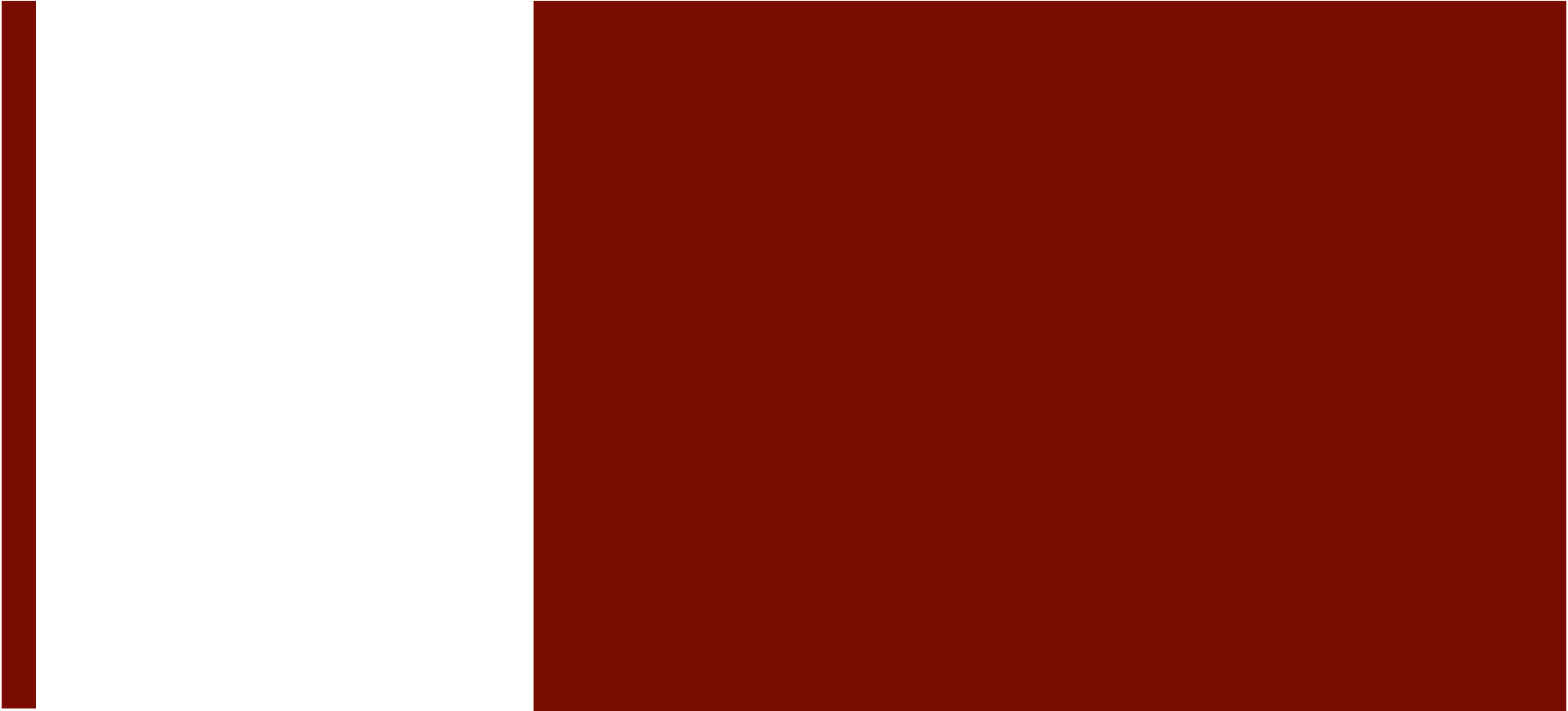
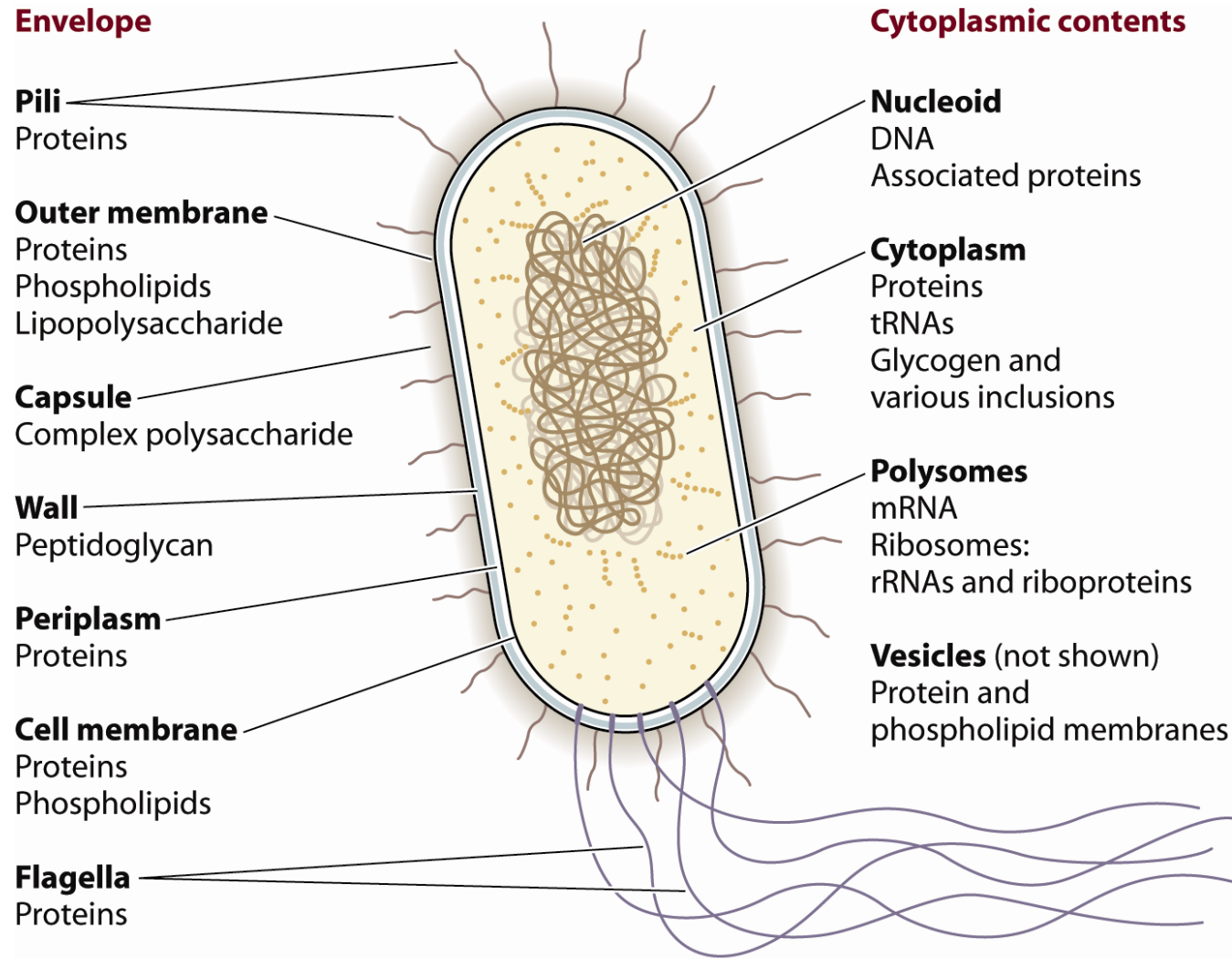




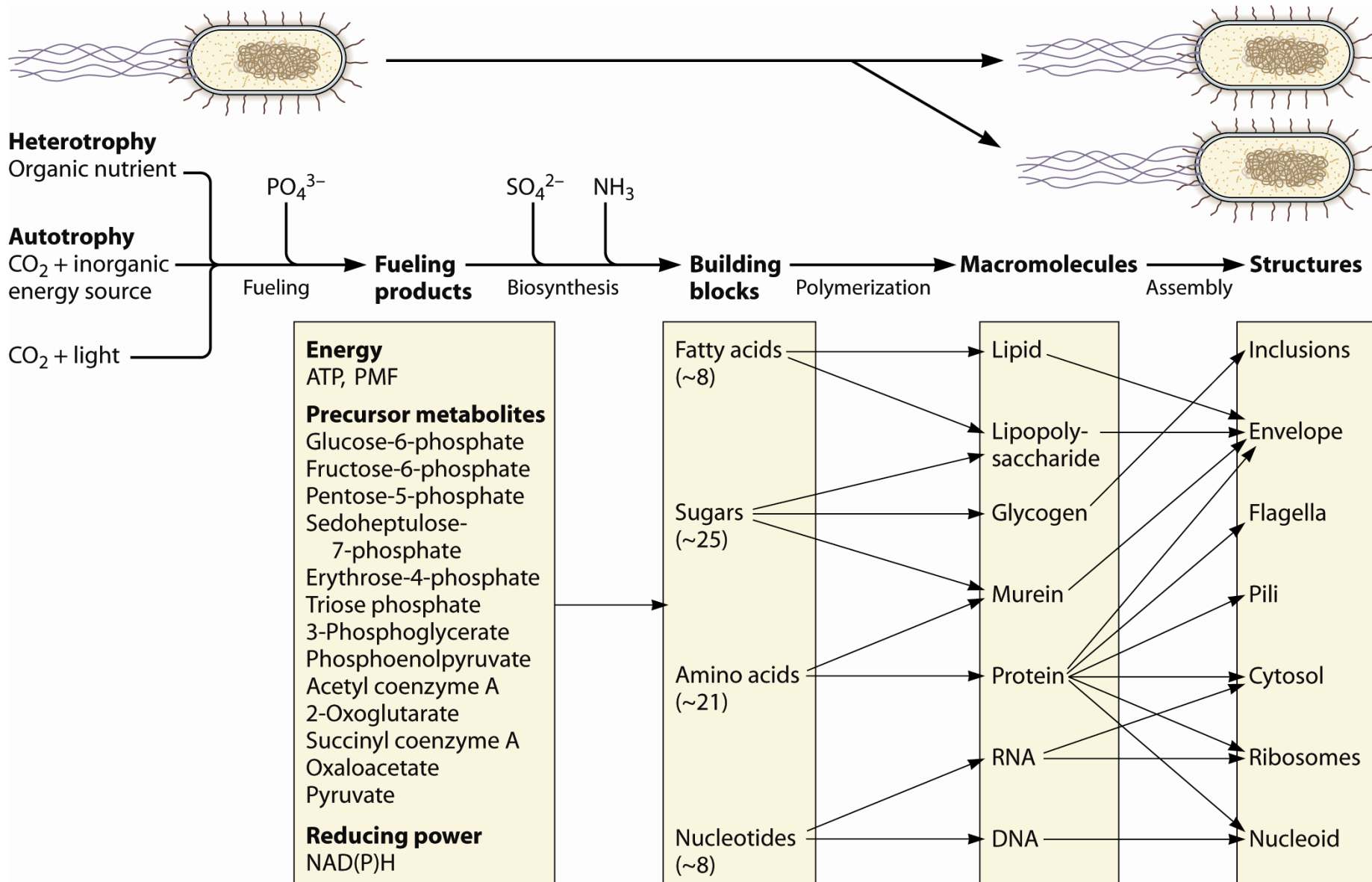
Metabolismo I:

Metabolismo heterotrófico

Como fazer uma célula bacteriana?

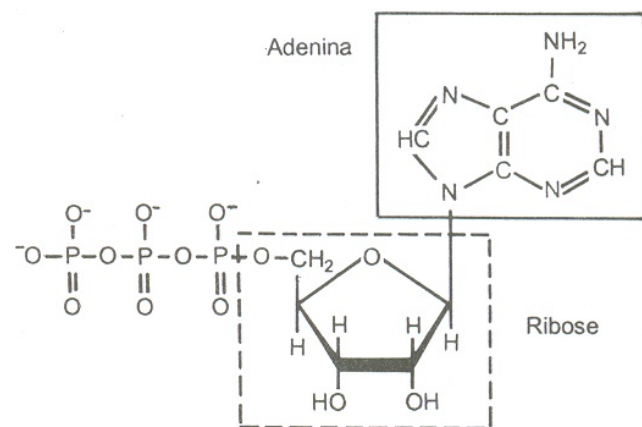


O que é metabolismo?

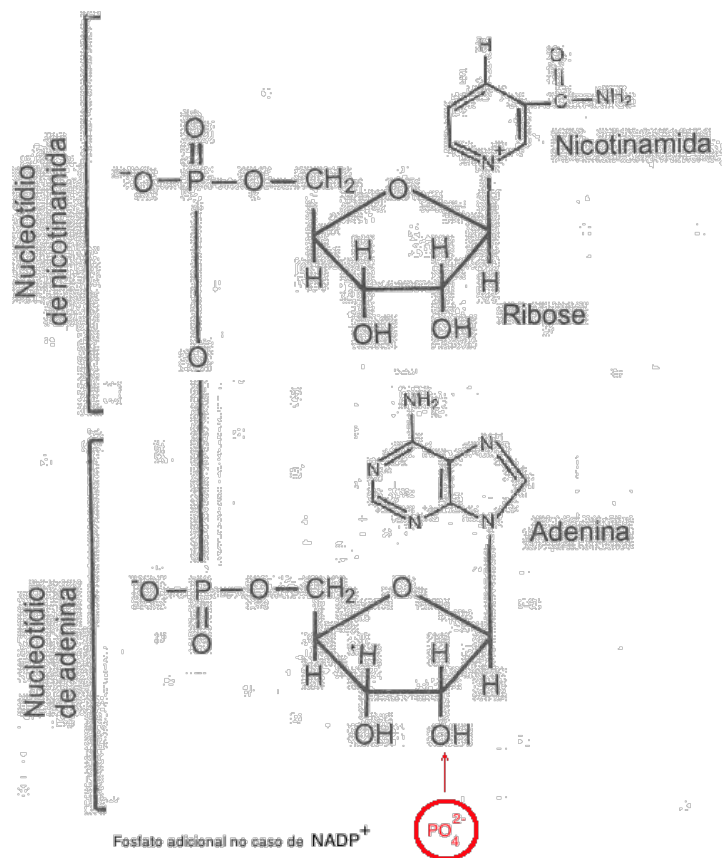


Destino dos precursores

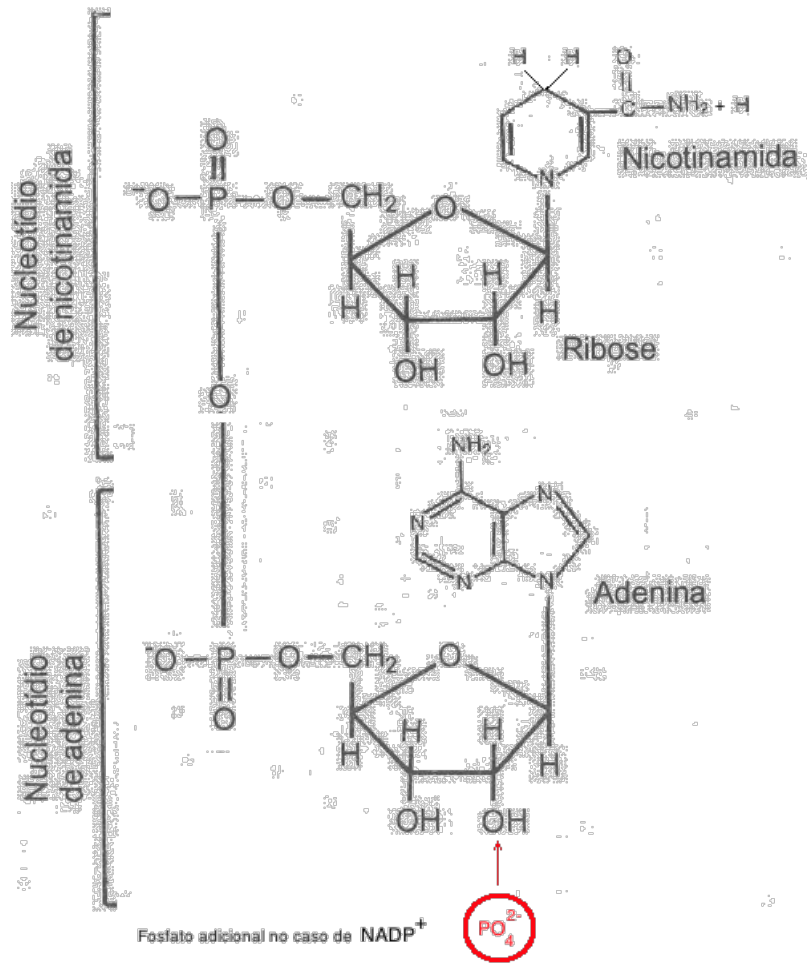
Nome	Estrutura	Precusores de:
1. Glicose-6-fosfato		Polímeros de carboidratos
2. Frutose-6-fosfato		<i>N</i> -acetilglicosamina, ácido <i>N</i> -acetilmurâmico, mureína
3. Ribose-5-fosfato		Ácidos nucleicos, histidina
4. Eritrose-4-fosfato		Aminoácidos aromáticos
5. Sedoheptulose-7-fosfato		Polímeros de carboidratos/polissacarídeos
6. Triose-fosfato		Precursor de dihidroxiacetona, lipídios
7. 3-fosfoglicerato		Aminoácidos da família da serina
8. Fosfoenolpiruvato		Aminoácidos aromáticos
9. Piruvato		Aminoácidos
10. Acetil-CoA		Lipídios
11. α-cetoglutarato		Aminoácidos da família do glutamato
12. Oxaloacetato		Aminoácidos da família do aspartato
13. Succinil-CoA		Heme



ATP



NADP⁺



NADPH

A célula bacteriana deve satisfazer três necessidades básicas:

- Energia
- 13 precursores
- Poder redutor
- ATP
- Intermediários do metabolismo de Carbono
- NADPH

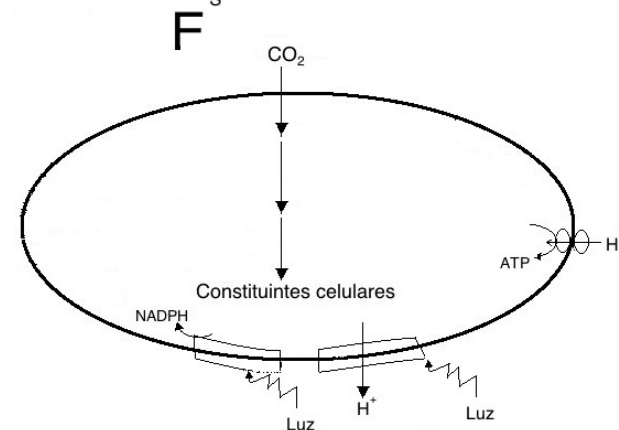
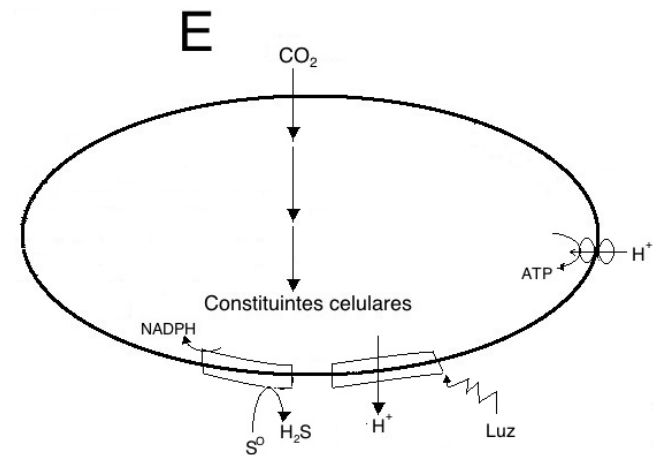
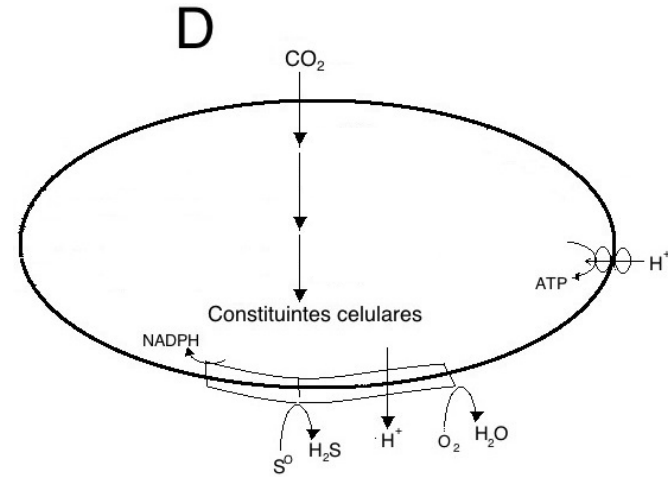
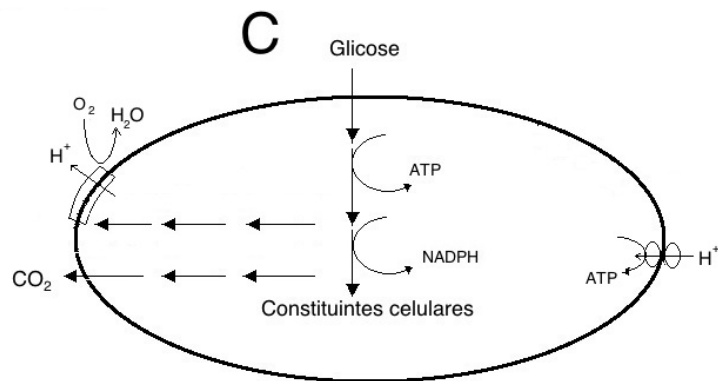
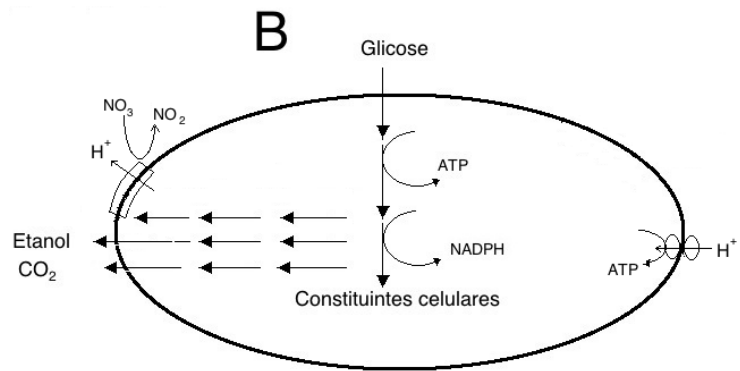
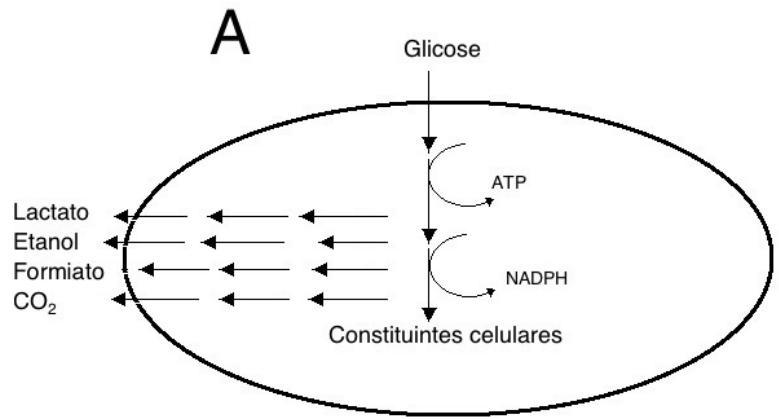
Diferentes estratégias de sobrevivência

