studies of archaeal glycolytic pathways have started only in early 1990s, a large number of open questions (including "missing" enzymes) remains.

Out of ten enzymatic steps, which constitute classical EMP seven are reversible and work in glyconeogenesis as well. However, glycolytic reactions catalyzed by 6-phosphofructokinase, pyruvate kinase and some forms of glyceraldehyde 3-phosphate dehydrogenase are not reversible (shown in red in the following slides). They are bypassed during glyconeogenesis via specific glyconeogenic enzymes (shown in blue) or by utilizing alternative routes of central carbon metabolism. Multiple alternative forms of enzymes exist in various organisms for nearly every functional role in this central pathway. Each variant is cataloged independently: each column in a Subsystem spreadsheet in SEED contains members of a single protein family assigned with a specific function. Alternative forms of enzymes can be grouped into subsets of functional roles (marked with "*") by using "ignore alternatives" tool on a SS page in SEED.

Comparative analysis of complete genomes in SEED revealed endless variations in the implementation of this all too familiar pathway in different organisms; allowed to project the accumulated knowledge from well studied organisms to many others; led to identification of missing genes and other open questions.

Functional roles and alternative forms of enzymes

Functional roles essential for both - glycolysis and glyconeogenesis - are in black, irreversible glycolytic enzymes are in red, glyconeogenic enzymes are in blue. Functional roles shown in grey are not part of the subsystem per se, but were included to facilitated analysis of variations in subsystem implementation in different organisms (functional variants). Alternative forms of enzymes are grouped and marked with "*". Alternative forms of enzymes unique for Archaea are highlighted in grey (next slide)

I. Subsystem: Embden-Meyerhof and Gluconeogenesis

Column	Alternative forms	Abbrev	Functional roles
1	*glk	**GlcK**	Glucokinase (EC 2.7.1.2)
2		**HxK**	Hexokinase (EC 2.7.1.1)
3		**PPgK**	Polyphosphate glucokinase (EC 2.7.1.63)
4	*pgi	**Pgi**	Glucose-6-phosphate isomerase (EC 5.3.1.9)
5		**Pgi_a2**	Glucose-6-phosphate isomerase, archaeal II (EC 5.3.1.9)
6	*pfk	**Pfk1**	6-phosphofructokinase (EC 2.7.1.11)
7		**Pfk2**	6-phosphofructokinase class II (EC 2.7.1.11)
8		**PP-PFKa**	Pyrophosphate--fructose 6-phosphate 1-phosphotransferase, alpha subunit (EC
9		**PP-PFKb**	Pyrophosphate--fructose 6-phosphate 1-phosphotransferase, beta subunit (EC 2
10	*fbp	**FBP_I**	Fructose-1,6-bisphosphatase, type I (EC 3.1.3.11)
11		**FBP_X**	Fructose-1,6-bisphosphatase, GlpX type (EC 3.1.3.11)
12		**FBP_B**	Fructose-1,6-bisphosphatase, Bacillus type (EC 3.1.3.11)
13	*fba	**FBA1**	Fructose-bisphosphate aldolase class I (EC 4.1.2.13)
14		**FBA2**	Fructose-bisphosphate aldolase class II (EC 4.1.2.13)
15		**Tpi**	Triosephosphate isomerase (EC 5.3.1.1)
16	*gap	**GAPDH**	NAD-dependent glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.12)
17		**GAPDH(P)**	NAD(P)-dependent glyceraldehyde 3-phosphate dehydrogenase (EC 1.2.1.59)
18		**GAPDH_P**	NADP-dependent glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.13)
19		**G3PNP**	Non-phosphorylating glyceraldehyde-3-phosphate dehydrogenase (NADP) (EC
20		**PgK**	Phosphoglycerate kinase (EC 2.7.2.3)
21	*pgm	**PgM**	Phosphoglycerate mutase (EC 5.4.2.1)
22		**BiPgM**	2,3-bisphosphoglycerate-independent phosphoglycerate mutase (EC 5.4.2.1)
23		**EnO**	Enolase (EC 4.2.1.11)
24		**PyK**	Pyruvate kinase (EC 2.7.1.40)
25	*pps	**PpS**	Phosphoenolpyruvate synthase (EC 2.7.9.2)
26		**PpD**	Pyruvate,phosphate dikinase (EC 2.7.9.1)
27		**GPDH**	Glucose-6-phosphate 1-dehydrogenase (EC 1.1.1.49)
28		**GS**	Glycogen synthase (EC 2.4.1.21)

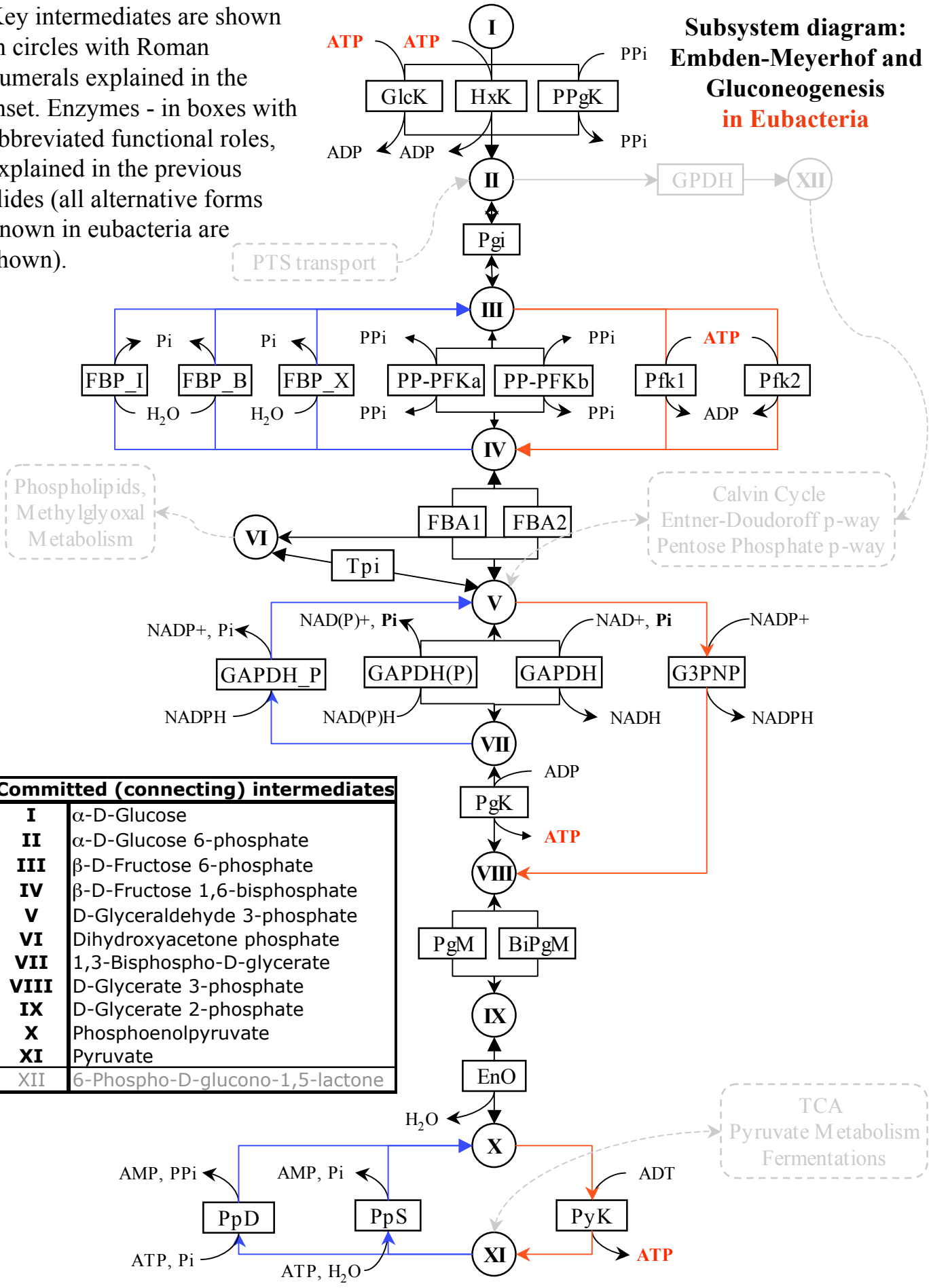
Functional roles and alternative forms of enzymes