- Vias metabólicas
- Processos metabólicos
 - Objetivo: obter ATP, precursores e poder redutor

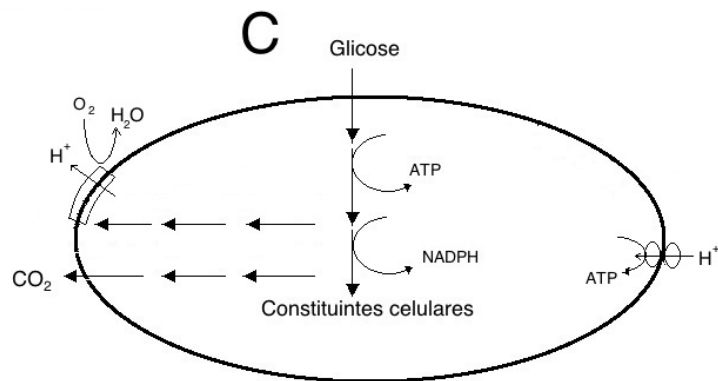
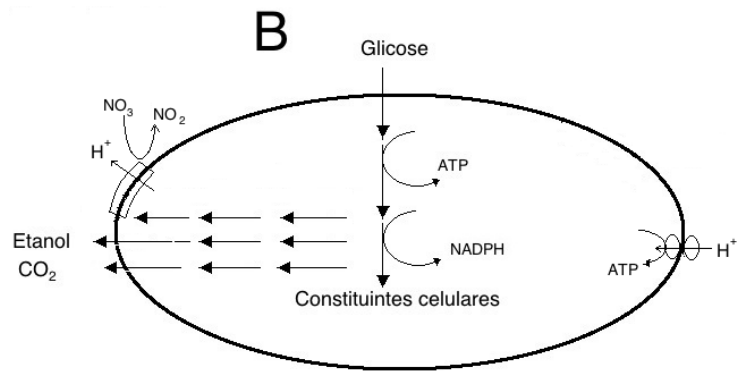
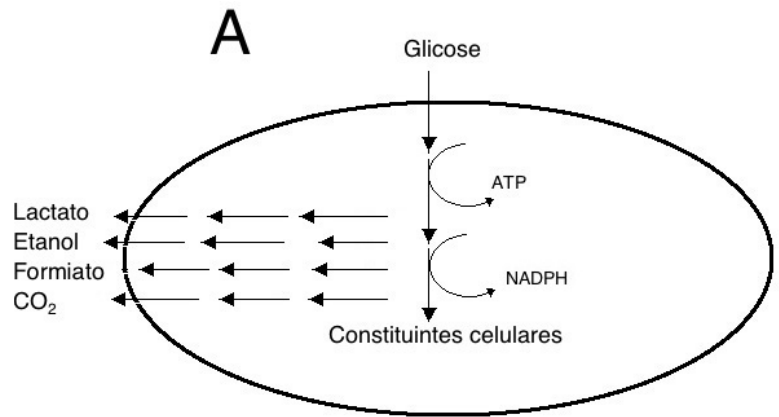
O que é metabolismo?

Heterotróficos

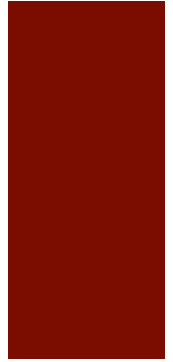
Autotróficos



Heterotróficos



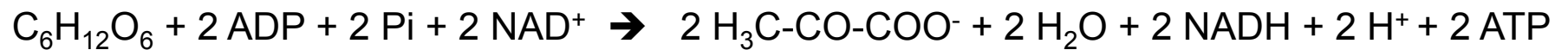
Metabolismo heterotrófico



- Obtenção dos 13 precursores

Glicólise

via de Embden-Meyerhof-Parnas (EMP)

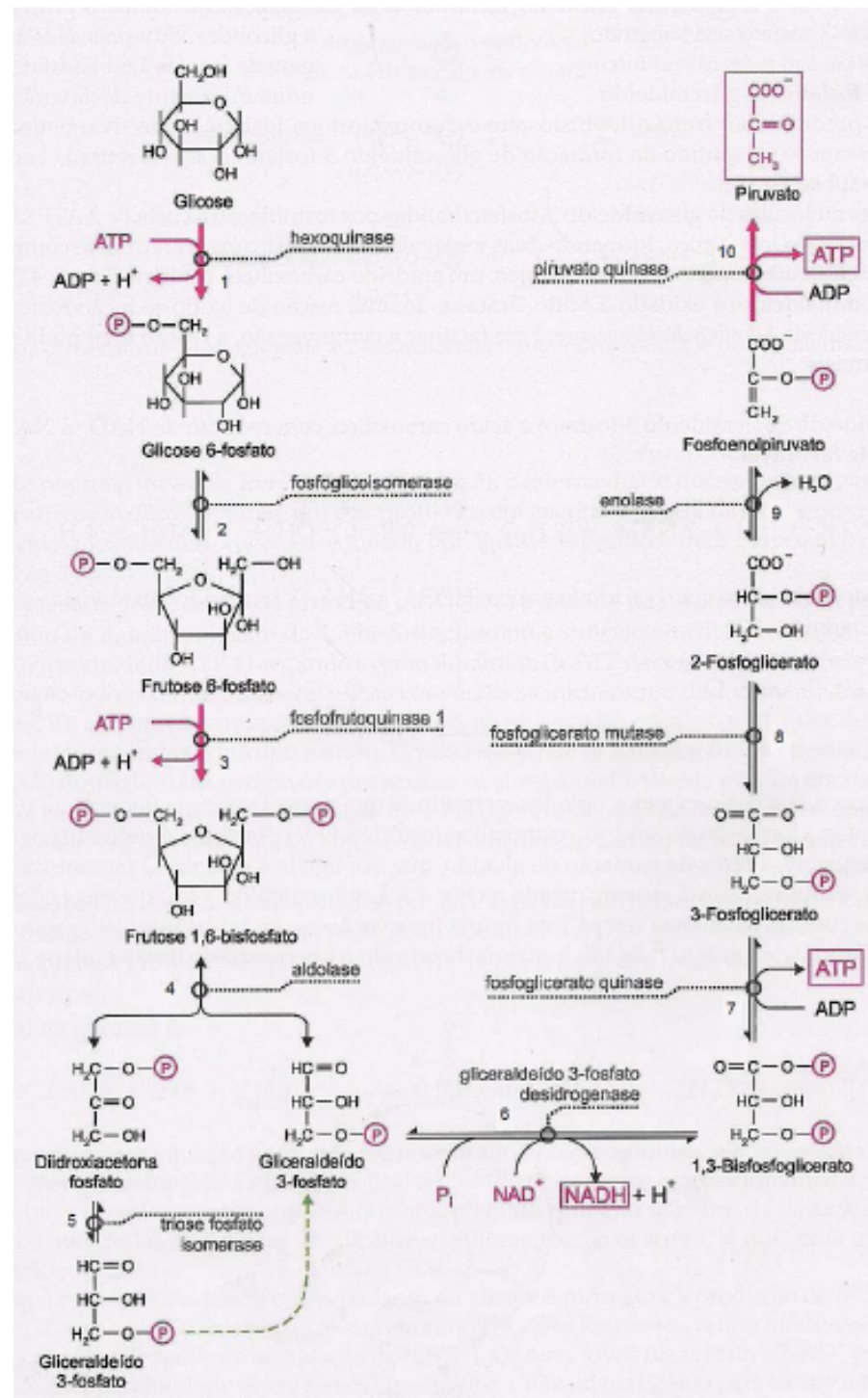


Glicose

Piruvato

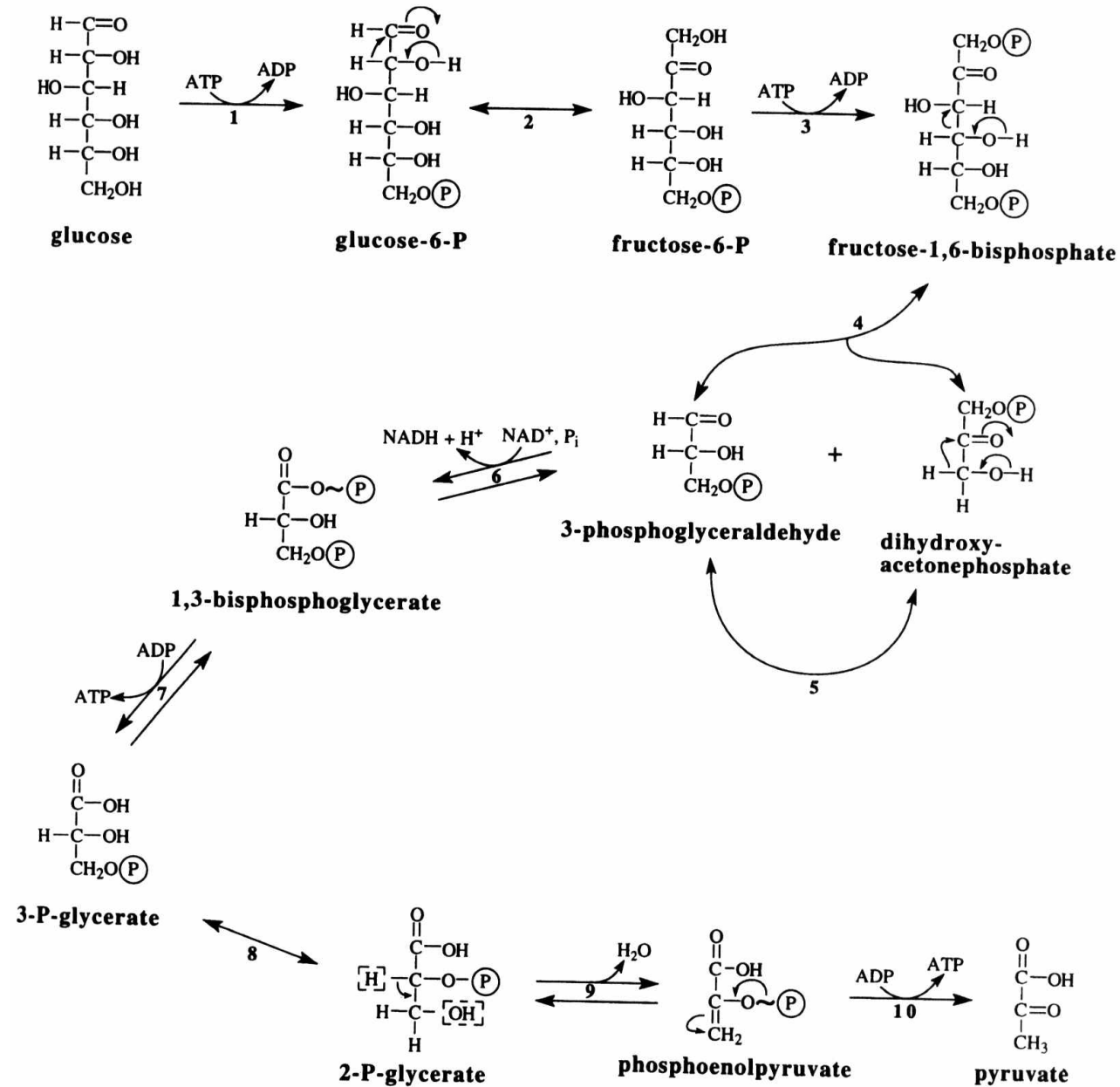
Uma célula bacteriana pode crescer fazendo exclusivamente a EMP?

EMP



ATP
NAD(P)H
Glicose-6-fosfato
Frutose-6-fosfato
Ribose-5-fosfato ou ribulose-5-fosfato
Eritrose-4-fosfato
Sedoheptulose-7-fosfato
Gliceraldeído-3-fosfato
3-Fosfoglicerato
Fosfoenolpiruvato
Piruvato
Acetil-CoA
Oxaloacetato
α-cetoglutarato
Succinil-CoA

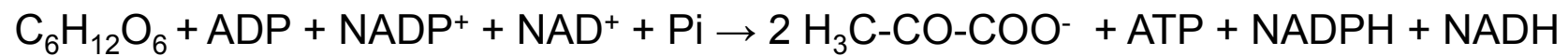
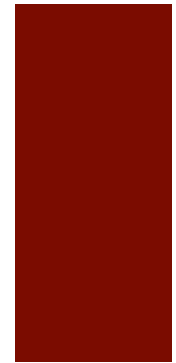
EMP



ATP
NAD(P)H
Glicose-6-fosfato
Frutose-6-fosfato
Ribose-5-fosfato ou ribulose-5-fosfato
Eritrose-4-fosfato
Sedoheptulose-7-fosfato
Gliceraldeído-3-fosfato
3-Fosfoglicerato
Fosfoenolpiruvato
Piruvato
Acetil-CoA
Oxaloacetato
α-cetoglutarato
Succinil-CoA

Metabólito	Via predominante de origem do metabólito*			
	EMP			
ATP	X			
NAD(P)H	-			
Glicose-6-fosfato	X			
Frutose-6-fosfato	X			
Ribose-5-fosfato ou ribulose-5-fosfato	-			
Eritrose-4-fosfato	-			
Sedoheptulose-7-fosfato	-			
Gliceraldeído-3-fosfato	X			
3-Fosfoglicerato	X			
Fosfoenolpiruvato	X			
Piruvato	X			
Acetil-CoA	-			
Oxaloacetato	-			
α -cetoglutarato	-			
Succinil-CoA	-			

Via de Entner-Doudoroff



Glicose

Piruvato

Uma célula bacteriana pode crescer fazendo ED?

Via de Entner-Doudoroff

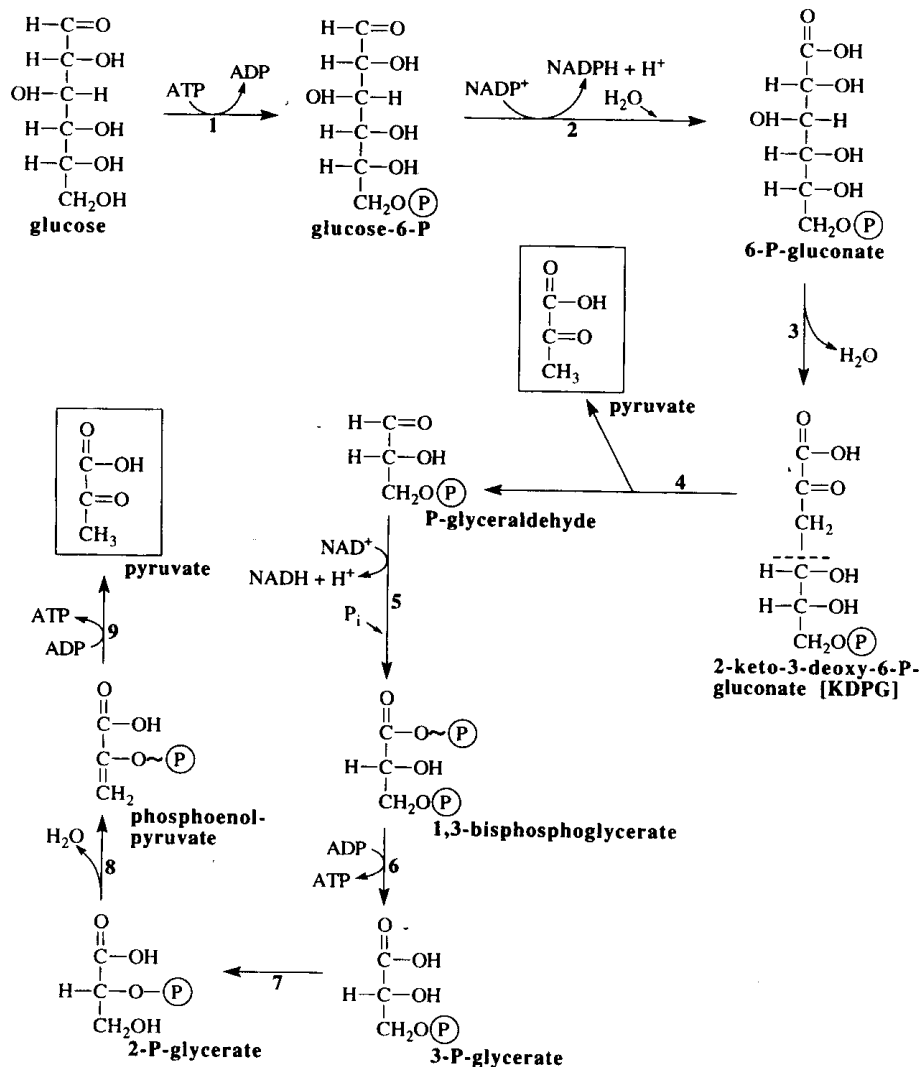
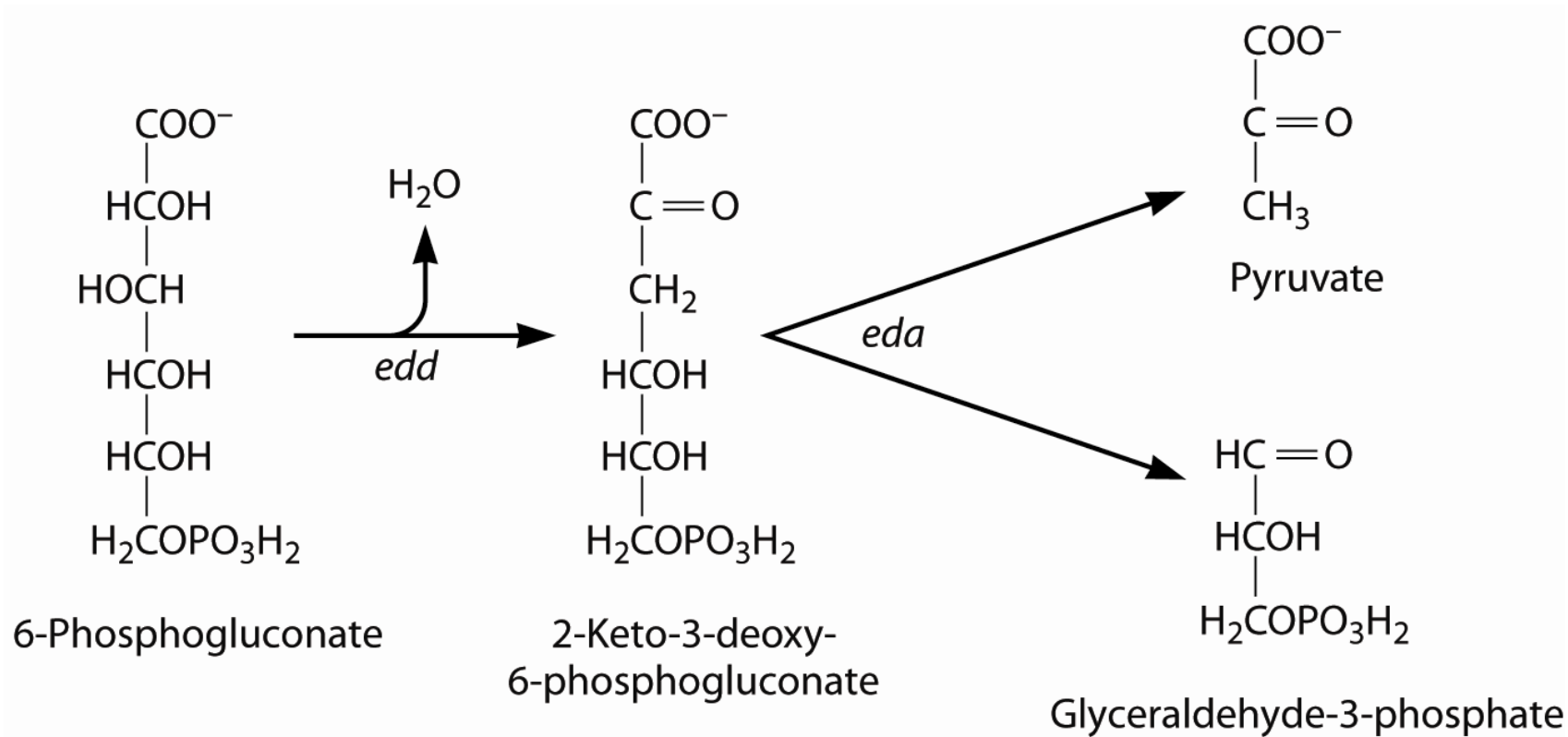


Fig. 8.12 The Entner-Doudoroff pathway. Because there is only one PGALD formed, there is only one ATP made. The enzymes unique to this pathway are the 6-phosphogluconate dehydratase (reaction 3) and the KDPG aldolase (reaction 4). The other enzymes are present in the pentose phosphate pathway and the glycolytic pathway. Enzymes: 1, hexokinase; 2, glucose-6-phosphate dehydrogenase; 3, 6-phosphogluconate dehydratase; 4, KDPG aldolase; 5, triose phosphate dehydrogenase; 6, PGA kinase; 7, mutase; 8, enolase; 9, pyruvate kinase.

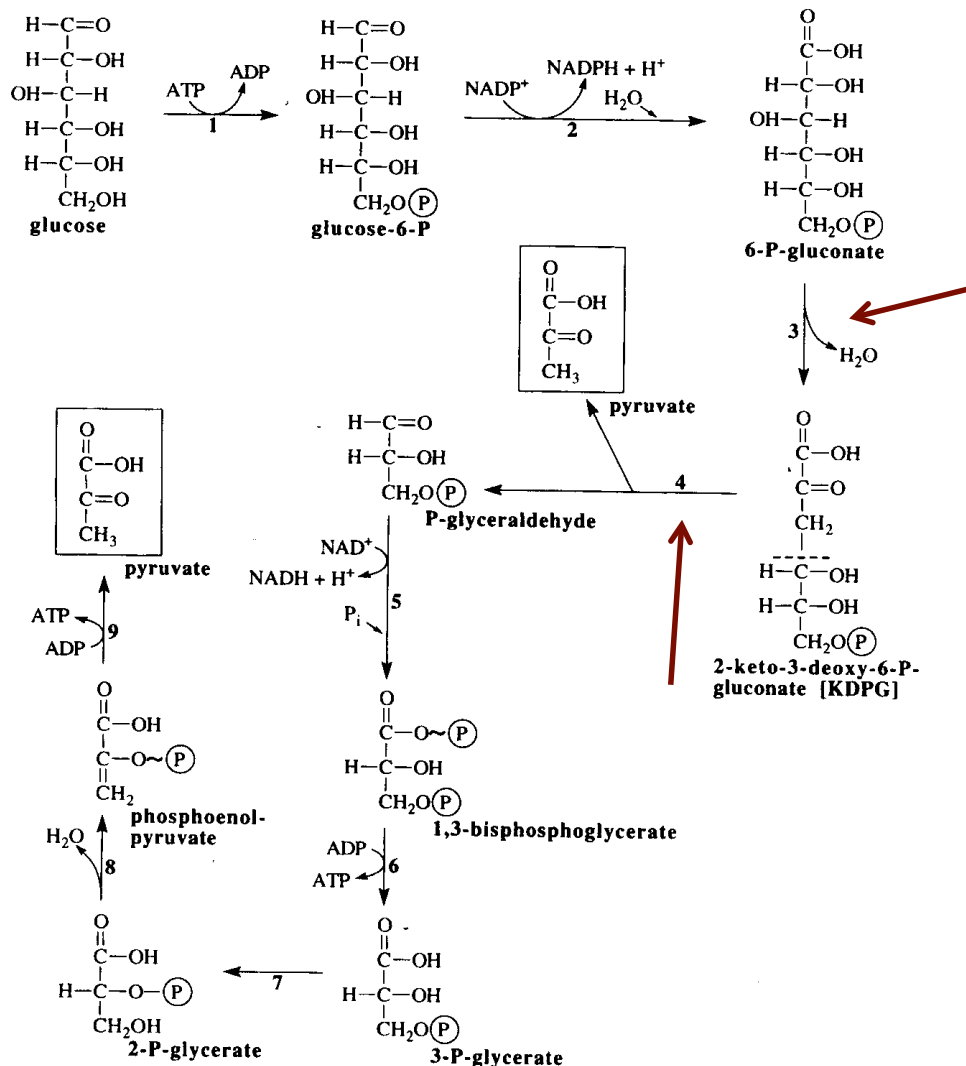
Via de Entner-Doudoroff



Reações específicas de ED

Via de Entner-Doudoroff

ED



ATP
NAD(P)H
Glicose-6-fosfato
Frutose-6-fosfato
Ribose-5-fosfato ou ribulose-5-fosfato
Eritrose-4-fosfato
Sedoheptulose-7-fosfato
Gliceraldeído-3-fosfato
3-Fosfoglicerato
Fosfoenolpiruvato
Piruvato
Acetil-CoA
Oxaloacetato
α -cetoglutarato
Succinil-CoA

Presença das vias Embden-Meyerhof-Parnas e Entner-Doudoroff em algumas bactérias

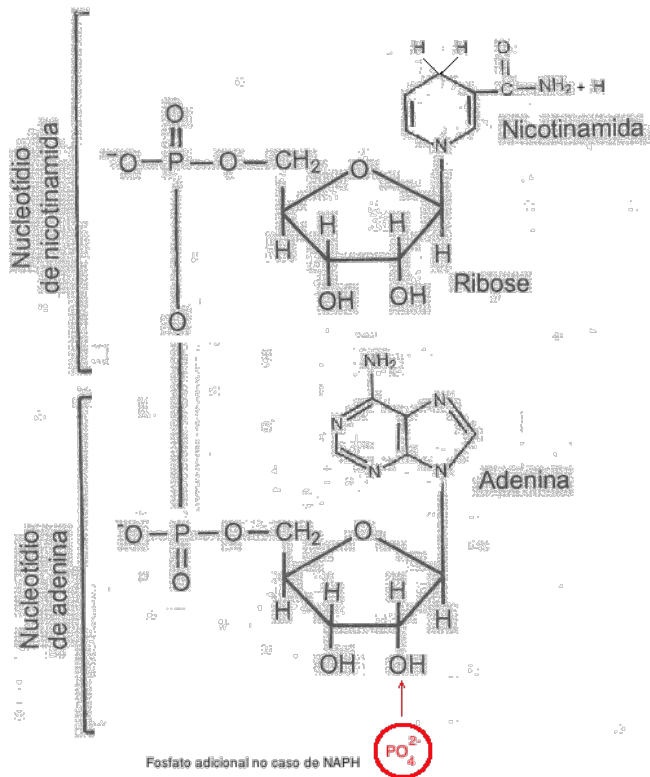
Organismo	EMP	ED
<i>Ralstonia eutropha</i>	-	+
<i>Pseudomonas aeruginosa</i>	-	+
<i>Pseudomonas saccharophila</i>	-	+
<i>Escherichia coli</i>	+	-/+*
<i>Xanthomonas phaseoli</i>	-	+
<i>Bradyrhizobium japonicum</i>	-	+
<i>Azotobacter choococcum</i>	+	-
<i>Bacillus subtilis</i>	+	-
<i>Arthrobacter sp</i>	+	-

**E. coli* somente expressa as enzimas de Entner-Doudoroff quando cresce em gliconato

Fig. 8.12 The Entner-Doudoroff pathway. Because there is only one PGALD formed, there is only one ATP made. The enzymes unique to this pathway are the 6-phosphogluconate dehydratase (reaction 3) and the KDPG aldolase (reaction 4). The other enzymes are present in the pentose phosphate pathway and the glycolytic pathway. Enzymes: 1, hexokinase; 2, glucose-6-phosphate dehydrogenase; 3, 6-phosphogluconate dehydratase; 4, KDPG aldolase; 5, triose phosphate dehydrogenase; 6, PGA kinase; 7, mutase; 8, enolase; 9, pyruvate kinase.

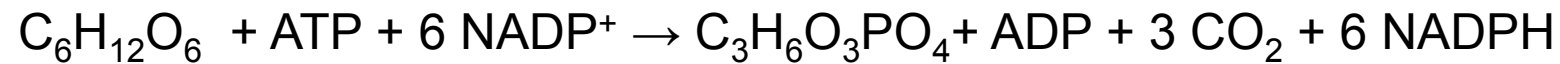
Metabólito	Via predominante de origem do metabólito*			
	EMP	ED		
ATP	X	X		
NAD(P)H	-	X		
Glicose-6-fosfato	X	X		
Frutose-6-fosfato	X	-		
Ribose-5-fosfato ou ribulose-5-fosfato	-	-		
Eritrose-4-fosfato	-	-		
Sedoheptulose-7-fosfato	-	-		
Gliceraldeído-3-fosfato	X	X		
3-Fosfoglicerato	X	X		
Fosfoenolpiruvato	X	X		
Piruvato	X	X		
Acetil-CoA	-	-		
Oxaloacetato	-	-		
α -cetoglutarato	-	-		
Succinil-CoA	-	-		

ED gera NADPH
Há outras fontes de NADPH?



Como obter NADPH?

Via das pentoses



Glicose

gliceraldeído-3-fosfato

Uma célula bacteriana pode crescer fazendo VP?

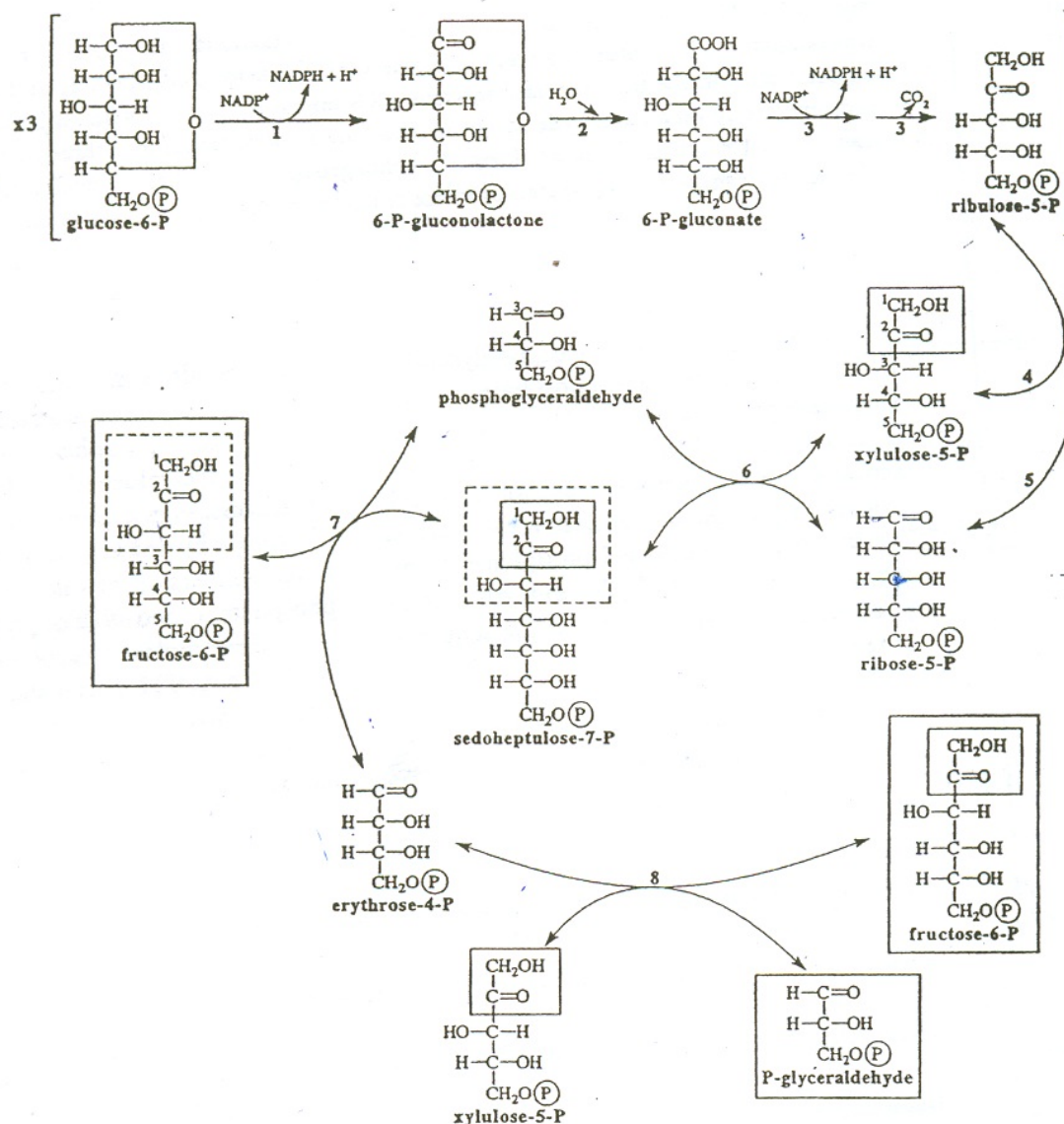


Fig. 8.11 The pentose phosphate pathway. Enzymes: 1, glucose-6-phosphate dehydrogenase; 2, lactonase; 3, 6-phosphogluconate dehydrogenase; 4, ribulose-5-phosphate epimerase; 5, ribose-5-phosphate isomerase; 6, 8, transketolase; 7, transaldolase. The two-carbon moiety transferred by the transketolase is shown in the boxed area. The three-carbon fragment transferred by the transaldolase is shown in the dashed box. The product of the glucose-6-phosphate dehydrogenase reaction is the lactone, which is unstable and hydrolyzes spontaneously to the free acid. However, there exists a specific lactonase that catalyzes the reaction.

ATP
NAD(P)H
Glicose-6-fosfato
Frutose-6-fosfato
Ribose-5-fosfato ou ribulose-5-fosfato
Eritrose-4-fosfato
Sedoheptulose-7-fosfato
Gliceraldeído-3-fosfato
3-Fosfoglicerato
Fosfoenolpiruvato
Piruvato
Acetil-CoA
Oxaloacetato
α -cetoglutaratato
Succinil-CoA



Metabólito	Via predominante de origem do metabólito*		
	EMP	ED	VP
ATP	X	X	-
NAD(P)H	-	X	X
Glicose-6-fosfato	X	X	X
Frutose-6-fosfato	X	-	X
Ribose-5-fosfato ou ribulose-5-fosfato	-	-	X
Eritrose-4-fosfato	-	-	X
Sedoheptulose-7-fosfato	-	-	X
Gliceraldeído-3-fosfato	X	X	X
3-Fosfoglicerato	X	X	-
Fosfoenolpiruvato	X	X	-
Piruvato	X	X	-
Acetil-CoA	-	-	-
Oxaloacetato	-	-	-
α -cetoglutarato	-	-	-
Succinil-CoA	-	-	-

*EMP – via de Embden Meyerhof Parnas; VP- via das pentoses ED- via de Entner -Doudoroff

Via da Fosfocetolase

(Hexose monofosfato)



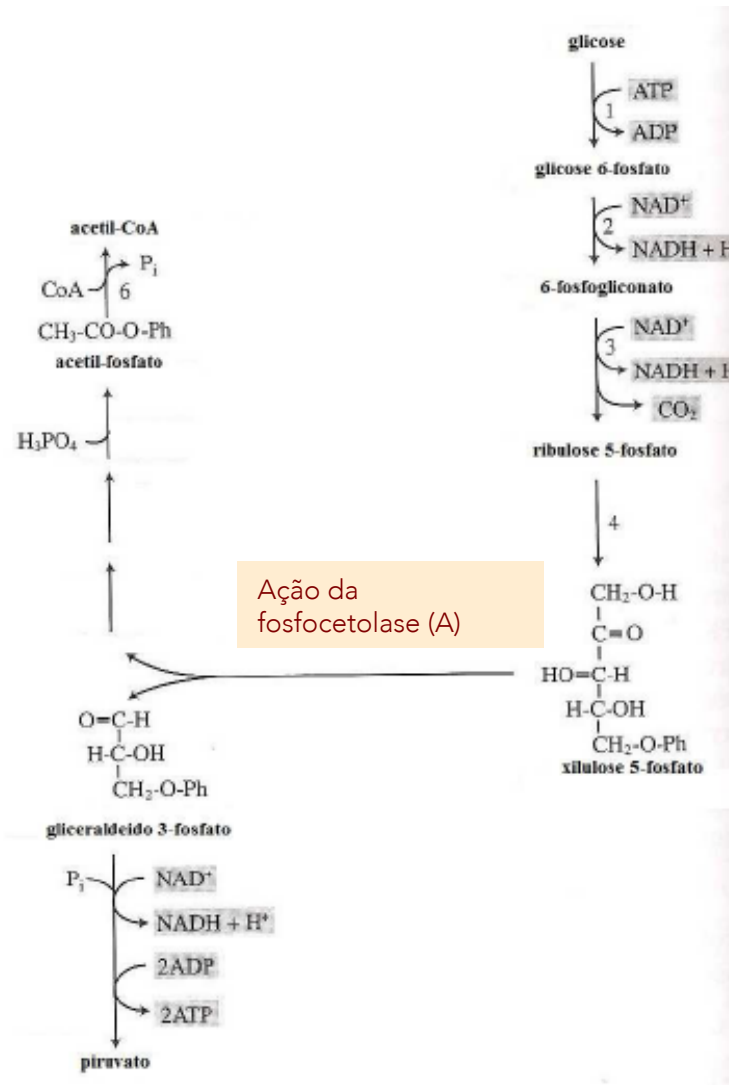
Uma célula bacteriana pode crescer fazendo VF?

Via da Fosfocetolase

Hexose monofosfato

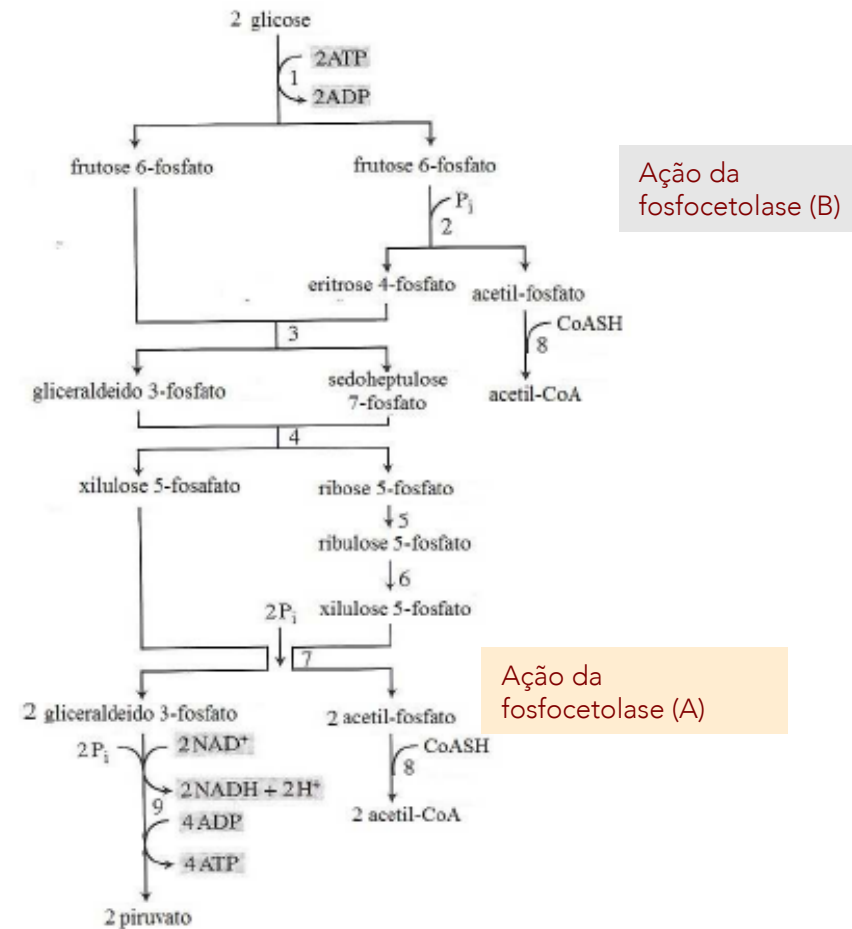


Ocorrência:
bactérias lácticas homofermentadoras



A

Leuconostoc mesenteroides

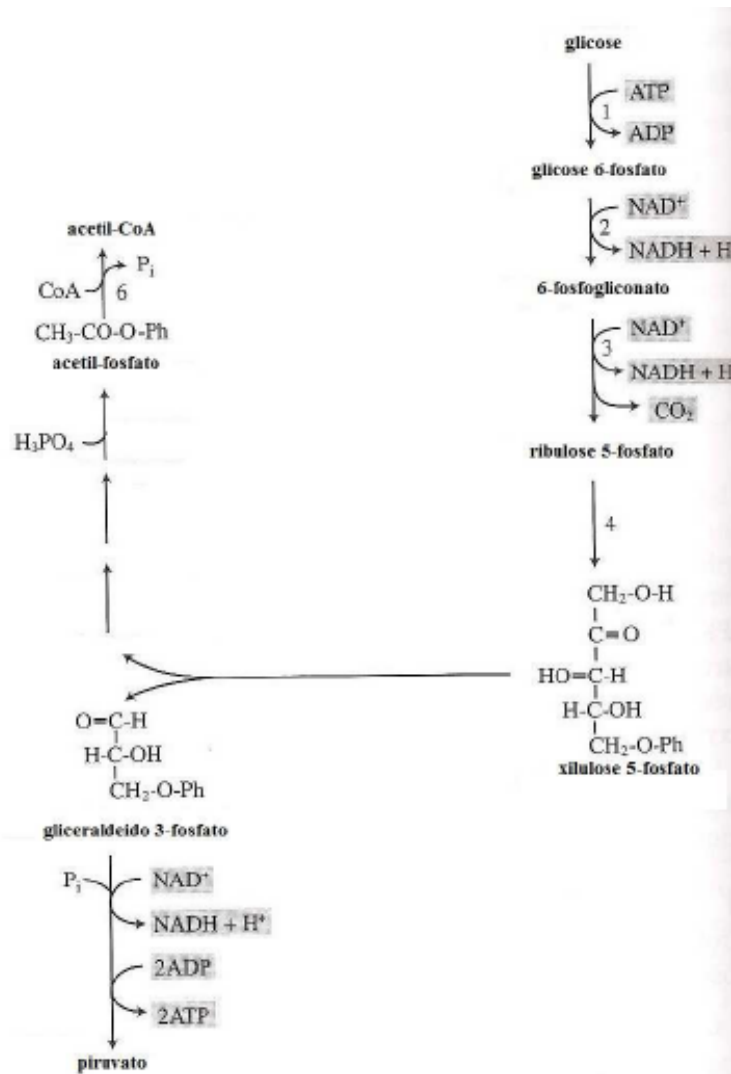


B

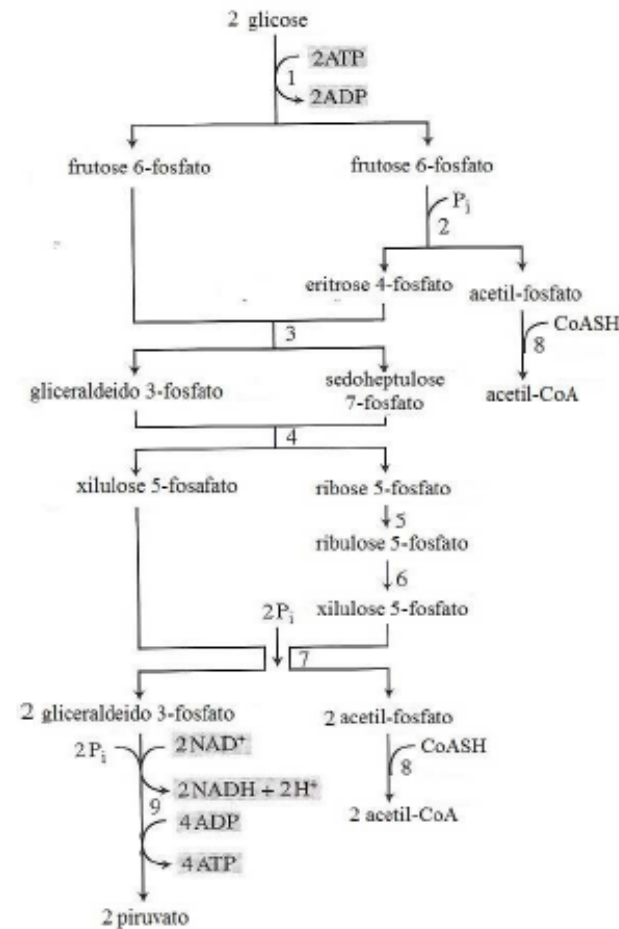
Bifidobacterium bifidum

Via da Fosfocetolase

(Hexose monofosfato)



A



B

ATP
NAD(P)H
Glicose-6-fosfato
Frutose-6-fosfato
Ribose-5-fosfato ou ribulose-5-fosfato
Eritrose-4-fosfato
Sedoheptulose-7-fosfato
Gliceraldeido-3-fosfato
3-Fosfoglicerato
Fosfoenolpiruvato
Piruvato
Acetil-CoA
Oxaloacetato
α-cetoglutarato
Succinil-CoA

Metabólito	Via predominante de origem do metabólito*			
	EMP	ED	VP	HMP
ATP	X	X	-	X
NAD(P)H	-	X	X	-
Glicose-6-fosfato	X	X	X	X
Frutose-6-fosfato	X	-	X	X
Ribose-5-fosfato ou ribulose-5-fosfato	-	-	X	X
Eritrose-4-fosfato	-	-	X	X
Sedoheptulose-7-fosfato	-	-	X	X
Gliceraldeído-3-fosfato	X	X	X	X
3-Fosfoglicerato	X	X	-	X
Fosfoenolpiruvato	X	X	-	X
Piruvato	X	X	-	X
Acetil-CoA	-	-	-	X
Oxaloacetato	-	-	-	-
α -cetoglutarato	-	-	-	-
Succinil-CoA	-	-	-	-