II. Subsystem: Embden-Meyerhof and Gluconeogenesis Archaeal

Column	Alternative forms	Abbrev	Functional roles
1	*glk	**GlkD**	ADP-dependent glucokinase (EC 2.7.1.147)
2		**HxK**	Hexokinase (EC 2.7.1.1)
3	*pgi	**Pgi_a**	Glucose-6-phosphate isomerase, archaeal (EC 5.3.1.9)
4		**Pgi_a2**	Glucose-6-phosphate isomerase, archaeal II (EC 5.3.1.9)
5		**Pgi**	Glucose-6-phosphate isomerase (EC 5.3.1.9)
7	*pfk	**Pfk1**	6-phosphofructokinase (EC 2.7.1.11)
8		**Pfk2**	6-phosphofructokinase class II (EC 2.7.1.11)
6		**PfkD**	ADP-dependent phosphofructokinase (EC 2.7.1.146)
9		**PP-PFKa**	Pyrophosphate--fructose 6-phosphate 1-phosphotransferase, alpha subunit (EC
	*fbp	**FBP_I**	Fructose-1,6-bisphosphatase, type I (EC 3.1.3.11)
		FBP_X	Fructose-1,6-bisphosphatase, GlpX type (EC 3.1.3.11)
		FBP_IV	Fructose-1,6-bisphosphatase, type IV, archaeal (EC 3.1.3.11)
		FBP_V	Fructose-1,6-bisphosphatase, type V, archaeal (EC 3.1.3.11)
13		**FBA_A**	Fructose-bisphosphate aldolase, archaeal class I (EC 4.1.2.13)
14		**Tpi**	Triosephosphate isomerase (EC 5.3.1.1)
17	*gap	**GAPDH(P)**	NAD(P)-dependent glyceraldehyde 3-phosphate dehydrogenase archaeal (EC
15		**GAPOR**	Glyceraldehyde-3-phosphate: ferredoxin oxidoreductase (EC 1.2.7.6)
16		**G3PNPa**	Non-phosphorylating glyceraldehyde-3-phosphate dehydrogenase (NAD)
18		**PgK**	Phosphoglycerate kinase (EC 2.7.2.3)
20	*pgm	**PgM**	Phosphoglycerate mutase (EC 5.4.2.1)
21		**BiPgM**	2,3-bisphosphoglycerate-independent phosphoglycerate mutase (EC 5.4.2.1)
19		**BiPgM_A**	2,3-bisphosphoglycerate-independent phosphoglycerate mutase, archaeal type
22		**EnO**	Enolase (EC 4.2.1.11)
23		**Pyk**	Pyruvate kinase (EC 2.7.1.40)
24	*pps	**PpS**	Phosphoenolpyruvate synthase (EC 2.7.9.2)
25		**PpD**	Pyruvate,phosphate dikinase (EC 2.7.9.1)
26		**GDH**	Glucose 1-dehydrogenase (EC 1.1.1.47)

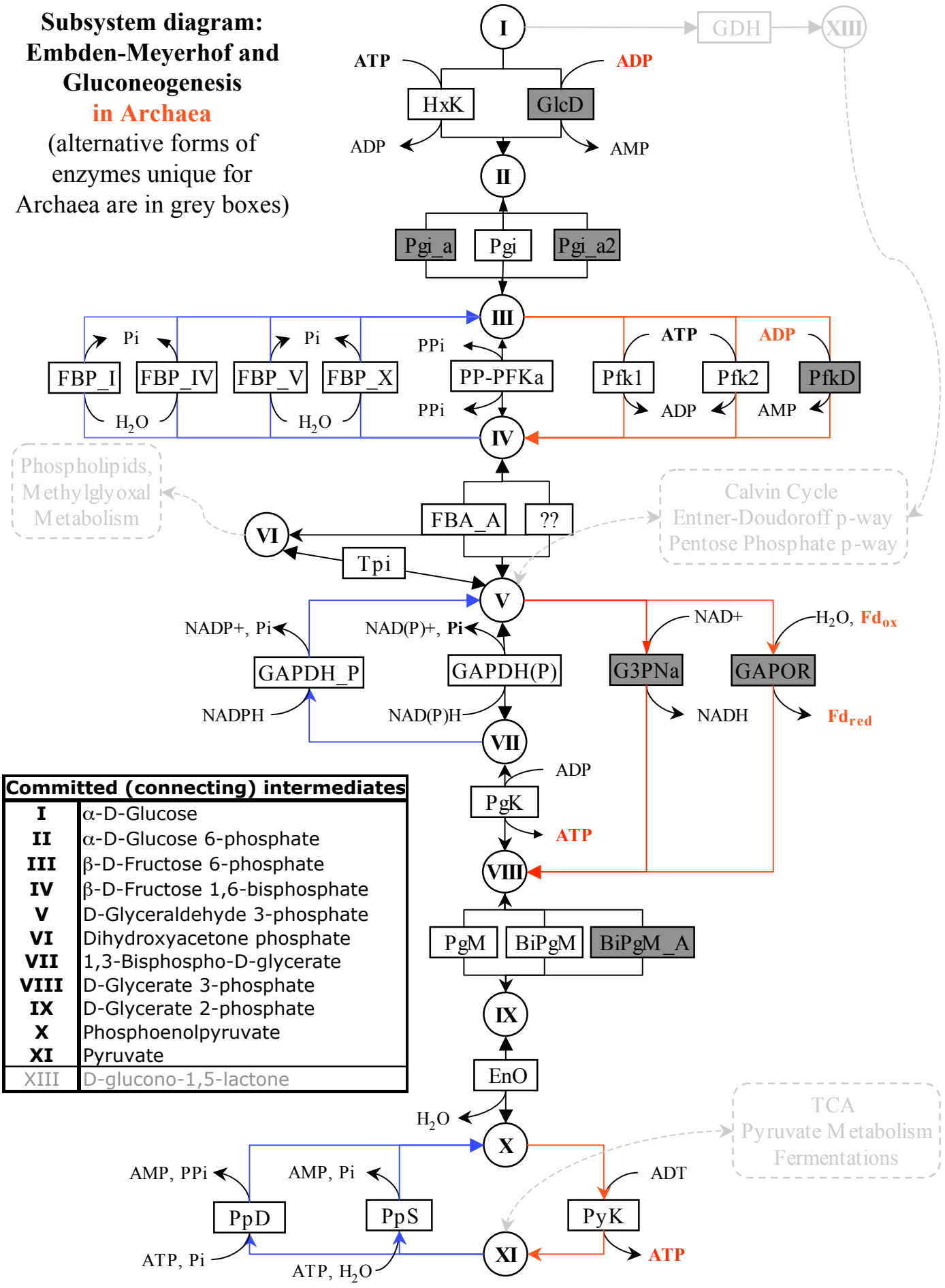
Key intermediates are shown in circles with Roman numerals explained in the inset. Enzymes - in boxes with abbreviated functional roles, explained in the previous slides (all alternative forms known in eubacteria are shown).