*EMP – via de Embden Meyerhof Parnas; VP- via das pentoses ED- via de Entner -Doudoroff

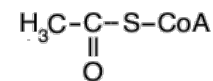
Os destinos do piruvato

- Precursor de biossíntese

- Oxidação a CO_2

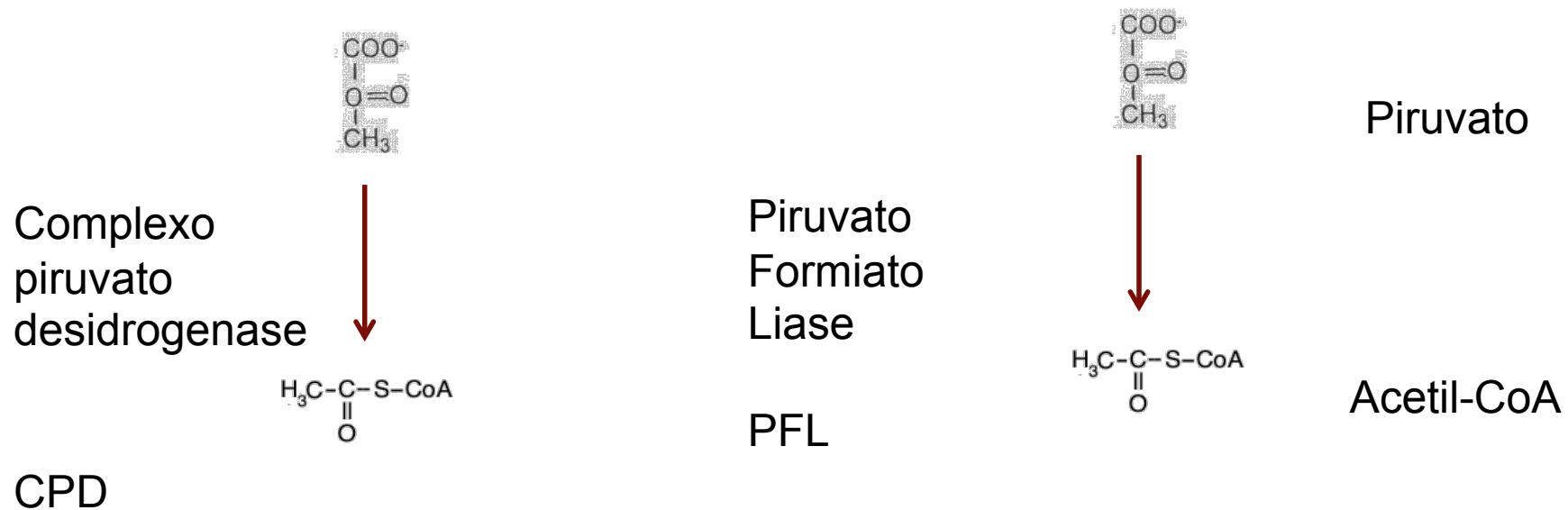


Piruvato

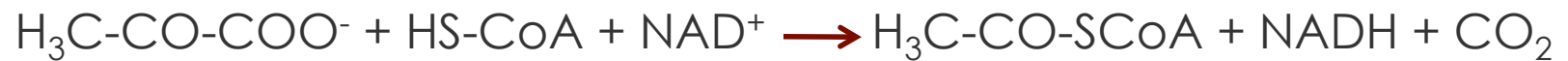
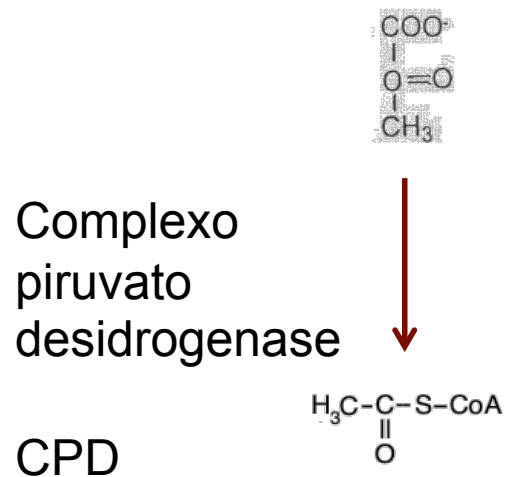


Acetil-CoA

Os destinos do piruvato



Os destinos do piruvato



Piruvato

Acetil-CoA

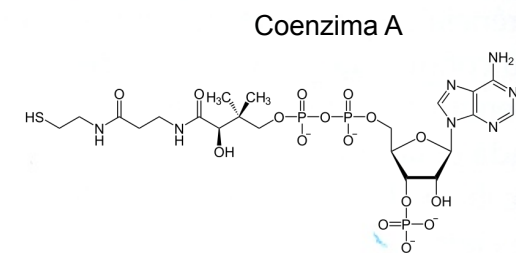
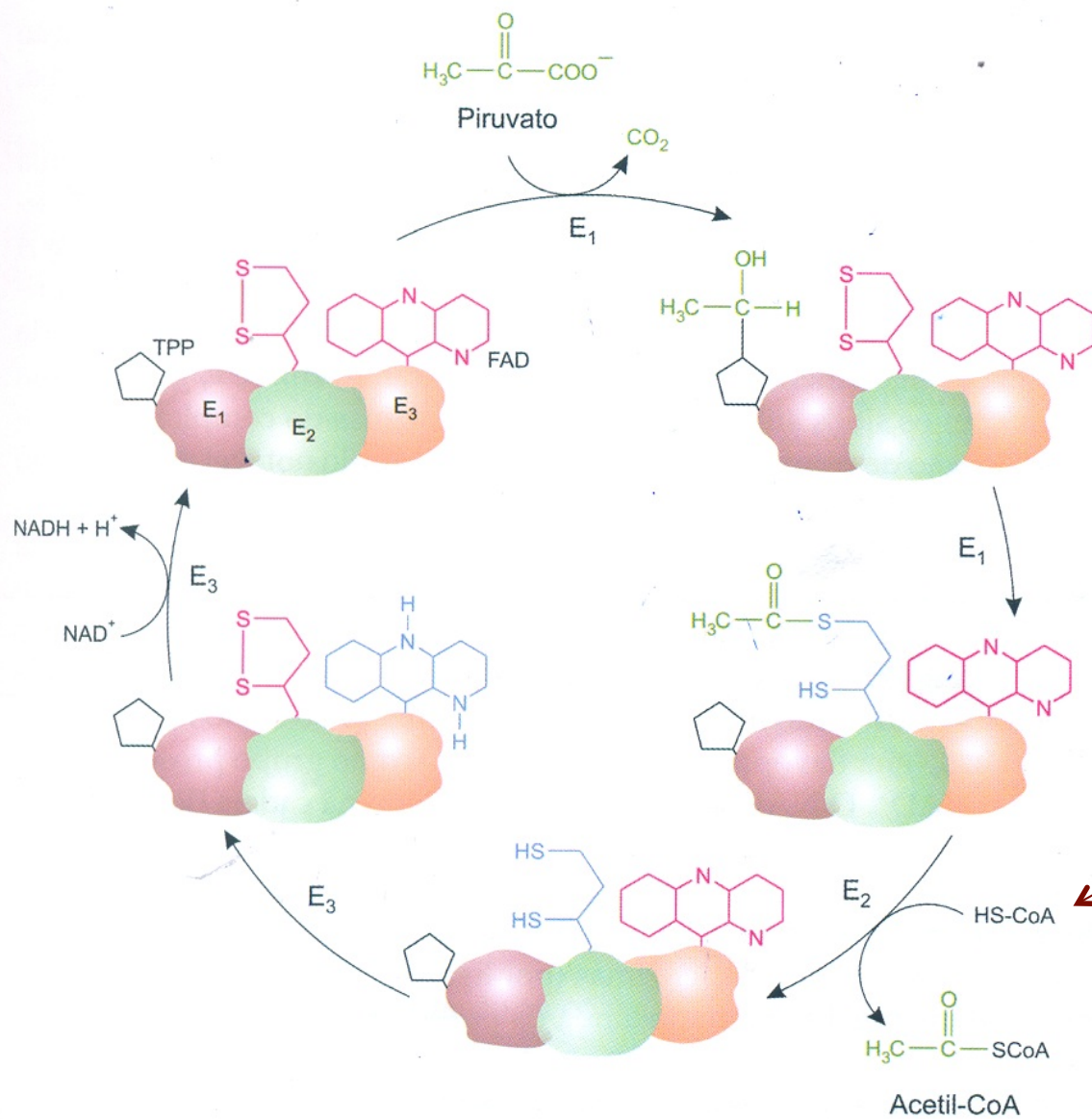


Fig. 9.9 Etapas da reação catalisada pelo complexo piruvato desidrogenase, onde E₁, E₂ e E₃ representam respectivamente as enzimas: piruvato desidrogenase (TPP), diidrolipoil transacetilase (ácido lipóico) e diidrolipoil desidrogenase (FAD).

Metabólito	Via predominante de origem do metabólito*				
	EMP	ED	VP	HMP	CPD
ATP	X	X	-	X	-
NAD(P)H	-	X	X	-	-
Glicose-6-fosfato	X	X	X	X	-
Frutose-6-fosfato	X	-	X	X	-
Ribose-5-fosfato ou ribulose-5-fosfato	-	-	X	X	-
Eritrose-4-fosfato	-	-	X	X	-
Sedoheptulose-7-fosfato	-	-	X	X	-
Gliceraldeído-3-fosfato	X	X	X	X	-
3-Fosfoglicerato	X	X	-	X	-
Fosfoenolpiruvato	X	X	-	X	-
Piruvato	X	X	-	X	-
Acetil-CoA	-	-	-	X	X
Oxaloacetato	-	-	-	-	-
α -cetoglutarato	-	-	-	-	-
Succinil-CoA	-	-	-	-	-

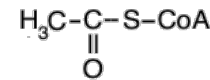
Os destinos do piruvato

Piruvato
Formiato
Liase

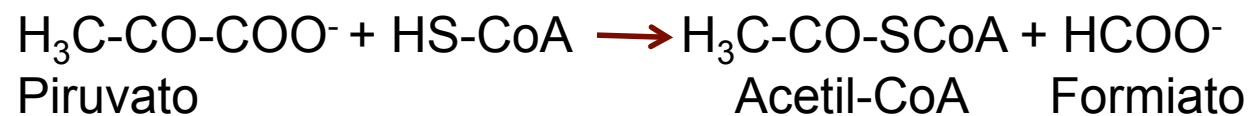
PFL



Piruvato

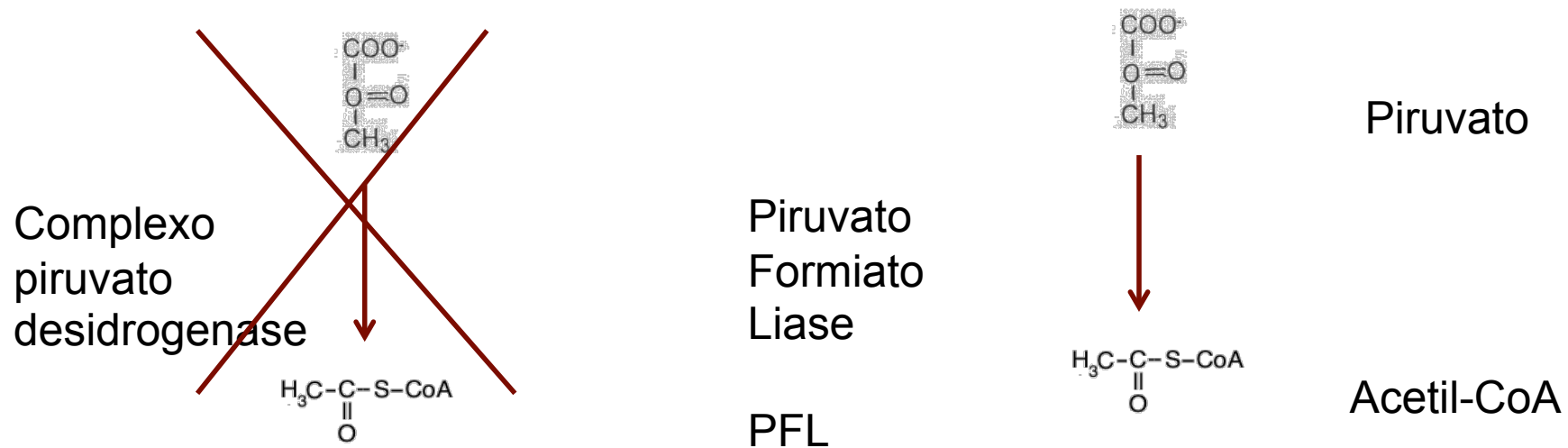


Acetil-CoA



Metabólito	Via predominante de origem do metabólito*				
	EMP	ED	VP	HMP	CPD/ PFL
ATP	X	X	-	X	-
NAD(P)H	-	X	X	-	-
Glicose-6-fosfato	X	X	X	X	-
Frutose-6-fosfato	X	-	X	X	-
Ribose-5-fosfato ou ribulose-5-fosfato	-	-	X	X	-
Eritrose-4-fosfato	-	-	X	X	-
Sedoheptulose-7-fosfato	-	-	X	X	-
Gliceraldeído-3-fosfato	X	X	X	X	-
3-Fosfoglicerato	X	X	-	X	-
Fosfoenolpiruvato	X	X	-	X	-
Piruvato	X	X	-	X	-
Acetil-CoA	-	-	-	X	X
Oxaloacetato	-	-	-	-	-
α -cetoglutarato	-	-	-	-	-
Succinil-CoA	-	-	-	-	-

Os destinos do piruvato



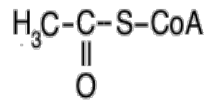
CPD



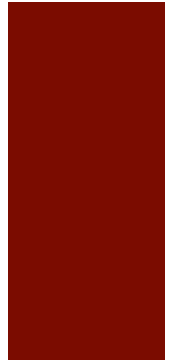
Situação em enterobactérias

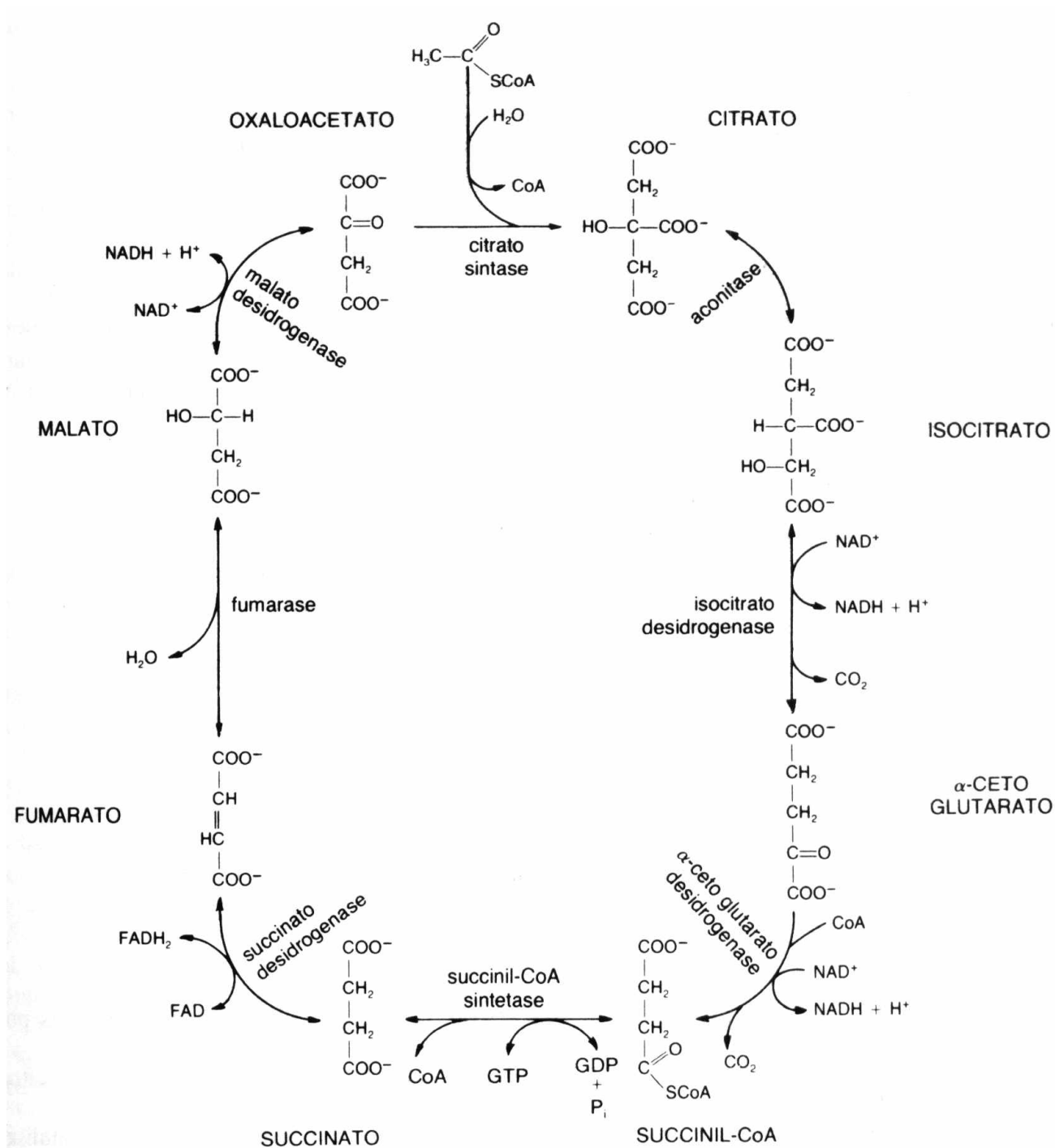
Destinos de acetil-coA

- Precursor do metabolismo
- Ciclo dos ácidos tricarboxílicos
- Ramos oxidativo e redutor



Ciclo dos ácidos tricarboxílicos (TCA ou ciclo de Krebs)

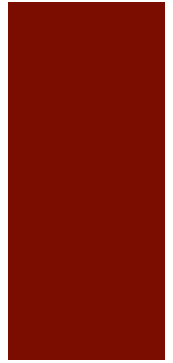


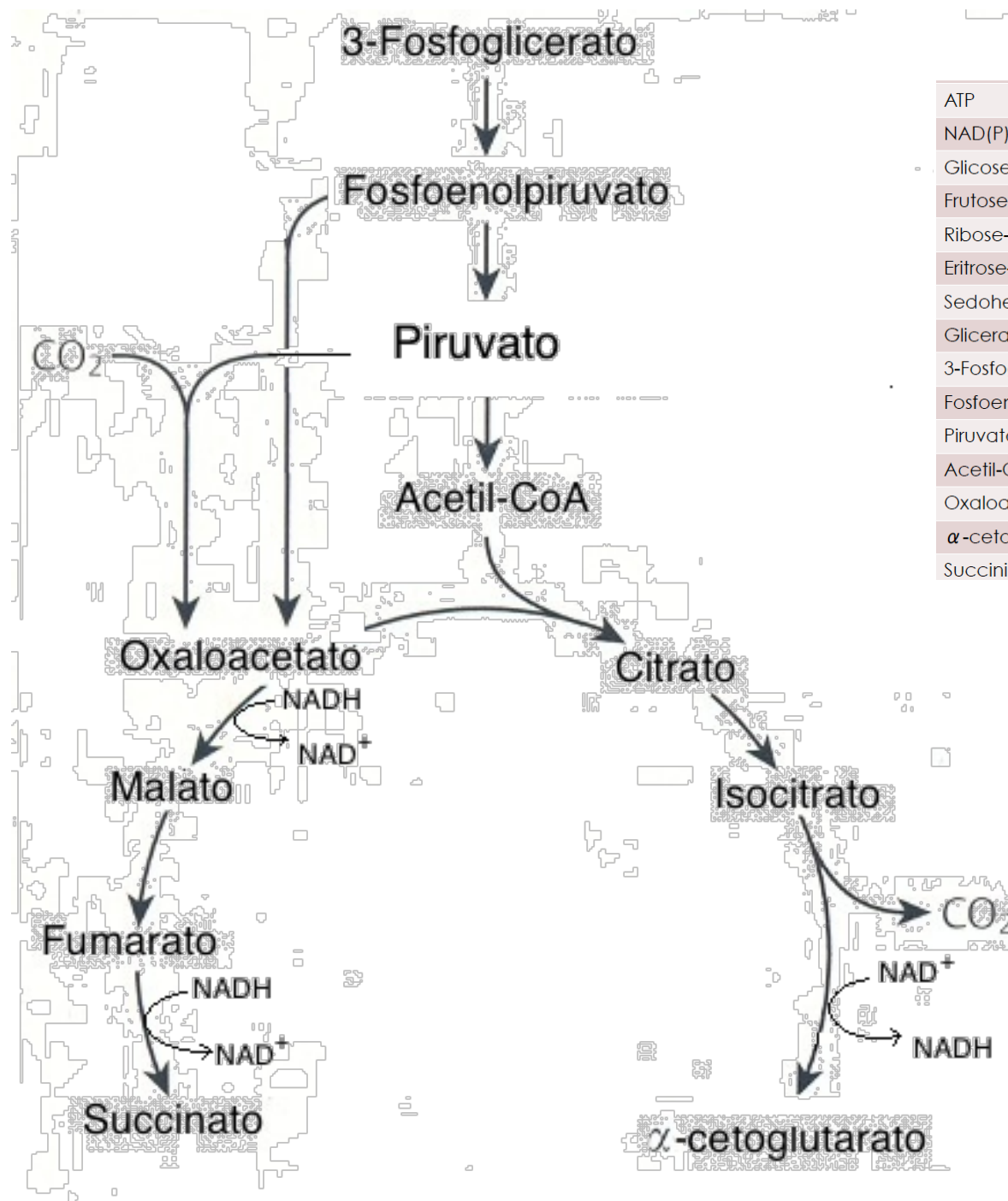


Ciclo de Krebs.