Subsystem diagram: Embden-Meyerhof and Gluconeogenesis in Eubacteria



Committed (connecting) intermediates	
I	α-D-Glucose
II	α-D-Glucose 6-phosphate
III	β-D-Fructose 6-phosphate
IV	β-D-Fructose 1,6-bisphosphate
V	D-Glyceraldehyde 3-phosphate
VI	Dihydroxyacetone phosphate
VII	1,3-Bisphospho-D-glycerate
VIII	D-Glycerate 3-phosphate
IX	D-Glycerate 2-phosphate
X	Phosphoenolpyruvate
XI	Pyruvate
XII	6-Phospho-D-glucono-1,5-lactone

Subsystem diagram:
Embden-Meyerhof and Gluconeogenesis
in Archaea
(alternative forms of enzymes unique for Archaea are in grey boxes)



Committed (connecting) intermediates	
I	α-D-Glucose
II	α-D-Glucose 6-phosphate
III	β-D-Fructose 6-phosphate
IV	β-D-Fructose 1,6-bisphosphate
V	D-Glyceraldehyde 3-phosphate
VI	Dihydroxyacetone phosphate
VII	1,3-Bisphospho-D-glycerate
VIII	D-Glycerate 3-phosphate
IX	D-Glycerate 2-phosphate
X	Phosphoenolpyruvate
XI	Pyruvate
XIII	D-glucono-1,5-lactone

SS: Embden-Meyerhof pathway and Gluconeogenesis in Archaea

Subsystem spreadsheet (fragment). Multipositional encoding of functional variants (appearing in **Variant code** column) is described in the last slide. Missing genes inferred by the functional context analysis are shown by "?". Several functional roles (marked with "*") aggregate two or more alternative enzyme families (as defined in slide 3). The occurrence of a specific form in an organism is shown by a role numbers (shown in black font), corresponding to those in slide 3. Cells within the same row highlighted by a matching color contain genes located in close vicinity of each other (clustering on the chromosome).

Organism	Variant Code	*glk	*pgi	*pfk	*fbp	FBA_A	Tpl	*gap	PgK	*pgm	EnO	PyK	*pps	GDH
Nanoarchaeum equitans Kin4-M [A]	-1													
Methanothermobacter thermautotrophicus str. Delta H [A]	9914*				1652-11	?	1031	968-16, 999-17	1032	1558-19, 416-19	41		1101-24, 458-24	
Methanopyrus kandleri AV19 [A]	9914*				950-11	?	1660	1104-16, 616-17	1658	1189-19	1643		252-24	
Archaeoglobus fulgidus DSM 4304 [A]	9*9*11*	?	1484-5	?	1432-11	?	1294	1721-17	1134	1415-19, 1740-19	1120		703-24	
Sulfolobus solfataricus P2 [A]	9914		2076-4		258-11	2954	2349	2925-16, 481-17	480	2038-20, 378-19	828	888	801-24, 2564-24	2739, 2776, 2934
Sulfolobus tokodaii str. 7 [A]	9914		2414-4		352-11	2518	2186	2646-16, 1477-17	1478	2283-20, 416-19	1312	1754	764-24, 1336-24	1845
Organism	**Variant Code**	***glk**	***pgi**	***pfk**	***fbp**	**FBA_A**	**Tpl**	***gap**	**PgK**	***pgm**	**EnO**	**PyK**	***pps**	**GDH**
Picrophilus torridus DSM 9790 [A]	1911*	1216-2	1226-4		807-11	?	348	742-17	1514	1271-19	1234	336	1519-24	1070, 639
Ferroplasma acidarmanus [A]	1911*	895-2	126-4		77-11	?	826	138-17	1891	1242-20, 417-19	61	745	1173-24	1190, 769
Halobacterium sp. NRC-1 [A]	1914	2212-2	1709-5		713-10	712	977	904-16, 257-17	1123	1627-21	1064	435	439-24	526
Haloarcula marismortui ATCC 43049 [A]	1911	530-2	2908-5		1065-10, 728-10	355	520	2078-17	2170	2597-20, 3080-21	104	529	1663-24	859
Methanococcoides burtonii DSM 6242 [A]	3311*	2595-1	923-5	2596-6	2612-12	?	2243	308-17	2602	2147-20, 1943-19, 1545-21	1253	1912	136-25	
Pyrococcus furiosus DSM 3638 [A]	3314	318-1	199-3	1834-6	628-11	2008	1970	476-15, 779-16, 1923-17	1094	2011-19	1689, 218	1229	43-24	
Methanocaldococcus jannaschii DSM 2661 [A]	3314	1651-1	1652-5	1651-6	309-11	1631	1573	1216-15, 1451-16, 1175-17	662	1659-19, 10-19	240	109	558-24	
Organism	**Variant Code**	***glk**	***pgi**	***pfk**	***fbp**	**FBA_A**	**Tpl**	***gap**	**PgK**	***pgm**	**EnO**	**PyK**	***pps**	**GDH**
Aeropyrum pernix K1 [A]	1114	1486-2	587-4	9-7	827-11	8	1116	1273-16, 126-17	127	1166-19	1731	382	18-24, 498-24, 17-24	
Methanosarcina mazei Go1 [A]	3311	472-1	1968-5	473-6	2181-12	714	1278	2782-17	485	2993-20, 1418-19, 904-21	2836	715	2723-24, 1770-25	

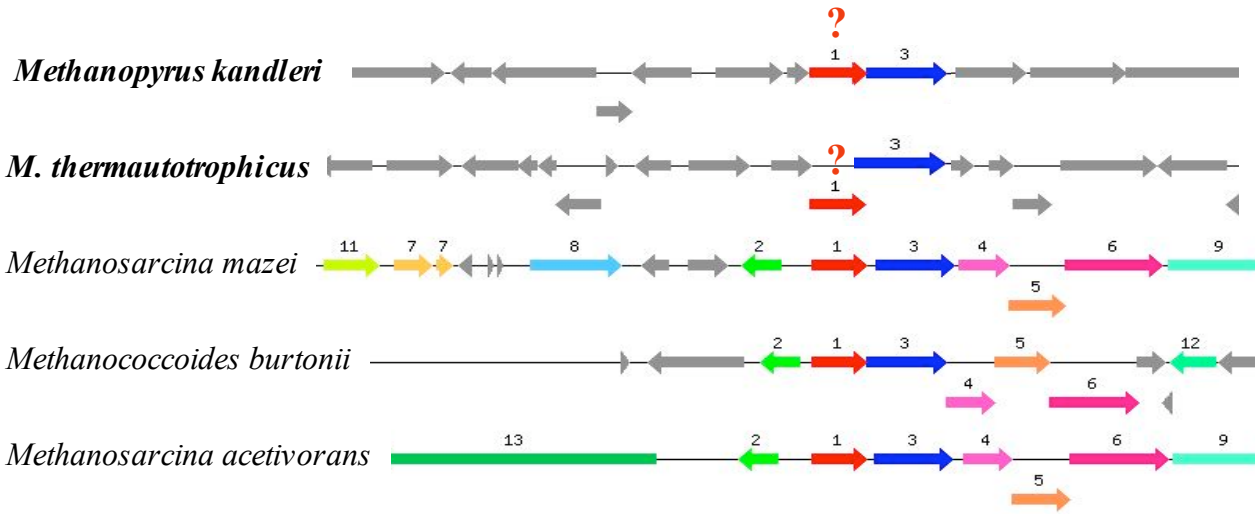
Open questions and comments

A number of "missing" genes (marked with a star in the **variant code**) still remain in archaeal variants of the EMP in spite the great progress achieved in the last decade in unraveling archaeal central carbon metabolism.