ATP
NAD(P)H
Glicose-6-fosfato
Frutose-6-fosfato
Ribose-5-fosfato ou ribulose-5-fosfato
Eritrose-4-fosfato
Sedoheptulose-7-fosfato
Gliceraldeído-3-fosfato
3-Fosfoglicerato
Fosfoenolpiruvato
Piruvato
Acetil-CoA
Oxaloacetato
α -cetoglutarato
Succinil-CoA

Em algumas condições o complexo α -cetoglutarato desidrogenase não está presente ou está inativado



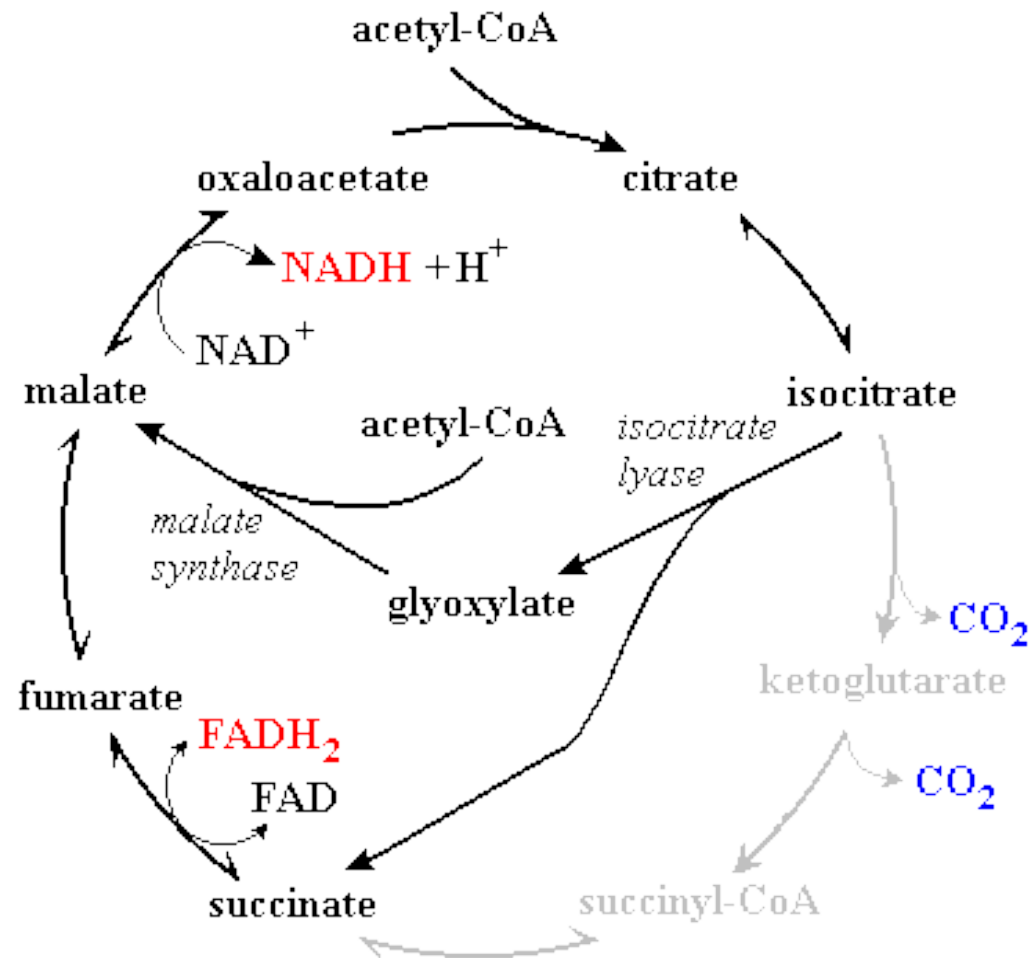


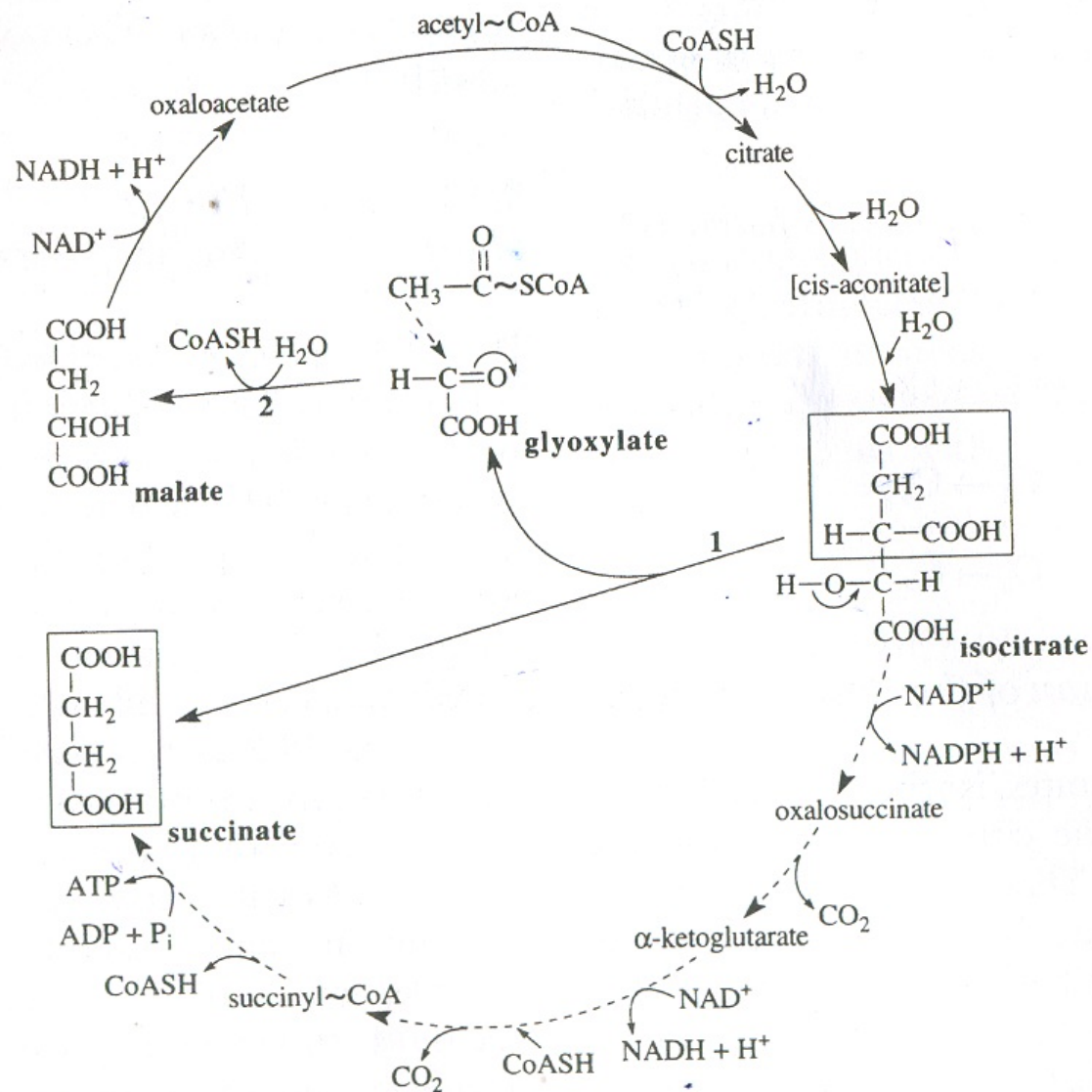
Ramo redutor

Ramo oxidativo

Metabólito	Via predominante de origem do metabólito*						
	EMP	ED	VP	HMP	CPD /PFL	TCA	RR/RO
ATP	X	X	-	X	-	X	-
NAD(P)H	-	X	X	-	-	-	-
Glicose-6-fosfato	X	X	X	X	-	-	-
Frutose-6-fosfato	X	-	X	X	-	-	-
Ribose-5-fosfato ou ribulose-5-fosfato	-	-	X	X	-	-	-
Eritrose-4-fosfato	-	-	X	X	-	-	-
Sedoheptulose-7-fosfato	-	-	X	X	-	-	-
Gliceraldeído-3-fosfato	X	X	X	X	-	-	-
3-Fosfoglicerato	X	X	-	X	-	-	-
Fosfoenolpiruvato	X	X	-	X	-	-	-
Piruvato	X	X	-	X	-	-	-
Acetil-CoA	-	-	-	X	X	-	-
Oxaloacetato	-	-	-	-	-	X	X
α -cetoglutarato	-	-	-	-	-	X	X
Succinil-CoA	-	-	-	-	-	X	X

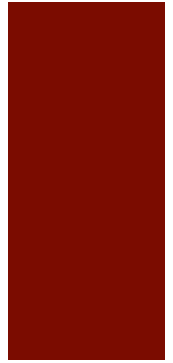
Shunt do glioxilato





The glyoxylate cycle. Enzymes: 1, isocitrate lyase; 2, malate synthase. The dashed arrows represent reactions of the citric acid cycle that are bypassed.

Como as bactérias crescem
quando não há glicose?



β -oxidação de ácidos graxos

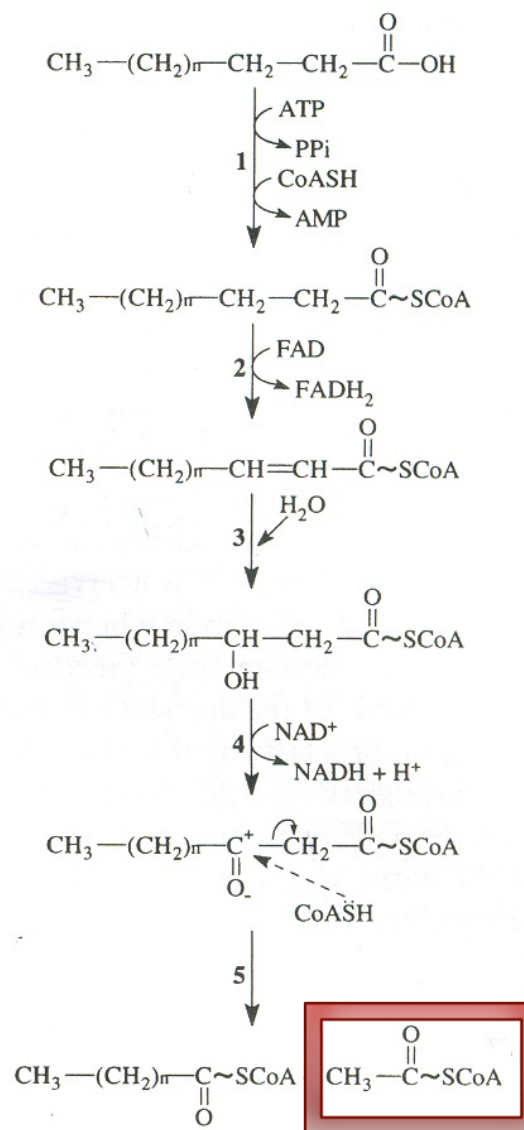
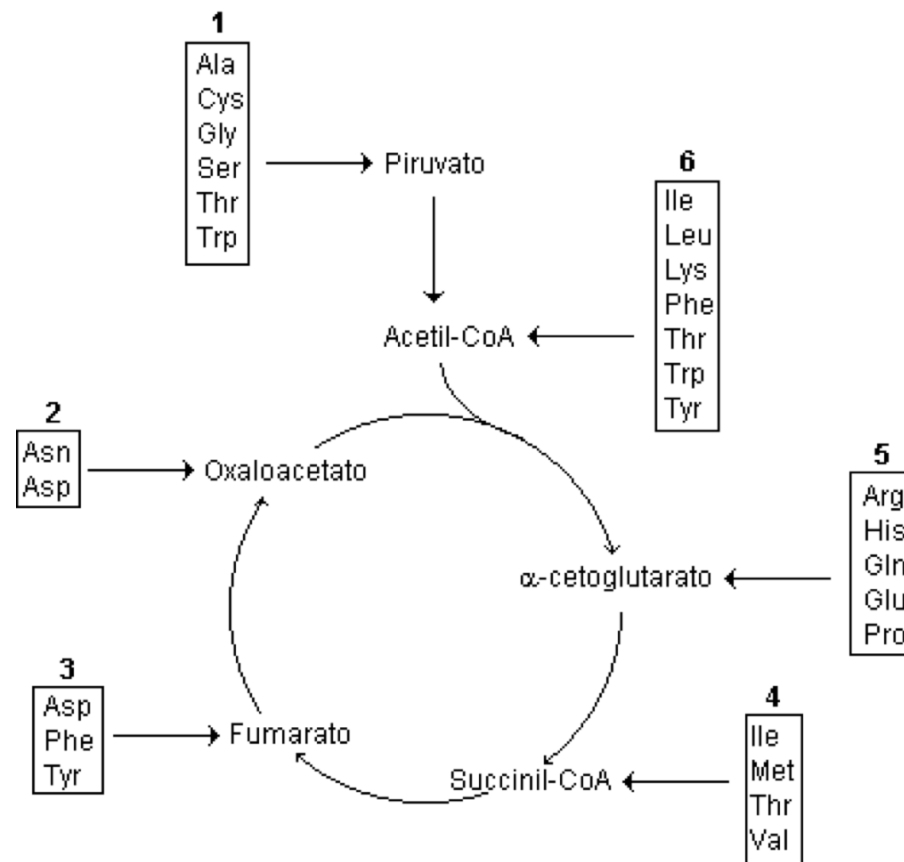


Fig. 9.1 β -Oxidation of fatty acids. Enzymes: 1, acyl-CoA synthetase; 2, fatty acyl-CoA dehydrogenase; 3, 3-hydroxyacyl-CoA hydrolyase; 4, L-3-hydroxyacyl-CoA dehydrogenase; 5, β -ketothiolase.

Como as bactérias crescem quando não há glicose?



Destino da cadeia carbônica dos aminoácidos, que foram repartidos em seis grupos (1 a 6) de acordo com o composto formado.

Gliconeogênese

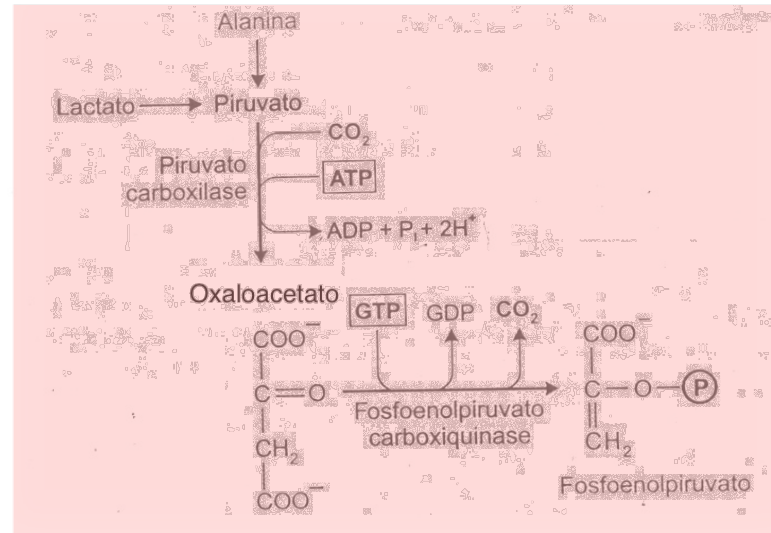
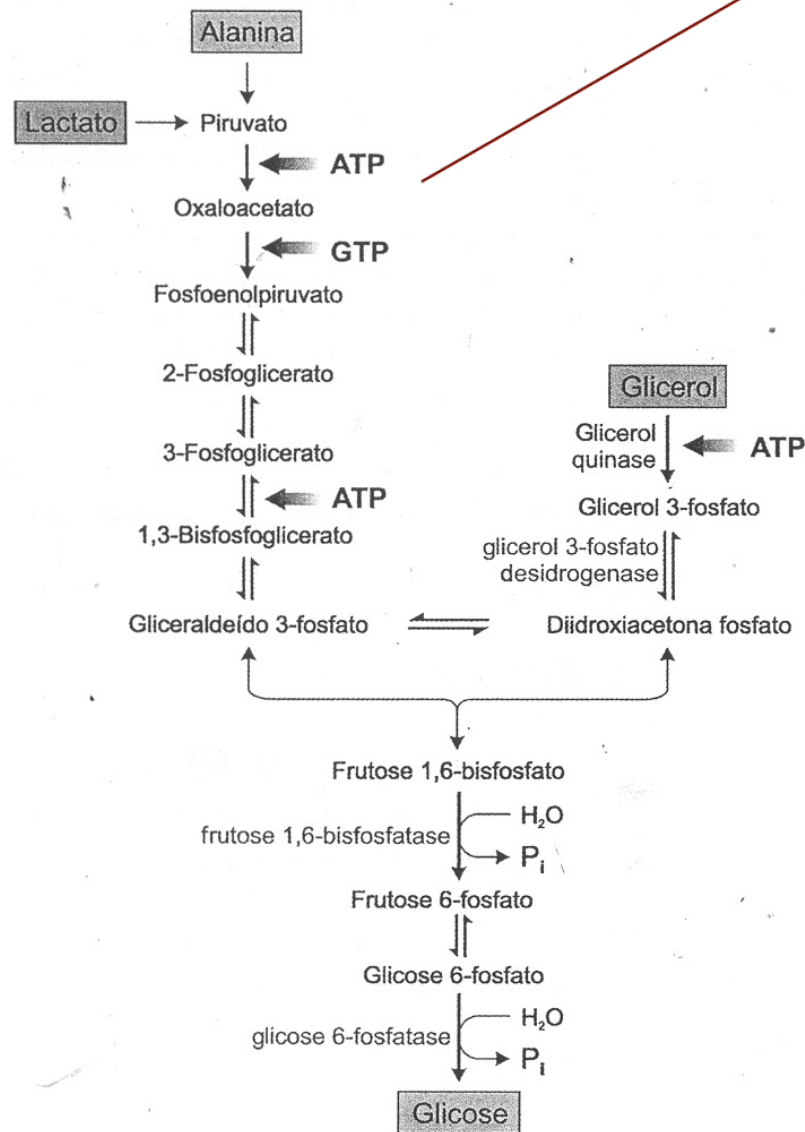


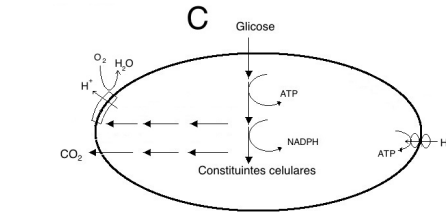
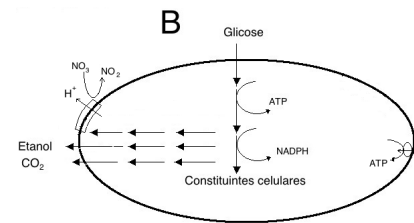
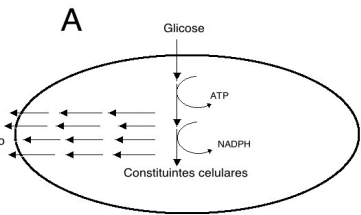
Fig. 14.4 Esquema simplificado da gliconeogênese. As reações que convertem piruvato a oxaloacetato e este a fosfoenolpiruvato estão detalhadas na Fig. 14.3. As reações comuns à via glicolítica podem ser encontradas na sua forma completa na Fig. 9.5 (Seção 9.1). Deve-se ressaltar que são necessárias *duas* moléculas de cada um dos compostos gliconeogênicos — alanina, lactato, glicerol — para sintetizar *uma* molécula de glicose.



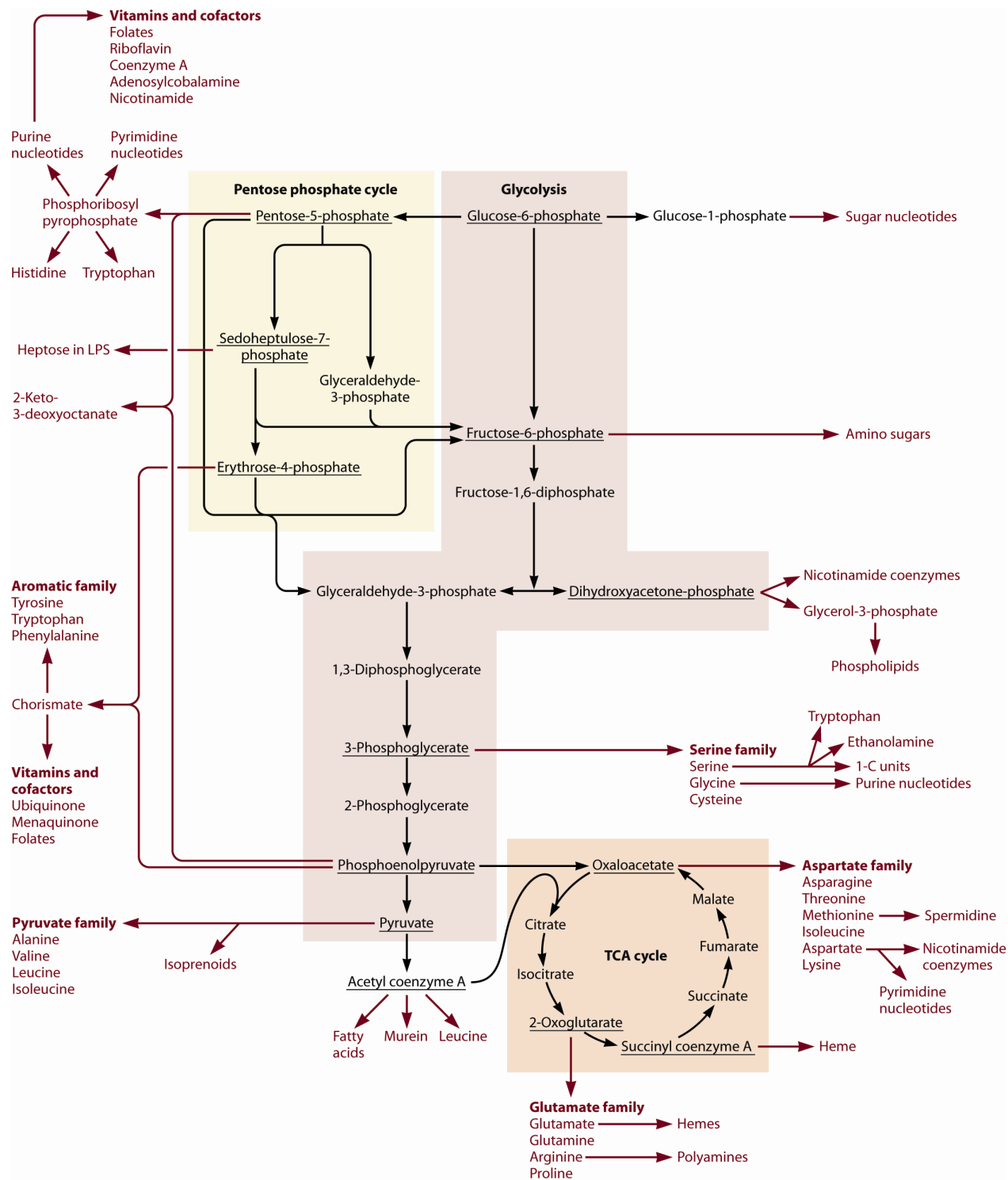
*Nenhuma das vias
isoladamente consegue
suprir os precursores
necessários ao metabolismo
bacteriano*