Missing Glk: Glucokinases are "missing" enzymes in several saccharolytic archaea, which lack a potential bypass (glucose 1-dehydrogenase, GDH, canalizing glucose into non-phosphorylating Entner-Doudoroff), and hence are expected to contain functional Glk, including: *Archaeoglobus fulgidus*, *Methanococcus maripaludis* (variant codes [9*___])

Missing PFK: in the majority of these organisms the presence of GDH, catalyzing the first step of alternative pathways of glucose catabolism indicates that archaeal non-phosphorylating Entner-Doudoroff is utilized in place of glycolysis. This is apparently the case in: *Ferroplasma acidarmanus, Picrophilus torridus, Halobacterium sp. NRC-1, Haloarcula marismortui*, *Sulfolobus* sp. and *Thermoplasma* sp. The absence of both enzymes - Pfk and GDH in an organism is characteristic of autotrophs *Methanopyrus kandleri and Methanothermobacter thermautotrophicus*, unable to utilize hexoses and apparently lacking internal glycogen cycle (accumulating cyclic 2,3-Diphosphoglycerate instead). On the other hand, Pfk is expected to be present, but is not found ("missing" gene) in genomes of *Pyrobaculum aerophilum* and *Archaeoglobus fulgidus* (variant codes [_9*__]).

Missing FBA: Archaea have their own class I FBA, unrelated to bacterial FBA I on the sequence level, but with the same Shiff base mechanism. FBA homologs are missing from the genomes of *Pyrobaculum aerophilum, Ferroplasma acidarmanus, Thermoplasma acidophilum and Thermoplasma volcanium*, *Picrophilus torridus* DSM 9790. In addition, in the following genomes none of the "aldolase of the DhnA family" homologs, albeit present, were annotated as FBA: *Archaeoglobus fulgidus DSM 4304*, *Methanopyrus kandleri* AV19, *Methanothermobacter thermautotrophicus*. These proteins appear to be phospho-2-dehydro-3-deoxyheptonate aldolases, rather then FBAs - based on (i) the strong clustering with other chorismate biosynthesis genes and on (ii) the absence of all other known types of phospho-2-dehydro-3-deoxyheptonate aldolase in these genomes. They are currently annotated in SEED as "Alternative step 1 of chorismate biosynthesis"



Clustering of the putative adolase homologs with enzymes of chorismate biosynthesis in selected archaeal genomes. Alignment of the chromosomal contigs of respective genomes around the homologs of the query ORF MK1409 (red arrow, #1). Homologous genes are shown by arrows with matching colors and numbers as follows: (1) Alternative step 1 of chorismate biosynthesis, (3) 3-dehydroquinate synthase (EC 4.2.3.4), (4) 3-dehydroquinate dehydratase (EC 4.2.1.10), (5) Shikimate 5-dehydrogenase (EC 1.1.1.25), (6) Prephenate dehydrogenase (EC 1.3.1.12). Genes not conserved within the cluster are colored grey.

SS: Embden-Meyerhof pathway and Gluconeogenesis in Eubacteria

Examples of subsystem variants, open questions, and comments

Variant code: 1113

Organism	Variant Code	*glk	*pgi	*pfk	*fbp	*fba	Tpi	*gap	PgK	*pgm	EnO	PyK	*pps	GPDH
Bacillus anthracis str. Ames [B]	1113	4140-1	4744-4	4475-6	4806-12, 5161-12	5164-14	4968	4970-16, 4458-17 793-19	4969	4967-22	4966	4474, 3096	2869-25	3145

Classic variant of glycolysis and glyconeogenesis, complete set of functional roles in both directions with several represented by alternative enzymes. Notably, two distinct GAPDHs, NAD-dependent (role #16) and NAD(P)H-dependent (role #17), catalyze glyceraldehyde-3P ←→ 1,3-bisP-glycerate conversion in the opposite directions. This is often the case in organisms with functional Calvin cycle, but has been recently demonstrated (Fillinger et al., 2000) in nonphotosynthetic bacteria, e.g. Bacillus as well. In addition, *B. anthracis* contains non-phosphorylating G3PNP (role # 19) which catalyses irreversible oxidation of glyceraldehyde-P to glycerate-3P in the direction of glycolysis (no ATP is produced).