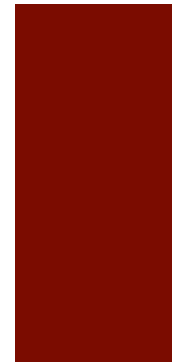
Uma combinação de vias é necessária



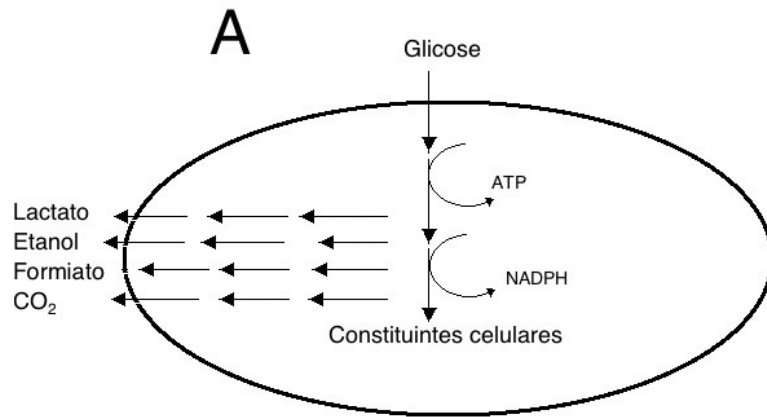
- Vias metabólicas
- Processos metabólicos
- Redes metabólicas



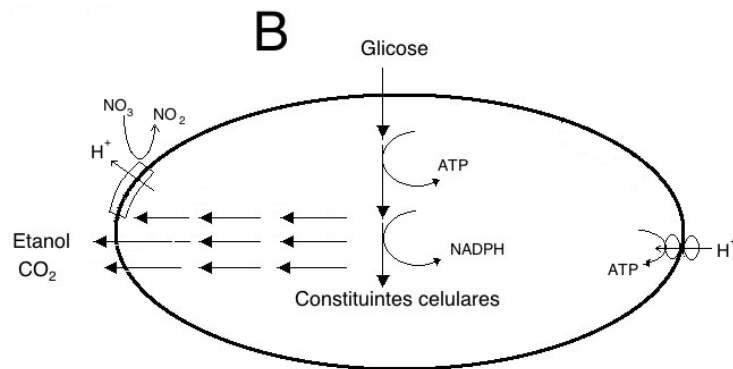
Obtenção de ATP



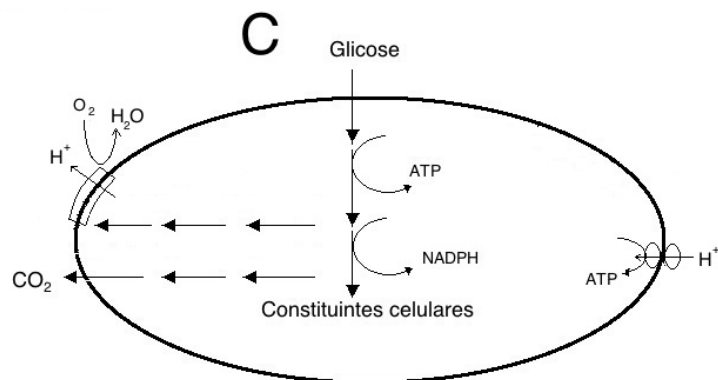
Heterotróficos



Sem O₂

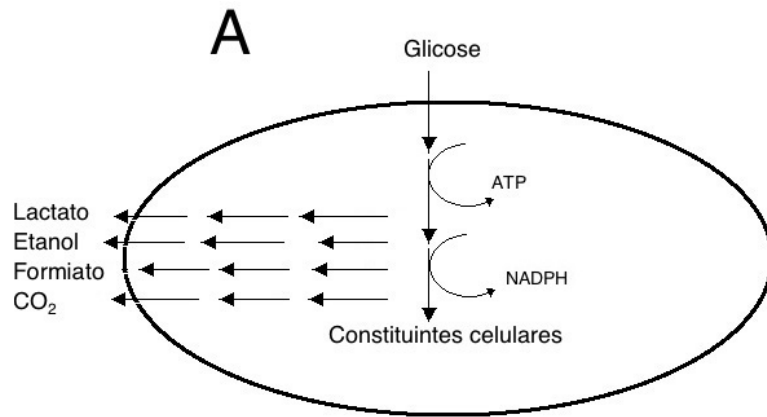


Sem O₂ com outro aceptor
final de eletrons



Com O₂

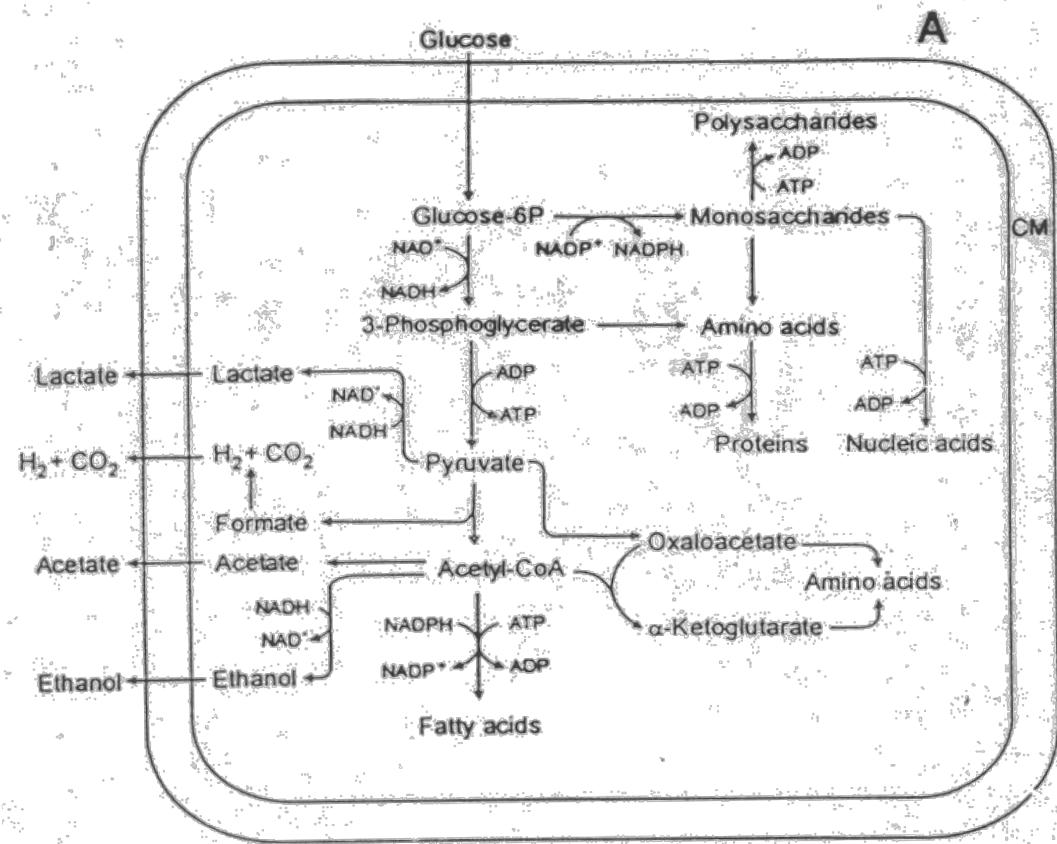
Heterotróficos



Sem O_2

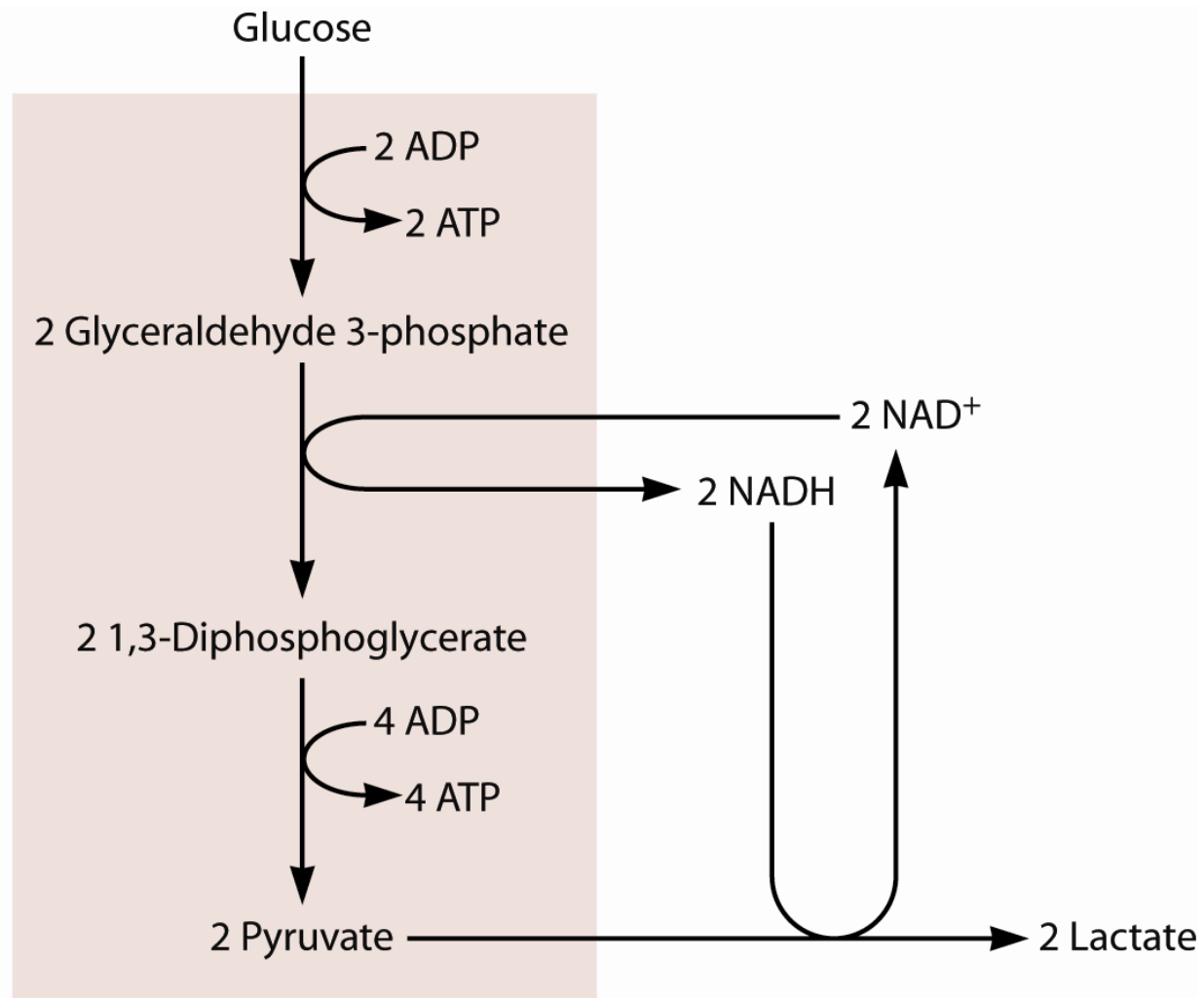
Semceptor de elétrons exógeno

FERMENTAÇÃO

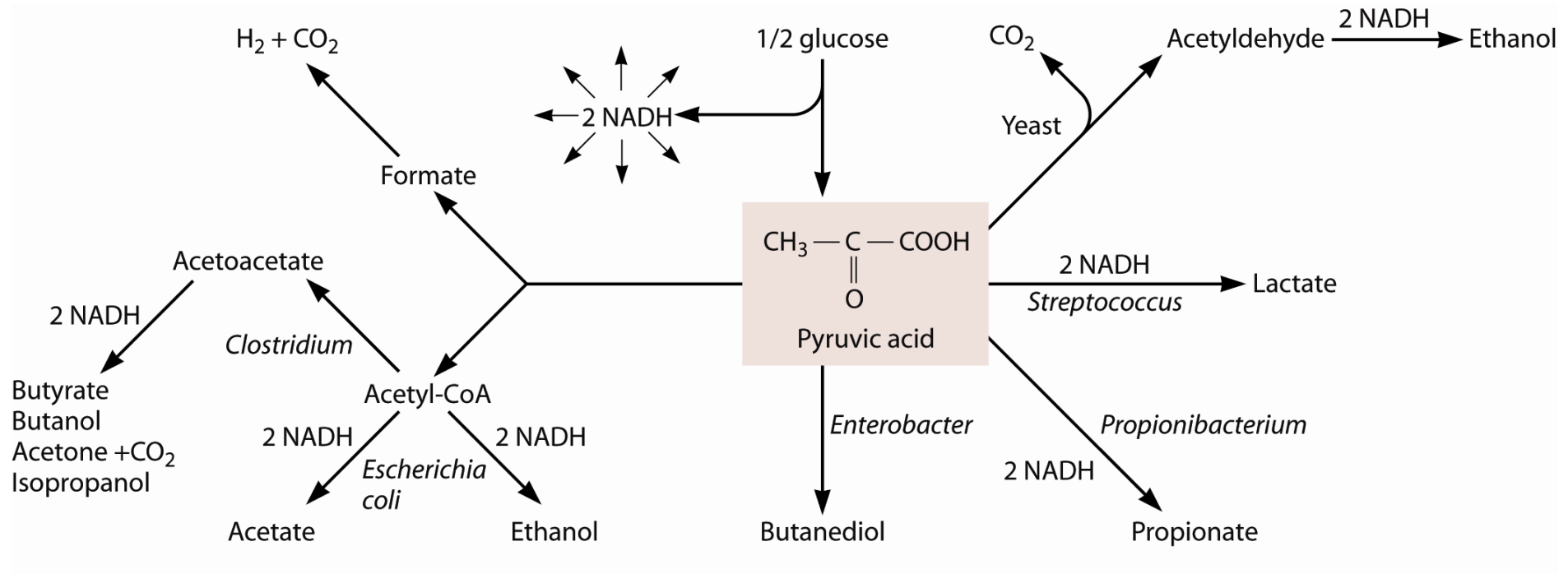


Reoxidação de coenzimas $NADH/NAD^+$

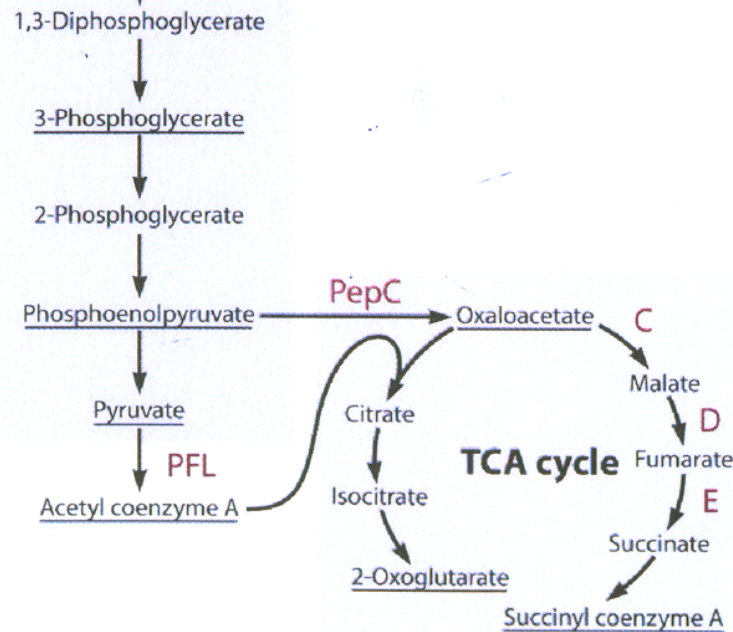
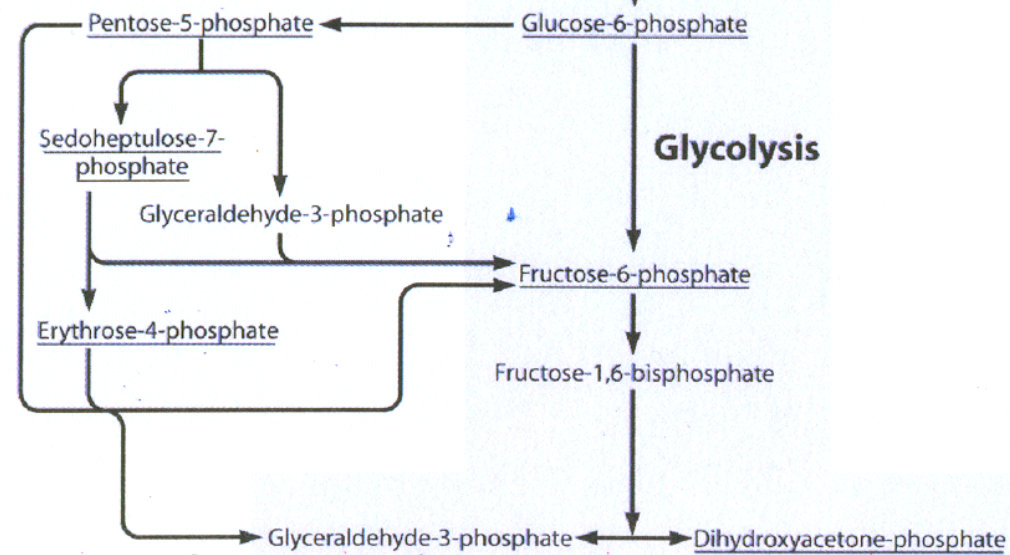
Fermentação



Fermentação

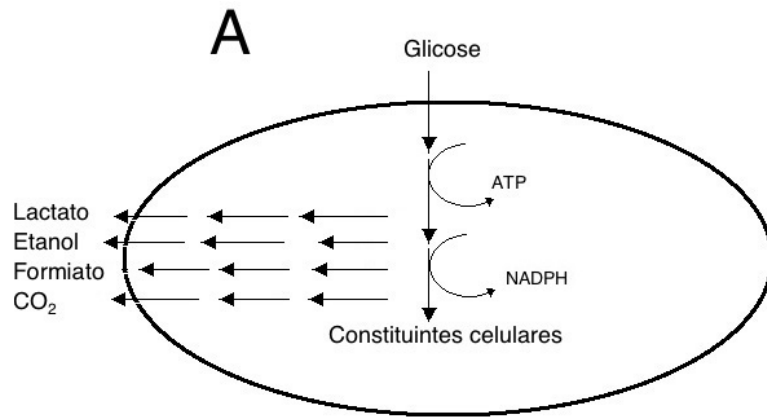


Pentose phosphate cycle

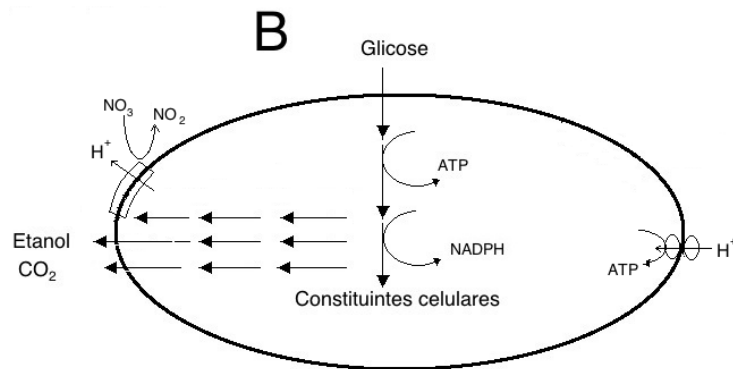


Formação de precursores durante a fermentação de glicose em *E. coli* (principais reações anapleróticas em vermelho)