Variant code: -1

Organism	Variant Code	*glk	*pgi	*pfk	*fbp	*fba	Tpi	*gap	PgK	*pgm	EnO	PyK	*pps	GPDH
Rickettsia prowazekii str. Madrid E [B]	-1												472-26	

An extreme, rare case of complete absence of glycolytic and glyconeogenic enzymes. Intracellular pathogen with minimal genome relying entirely on the host for energy and anabolic precursors. Surprising presence of pyruvate, phosphate dikinase (EC 2.7.9.1).

Variant code: 1911

Organism	Variant Code	*glk	*pgi	*pfk	*fbp	*fba	Tpi	*gap	PgK	*pgm	EnO	PyK	*pps	GPDH
Helicobacter pylori J99 [B]	1911	1024-1	1088-4		1436-10	161-14	179	1261-16	1260	904-22	141		110-25	1022

Functional glyconeogenesis can be asserted, but not the EMP (due to the absence of PGK). The presence of glucose-6-phosphate 1-dehydrogenase (GPDH, included in this SS) catalyzing the first step of alternative pathways of glucose catabolism indicates that Entner-Doudoroff and/or Pentose Phosphate pathways are used in place of glycolysis. This is apparently the case in all species of *Neisseria, Bordetella, Bifidobacterium,* and *Pseudomonas* where genome sequence data are available, and other microorganisms

Variant code: 99110

Organism	Variant Code	*glk	*pgi	*pfk	*fbp	*fba	Tpi	*gap	PgK	*pgm	EnO	PyK	*pps	GPDH
Helicobacter hepaticus ATCC 51449 [B]	9911**		491-4		1344-10	106-14	1315	1157-16, 492-16	327	1169-22	631		1824-25	

Functional glyconeogenesis can be asserted, but the absence of GPDH in addition to PGK renders an organism non-glycolytic. This is likely the case in: all *Bordetella* species, *Campylobacter jejuni, Acinetobacter sp., Psychrobacter sp.*, etc.

Variant code: 9271

Organism	Variant Code	*glk	*pgi	*pfk	*fbp	*fba	Tpl	*gap	PgK	*pgm	EnO	PyK	*pps	GPDH
Chlamydophila pneumoniae J138 [B]	9271		1021-4	160-9, 208-9		281-13	1059	621-16	676	861-21	798	97		238

In this case, in spite the absence of any known form of FBP, both - glycolysis and glyconeogenesis can be asserted, due to the presence of Pyrophosphate--fructose 6-phosphate 1-phosphotransferase (role #9, PPi-PFK). Since PPi-PFK is capable of catalyzing the reverse reaction (Deng et al, 1999), it can also act in gluconeogenesis. This is the case in all *Chlamydophila, Borrelia, Treponema* species with genome sequences available to date.

Missing FBP?

Organism	Variant Code	*glk	*pgi	*pfk	*fbp	*fba	Tpl	*gap	PgK	*pgm	EnO	PyK	*pps	GPDH
Streptococcus pyogenes MGAS315 [B]	1193	1180-1	156-4	913-6	?	1630-14	433	201-16, 1045-19	1624	1090-21	479	912		
Xylella fastidiosa Ann-1 [B]	1191	875-1	1375-4	1651-6	?	1095-13	1676	829-16	1093	2023-21	381	1094	689-25	876

Variant code [**9*]: In a number of organisms gluconeogenesis appears to be incomplete due to the absence of all known types of FBP: *Propionibacterium acnes, Clostridium perfringens, Ureaplasma parvum*, all sequenced species of *Streptococcus* and *Xylella fastidiosa*. This implies either the presence of a novel non-orthologous FBP variant in these organisms, or the existence of yet unknown compensating pathway, or strict dependency on exogenous carbohydrates for essential anabolic precursors, which is a possible scenario in these pathogenic organisms.

Gene candidates for the missing functional role: distant homologs of archaeal Fructose-1,6-bisphosphatase, type IV, archaeal (EC 3.1.3.11) / Inositol-1- monophosphatase (EC 3.1.3.25) (ref 6) can be identified in these genomes. Glycolytic pathway appears functional.