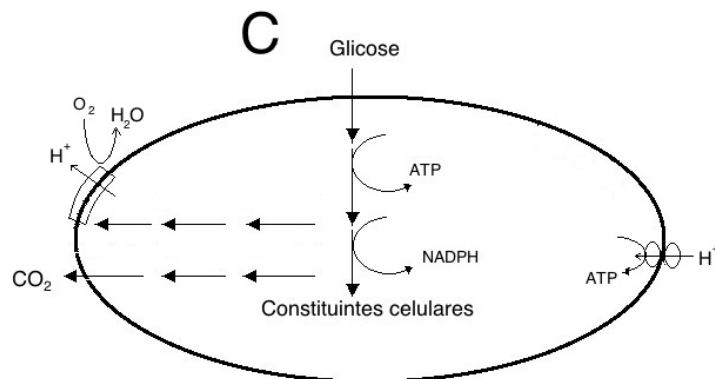
Heterotróficos



Sem O_2 **FERMENTAÇÃO**

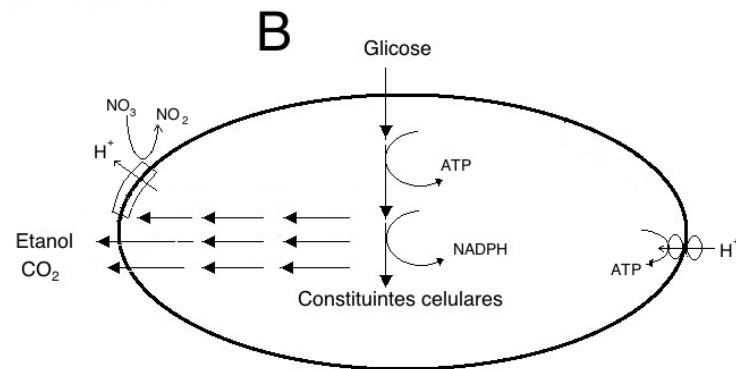


Sem O_2 com outro acceptor final de eletrons

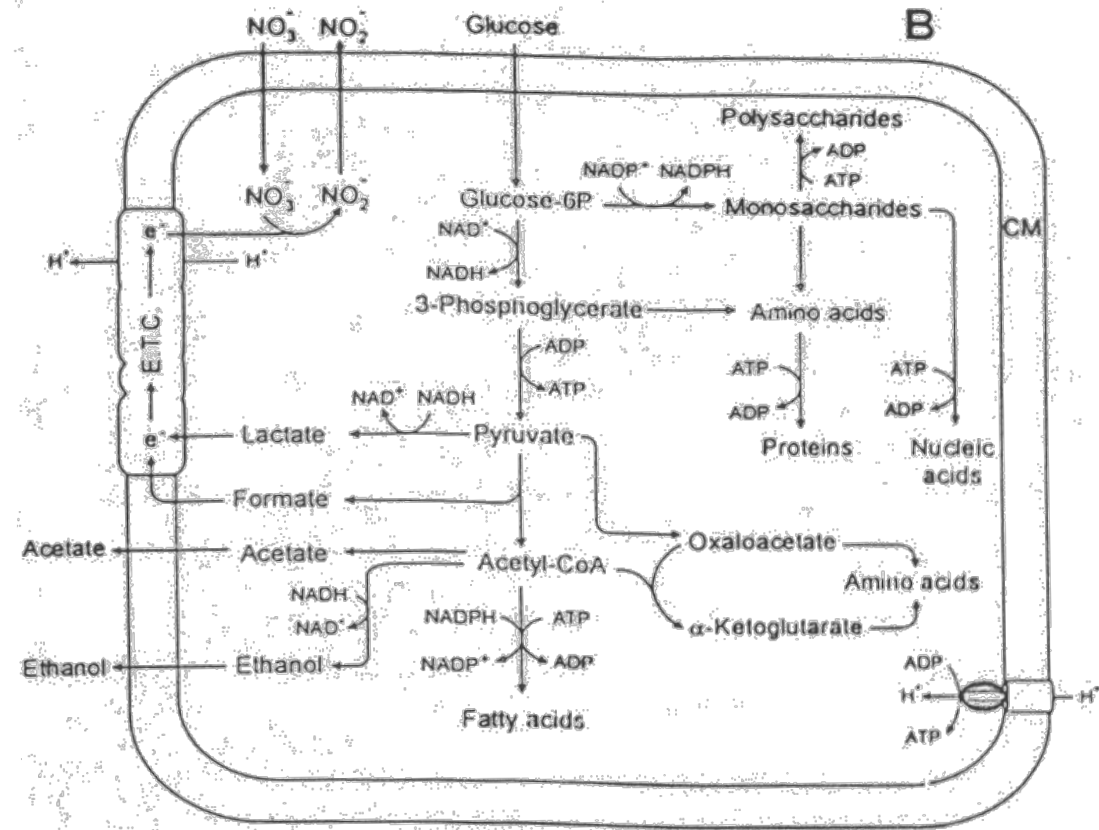


Com O_2

Heterotróficos

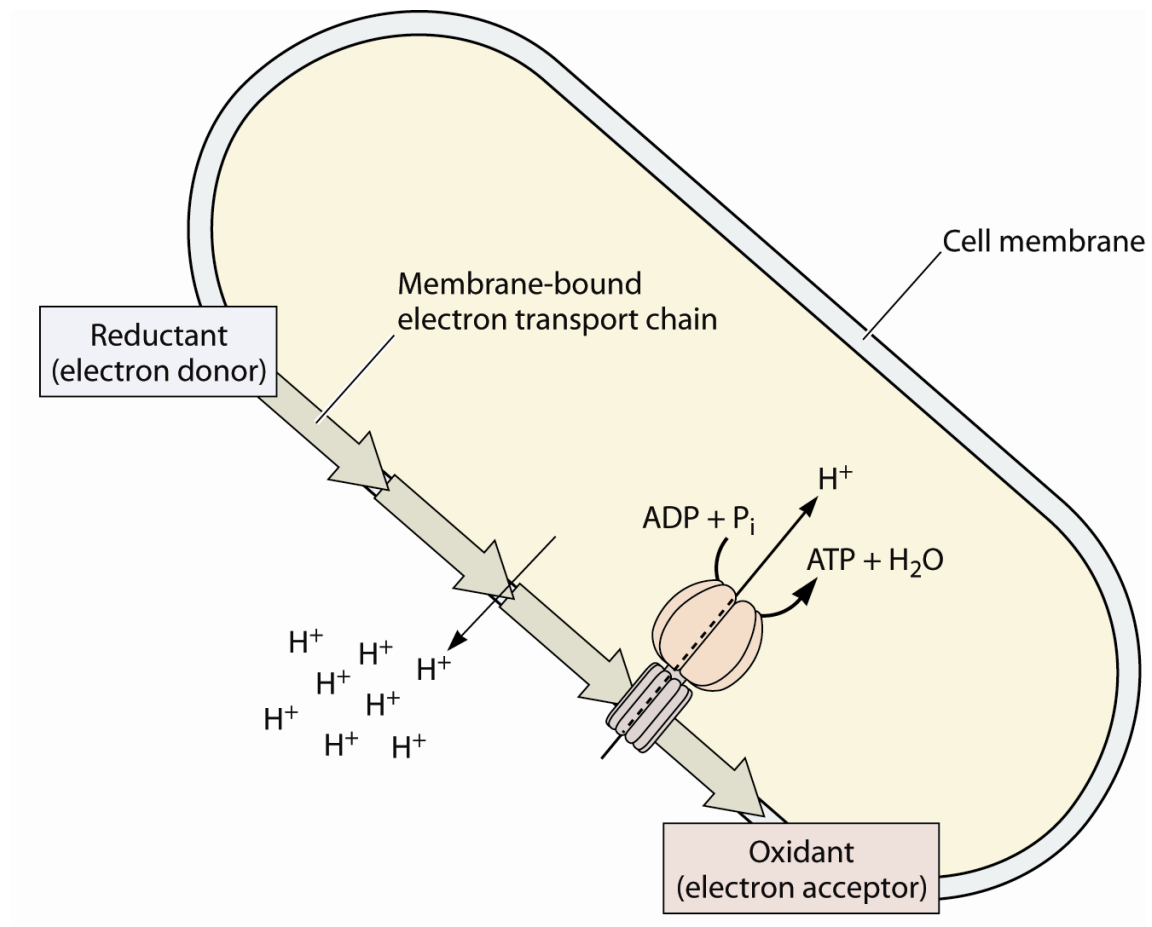


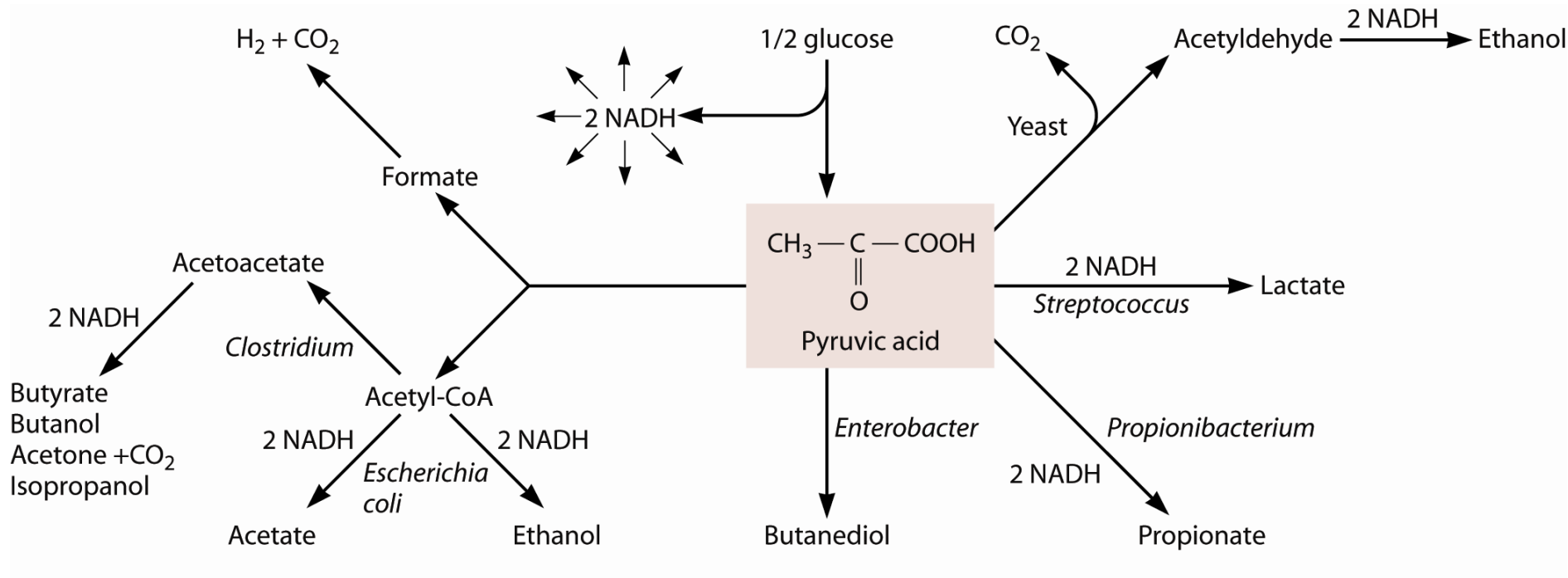
Sem O_2 com outro aceptor final de elétrons



RESPIRAÇÃO ANAERÓBIA

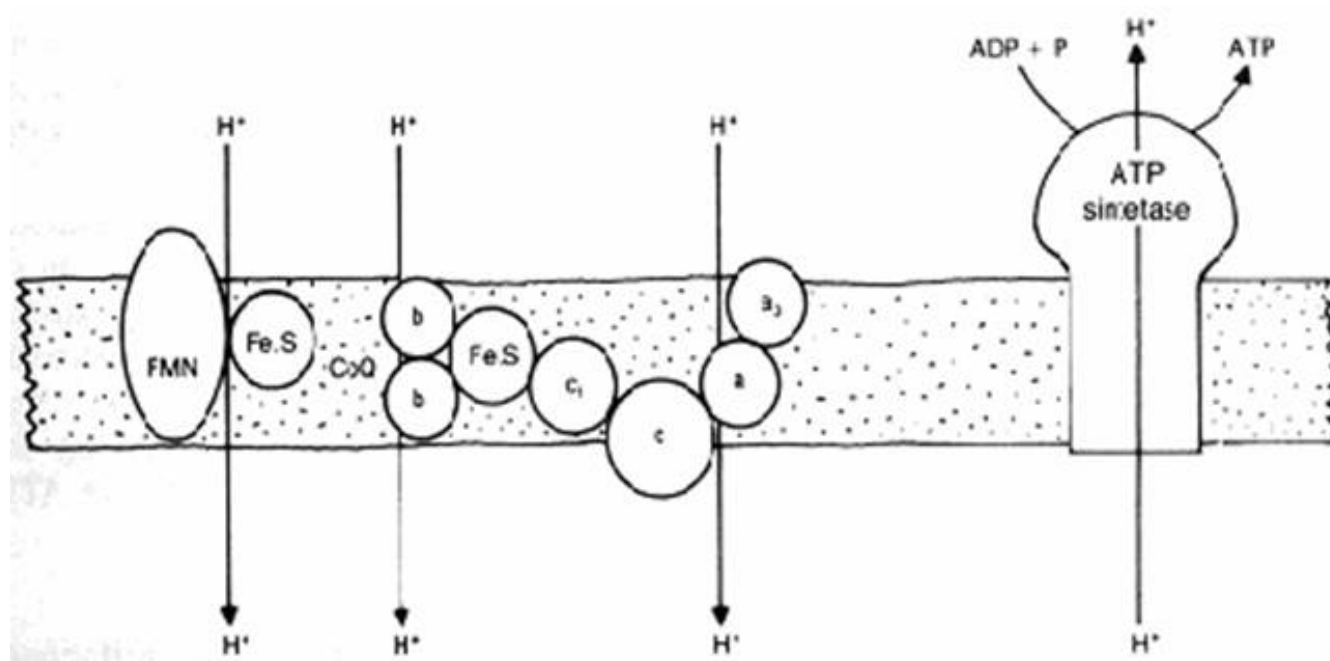
Cadeias de transporte de elétrons e fosforilação oxidativa



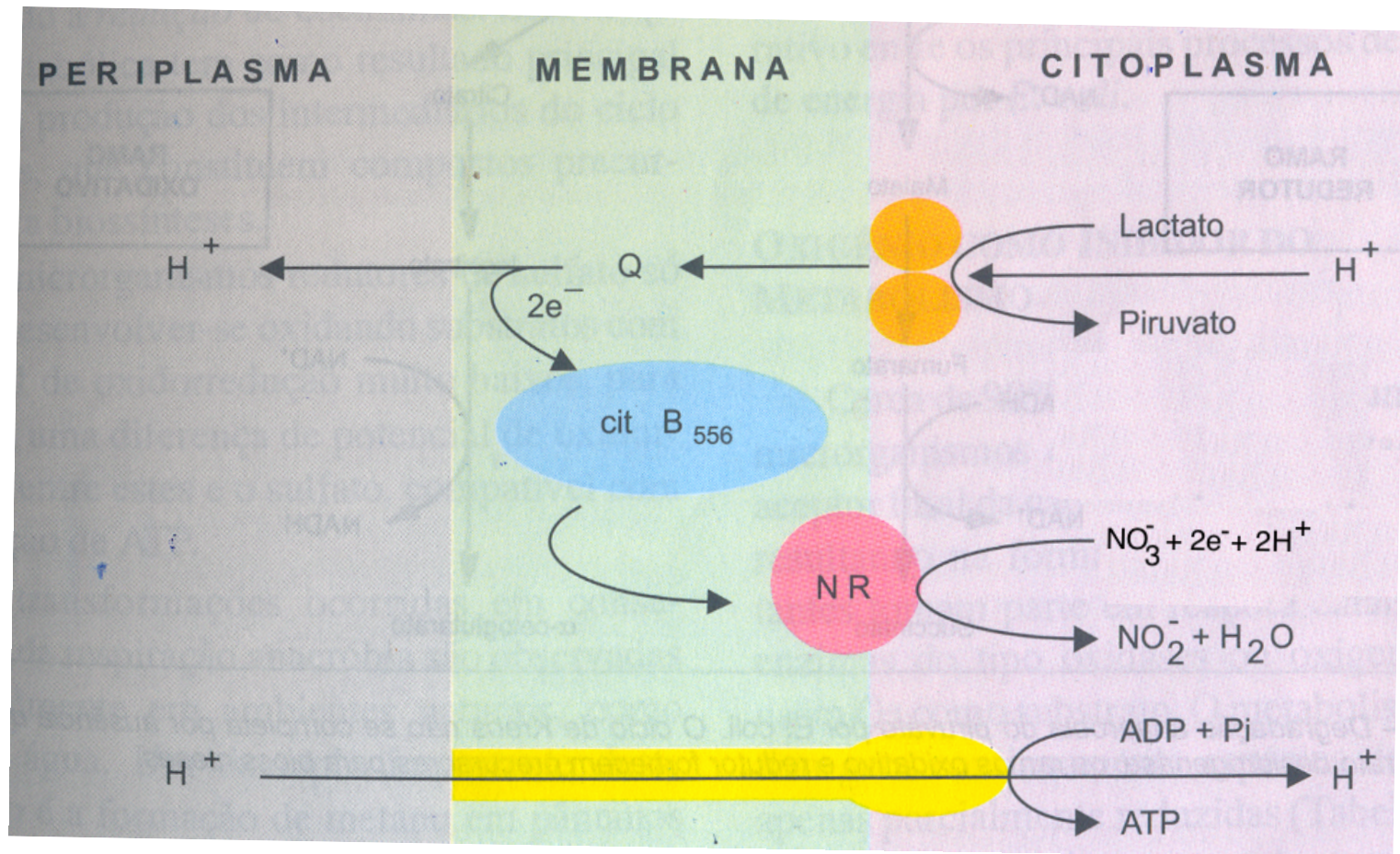


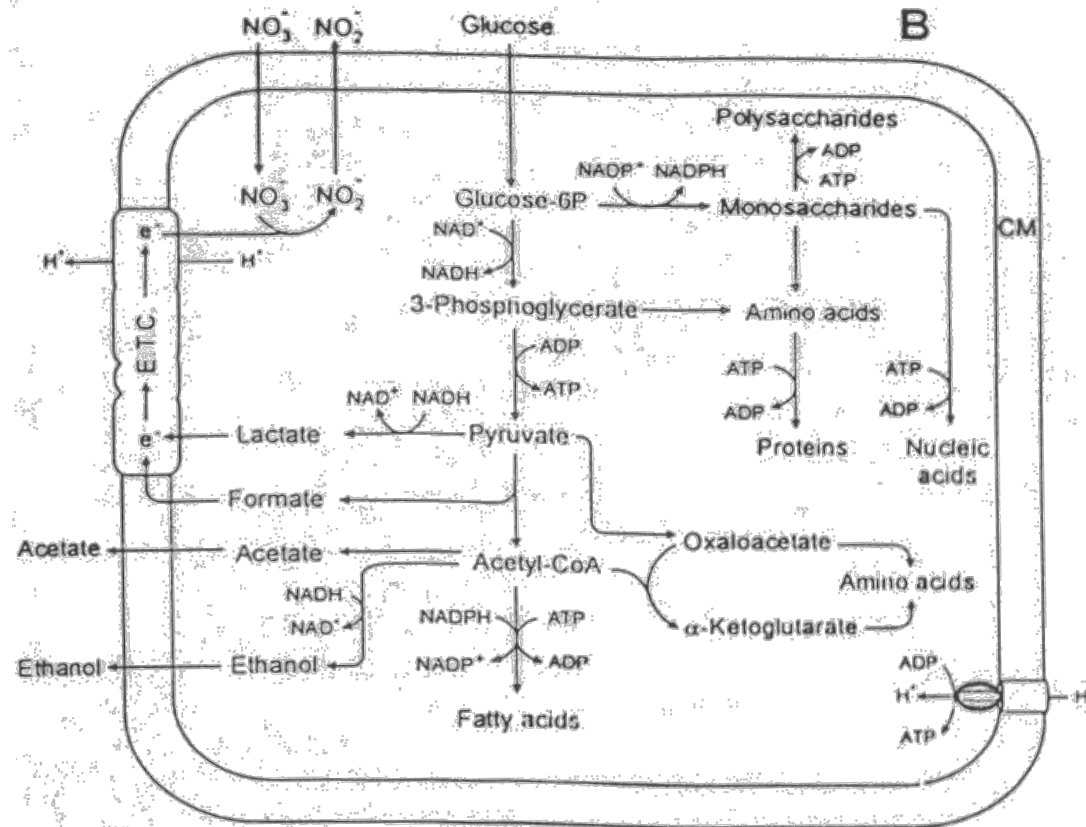
Produtos da fermentação não foram completamente oxidados
Podem gerar mais energia

CTE esquema geral



CTE em *E. coli* quando nitrato é o aceptor final de elétrons



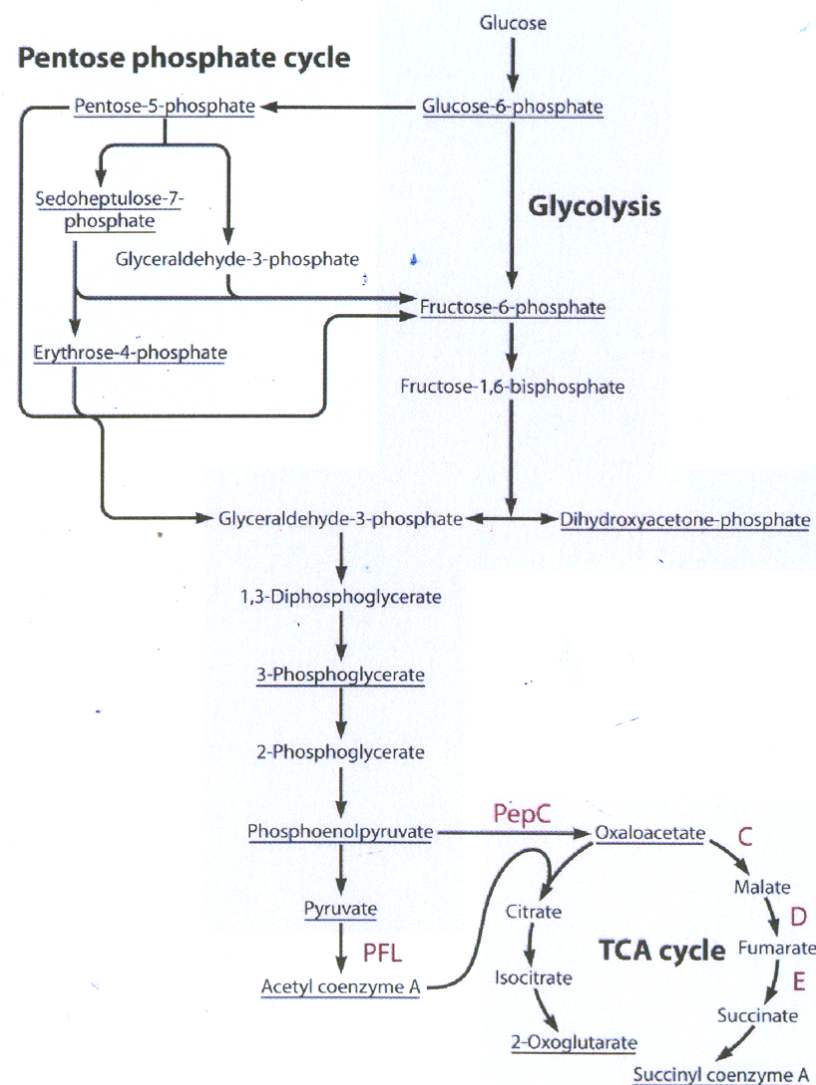


RESPIRAÇÃO ANAERÓBIA

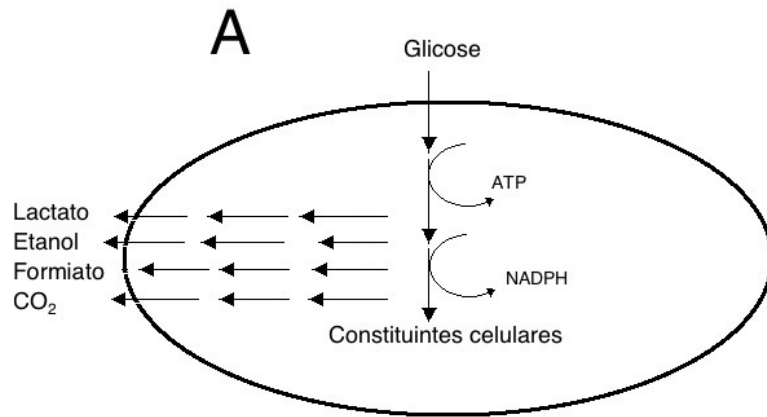
Table 6.3 Compounds that can serve as electron acceptors in anaerobic respiration, replacing oxygen

Organic compounds	Inorganic compounds
Fumarate	Nitrate (NO_3^-)
Dimethylsulfoxide (DMSO)	Nitrite (NO_2^-)
Trimethylamine <i>N</i> -oxide (TMAO)	Nitrous oxide (N_2O)
	Chlorate (ClO_3^-)
	Perchlorate (ClO_4^-)
	Manganic ion (Mn^{4+})
	Ferric ion (Fe^{3+})
	Gold (Au^{3+})
	Selenate (SeO_4^{2-})
	Arsenate (AsO_4^{3-})
	Sulfate (SO_4^{2-})
	Sulfur (S^0)

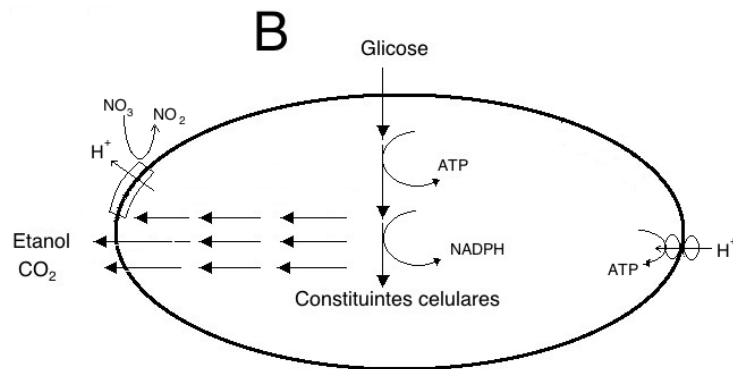
Obtenção de precursores na respiração anaeróbica



Heterotróficos

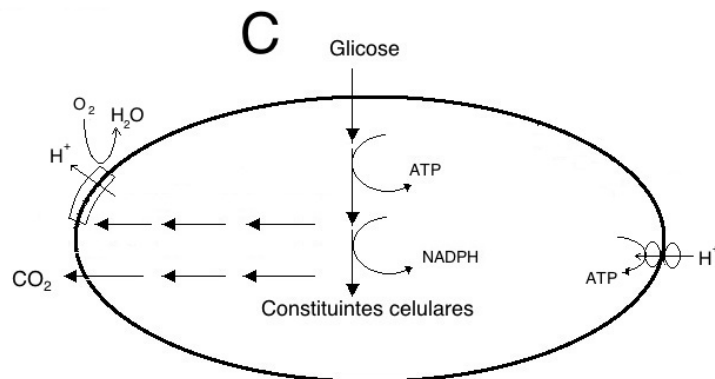


Sem O_2 **FERMENTAÇÃO**



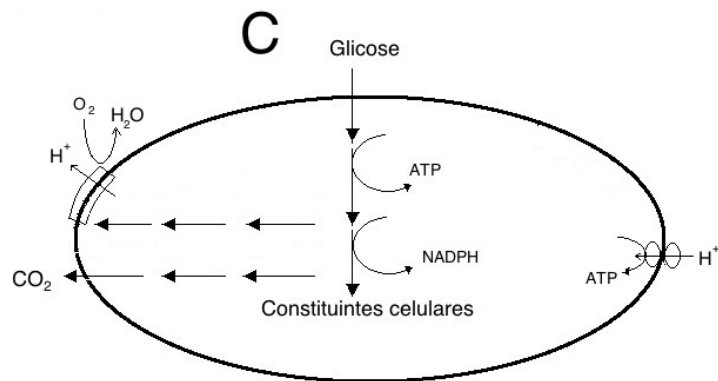
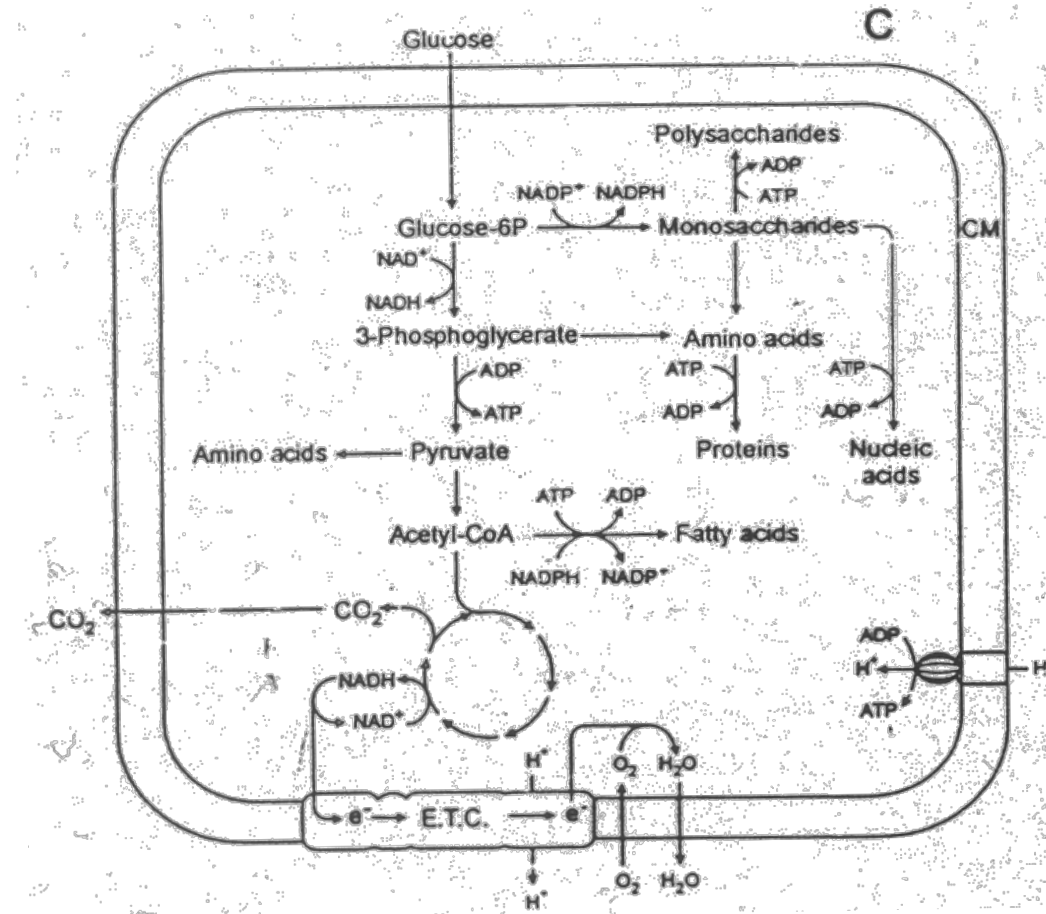
Sem O_2 com outro acceptor final de eletrons

RESPIRAÇÃO ANAERÓBIA



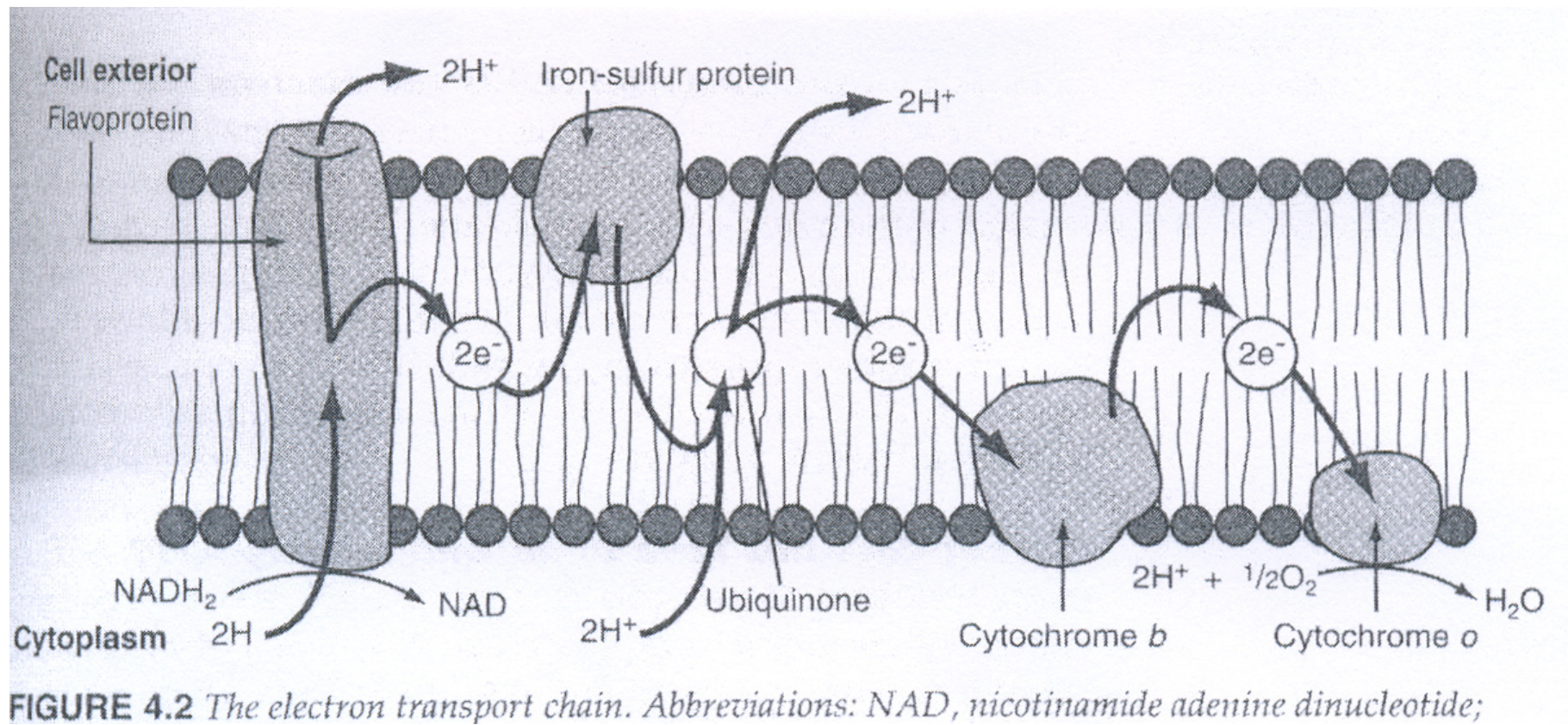
Com O_2

Heterotróficos



Com O₂

Cadeia de transporte de elétrons aeróbica



Quadro 8.2 Potenciais de óxido-redução padrão dos componentes da cadeia de transporte de elétrons

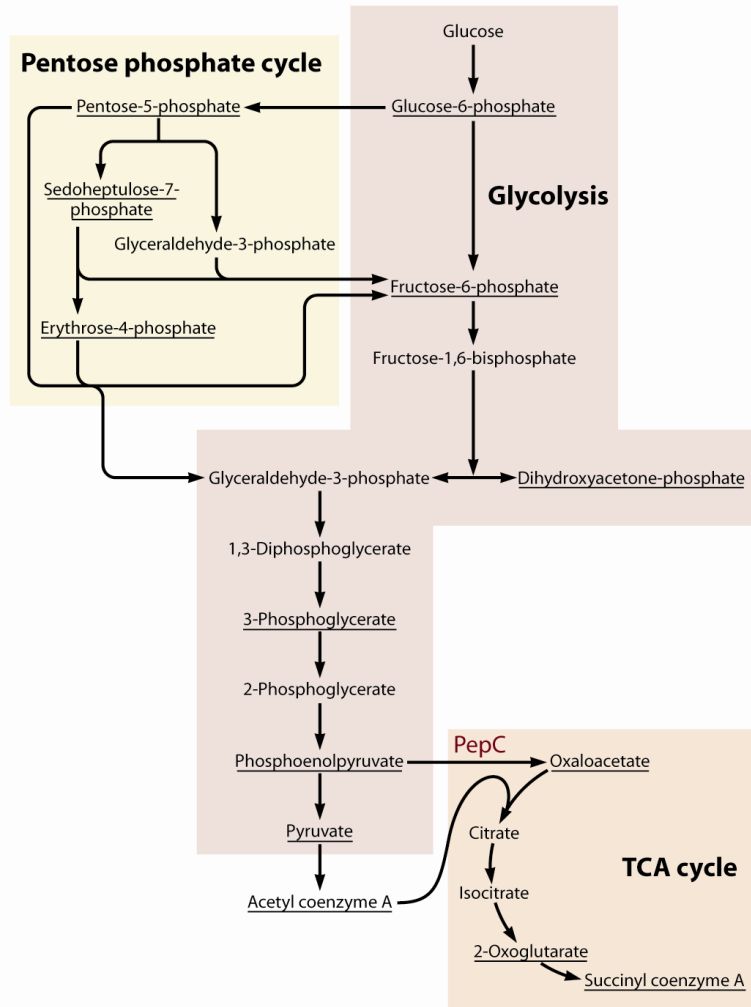
Par oxidado/reduzido	E°' (volts)
NAD ⁺ /NADH	– 0,32
FMN/FMNH ₂	– 0,30*
FAD/FADH ₂	– 0,18**
CoQ/CoQH ₂	+ 0,04
Citocromo b (Fe ³⁺)/citocromo b (Fe ²⁺)	+ 0,06
Citocromo c ₁ (Fe ³⁺)/citocromo c (Fe ²⁺)	+ 0,23
Citocromo c (Fe ³⁺)/citocromo c (Fe ²⁺)	+ 0,25
Citocromo a (Fe ³⁺)/citocromo a (Fe ²⁺)	+ 0,29
Citocromo a ₃ (Fe ³⁺)/citocromo a ₃ (Fe ²⁺)	+ 0,55
O ₂ /H ₂ O	+ 0,82

*O valor refere-se à coenzima ligada à NADH desidrogenase.

**O valor refere-se à coenzima livre; quando ligada a proteínas, seu valor varia entre 0,0 e +0,3, dependendo da proteína.

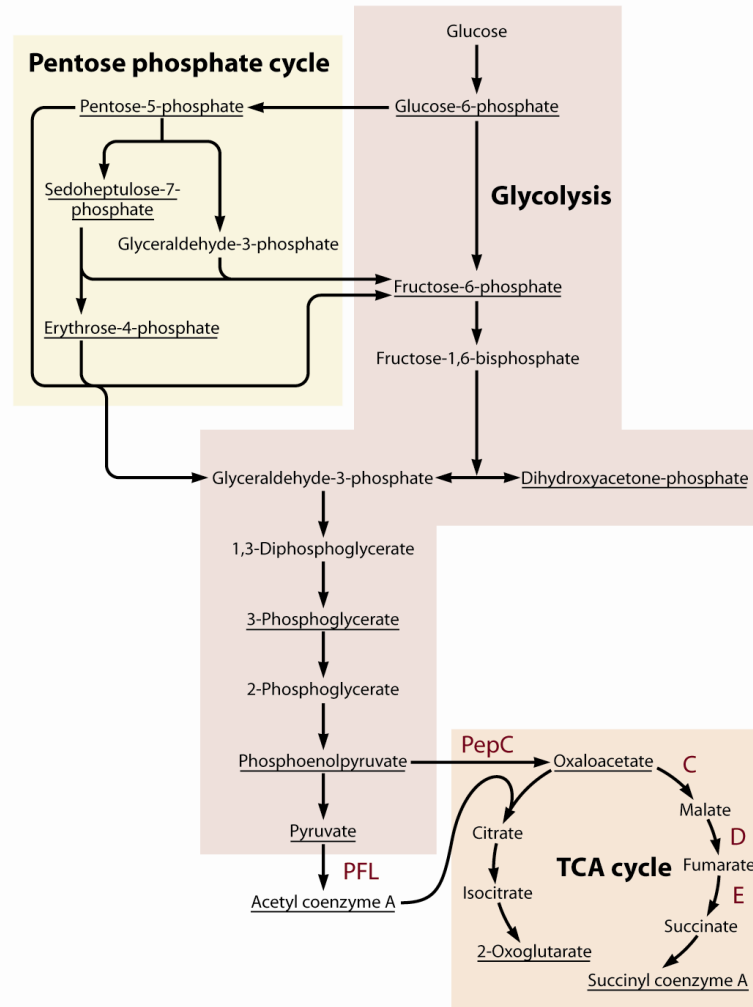
Precursores/Poder redutor/ATP

A

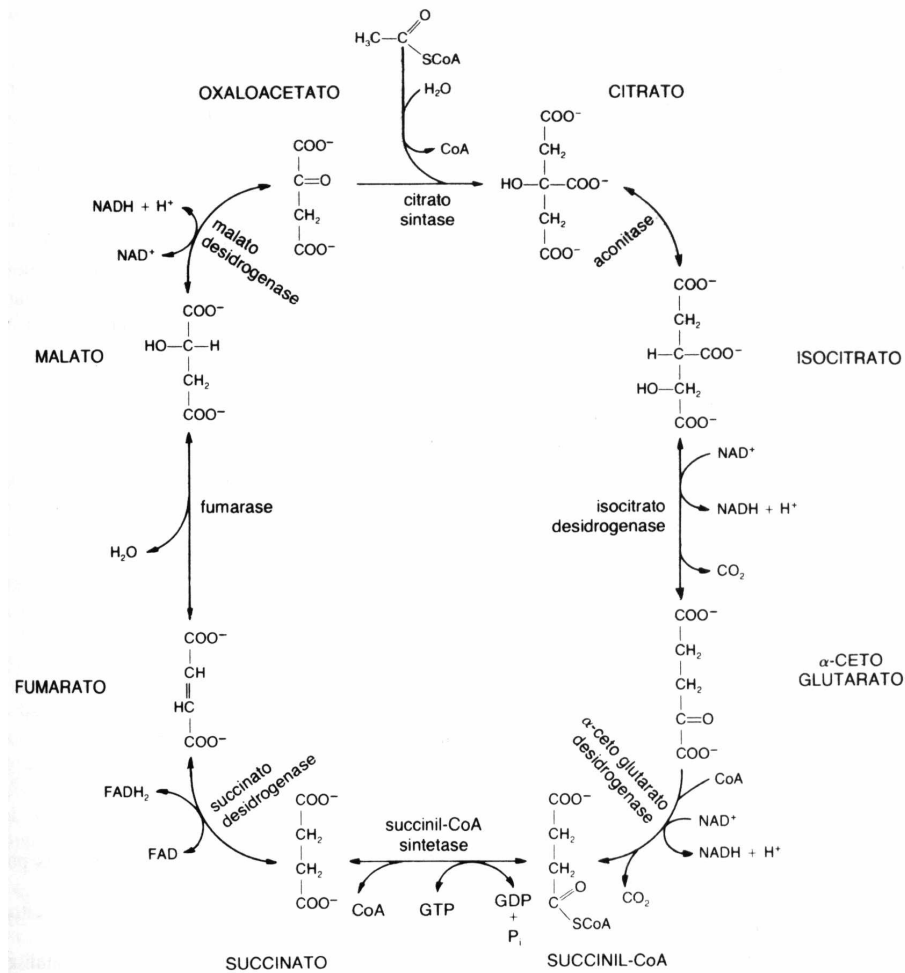


Aerobiose

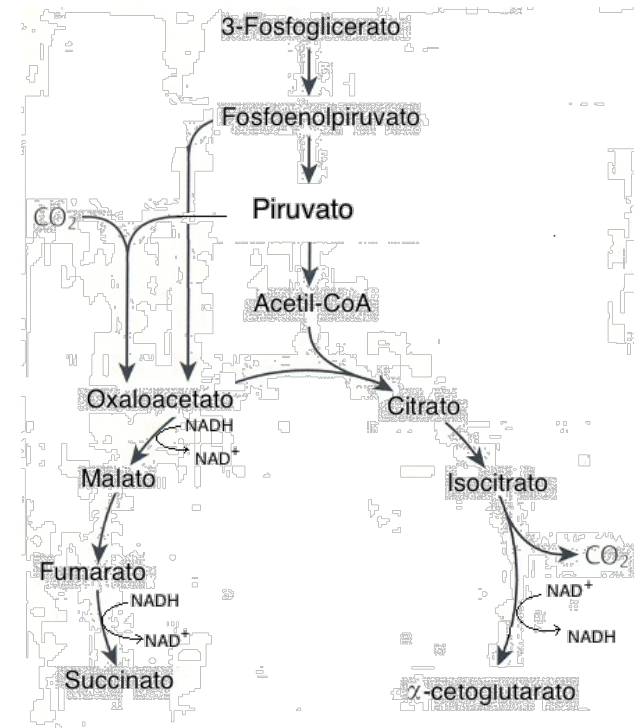
B



Anaerobiose

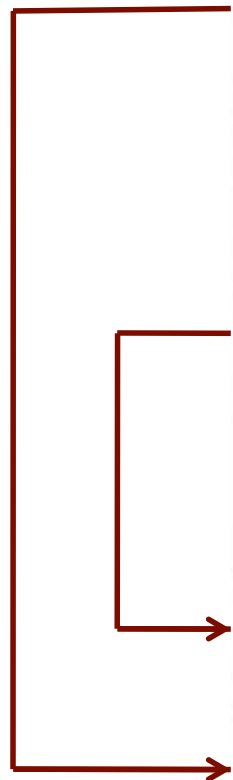


Ciclo de Krebs.

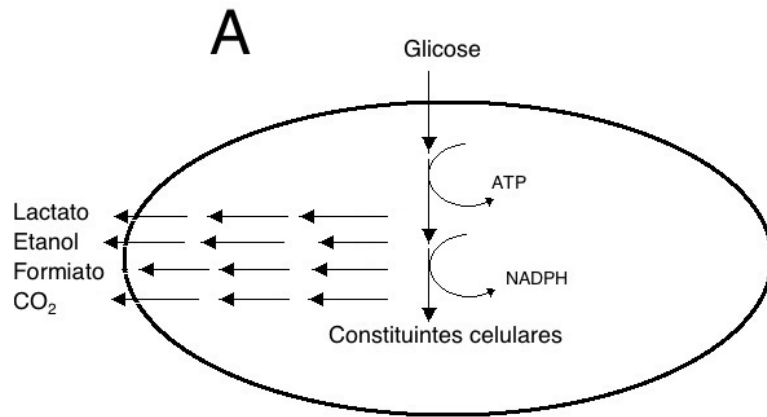


**Alguns Pares Redox de Importância Biológica e
seus Potenciais de Oxidorredução Padrão**

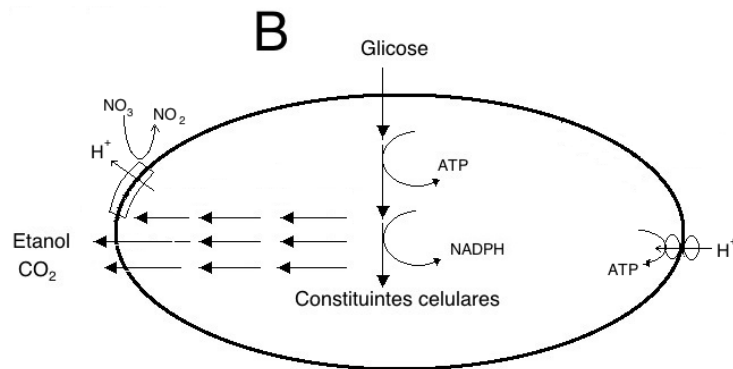
<i>Par Redox</i>	<i>E°' (V)</i>
2H ⁺ /H ₂	- 0,41
NAD ⁺ /NADH	- 0,32
S ⁰ /HS ⁻	- 0,27
CO ₂ /CH ₄	- 0,24
SO ₄ ²⁻ /HS ⁻	- 0,22
Piruvato/lactato	- 0,19
Fumarato/succinato	+ 0,03
Ubiquinona ox/red.	+ 0,11
Citocromo aa3 ox/red	+ 0,39
NO ₃ ⁻ /NO ₂ ⁻	+ 0,43
Fe ³⁺ /Fe ²⁺	+ 0,77
O ₂ /H ₂ O	+ 0,82



Heterotróficos

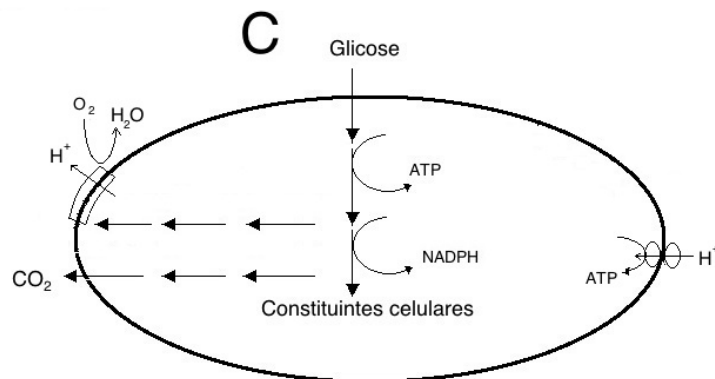


Sem O₂ **FERMENTAÇÃO**



Sem O₂ com outro acceptor final de eletrons

RESPIRAÇÃO ANAERÓBIA



Com O₂

RESPIRAÇÃO AERÓBIA