Missing FBA

Organism	Variant Code	*glk	*pgi	*pfk	*fbp	*fba	Tpl	*gap	PgK	*pgm	EnO	PyK	*pps	GPDH
Desulfotalea psychrophila LSv54 [B]	1181	1060-1	796-4	1909-6	1666-11	FBA_A	100	822-16	101	2472-22	1799	3116	1368-26	
Geobacter sulfurreducens PCA [B]	1111	1691-1	1302-4	2055-6, 1692-6	1640-10	?	1617	1618-16	1617	1601-21, 3186-22	2273, 71	3309	798-25, 576-26	

FBA is essential for both, EMP and glyconeogenesis. It is still a "missing" gene in the genomes of *Geobacter sulfurreducens* PCA (finished to one contig) and *Geobacter metallireducens* (unfinished), where an otherwise complete set of EMP/glyconeogenetic genes can be asserted. No clear homologs of any known forms of FBA (including archaeal) can be identified in these genomes. On the other hand, *Desulfotalea psychrophila*, missing all forms of bacterial FBA, contains Fructose-bisphosphate aldolase, archaeal class I ortholog.

Variant codes used in the two Subsystems

[-1]: the majority of enzymes are absent, no functional EMP or glyconeogenesis can be asserted

First digit in a multipositional variant code reflects the type of sugar kinase catalyzing formation of glucose-6-P in an organism:

[1___] = an ATP-dependent hexo- or glucokinase(s) is present
[3___] = an ADP-dependent glucokinase is present
[8___] = different types of kinases (ADP - ATP- , or PPi-dependent) can be assertred
[9___] = no sugar kinase could be identified.

Second digit reflects a type of 6-phosphofructokinase (Pfk) present:

[_1__] = ATP-dependent Pfk is present (one or several types)
[_2__] = PPi-dependent Pfk is present. ATP yield of glycolysis is higher in this case.
[_3__] = an ADP-dependent Pfk is present
[_8__] = different types of kinases (ADP - ATP- , or PPi-dependent) can be asserted
[_9__] = no ortholog of known PFKs can be detected in a genome.

Third digit reflects the presence/ absence of some form of Fructose-1,6-bisphosphatase (FBP):

[__1_] = a clear ortholog of at least one form of FBP is present
[__8_] = several FBPs of different types are present (redundancy)
[__9_] = no FBP can be detected in a genome.

Fourth digit reflects a type of glyceraldehyde 3-phosphate dehydrogenase (GAPDH) present:

[___1] = a single universal GAPD(P)H acts in both directions - in glycolysis and glyconeogenesis
[___2] = two distinct GAPDHs with different cofactor requirements catalyze glyceraldehyde-3P <-> 1,3-bisP-glycerate conversion in opposite directions.
[___3] = as #2, but non-phosphorylating G3PNP catalyses irreversible oxidation of G3P in the direction of glycolysis. No ATP is produced in this reaction.
[___4] = in archaea: GAPDHs catalyze 1,3-bisP-glycerate → glyceraldehyde-3P conversion in glyconeogenesis, while GAPOR or/and G3PNPa catalyze irreversible oxidation of glyceraldehyde-P to glycerate-3P in the direction of glycolysis. No ATP is produced in this reaction.

References

1. T. Dandekar, S. Schuster, B. Snel, M. Huynen, and P. Bork. 1999. Pathway alignment: application to the comparative analysis of glycolytic enzymes. Biochem. J. 343, 115–124
2. Verhees CH, Kengen SW, Tuininga JE, Schut GJ, Adams MW, De Vos WM, Van Der Oost J. 2003. The unique features of glycolytic pathways in Archaea. Biochem J. 375:231-46.
3. Iddar A, Serrano A, and Soukri A. 2002. A phosphate-stimulated NAD(P)+-dependent glyceraldehyde-3-phosphate dehydrogenase in Bacillus cereus. FEMS Microbiol Lett. 211(1):29-35.
4. Fillinger et al, 2000. Two GAPDHs with opposite physiological roles in a nonphotosynthetic bacterium . JBC 275(19): 14031-37
5. Ronimus RS, Morgan HW. 2003. Distribution and phylogenies of enzymes of the Embden-Meyerhof-Parnas pathway from archaea and hyperthermophilic bacteria support a gluconeogenic origin of metabolism. Archaea 1(3):199-221. Review.
6. Stec, B., Yang, H., Johnson, K. A., Chen, L. and Roberts, M. F. 2000. MJ0109 is an enzyme that is both an inositol monophosphatase and the 'missing' archaeal fructose-1,6-bisphosphatase. Nat. Struct. Biol. 7, 1046–1050

Due to the space constrains only a small fraction of relevant references could be listed here, many others are quoted as links on the corresponding PEG pages.