Lactic metabolism revisited: Metabolism of lactic acid bacteria in food fermentations and food spoilage

Michael G. Gänzle

University of Alberta, Department of Agricultural, Food and Nutritional Science, Edmonton, Canada

Short title: **Lactic metabolism revisited**

Michael Gänzle

University of Alberta, Dept. of Agricultural, Food and Nutritional Science

4-10 Agriculture/Forestry Centre

Edmonton, AB,

Canada, T6G 2P5

phone: + 1 780 492 0774

fax: + 1 780 492 4265

e-mail: mgaenzle@ualberta.ca

Abstract

Sensory properties, shelf life, and safety of a majority of fermented foods are determined by the metabolic activity of food fermenting lactic acid bacteria. This communication reviews major metabolic routes of lactic acid bacteria, and indicates how metabolism is influenced by the environmental conditions or manipulated for improved control of food fermentations. Emphasis is placed on homofermentative and heterofermentative metabolism of carbohydrates, organic acids, and the conversion of amino acids with major impact on food safety and quality. In addition to the role of lactic metabolism in food fermentations, their implications for food spoilage is discussed.

Highlights

- Homolactic metabolism generally generates lactate as main metabolite.
- Pyruvate can be diverted to acetate or acetoin as alternative end products
- Heterolactic metabolism generates lactate and acetate or ethanol as main metabolites
- The availability of substrates for cofactor regeneration determines acetate formation
- Catabolism of arginine and glutamine contributes to acid resistance of LAB

Introduction.

The term "lactic acid bacteria" (LAB) describes as group of Gram-positive bacteria that share metabolic and physiological characteristics [1, 2, 3]. Suitable criteria to define the term LAB have been lacking for most of the 20th century and the term has been associated with food-fermenting or probiotic organisms, often including bifidobacteria. Currently, the term LAB describes organisms in the order *Lactobacillales* [4], confirming the suggestion that LAB constitute a phylogenetically homogenous group [1]. LAB include environmental organisms, members of plant microbiota, commensals of humans and animals, and opportunistic or obligate pathogenic organisms [4]. Five of the 6 families of LAB also include food fermenting organisms [4]; *Lactobacillaceae* and *Leuconostococcaceae* comprise predominantly non-pathogenic organisms with a safe tradition of use in food fermentations (Fig. 1) [4]. Food-fermenting LAB excel at exploitative competition and inhibit competitors by combining rapid utilization of abundant carbohydrates with accumulation of lactic and acetic acids. The evolution of LAB is shaped by reduction of genome size to achieve niche adaptation [5]. The reduction of the genome size was associated with abandoning the metabolic efficiency and versatility that are characteristic of the closely related bacilli. Abandoning the metabolic efficiencies of aerobic or anaerobic electron transfer chains, however, enables LAB to adhere to an "iron free diet" and to occupy plant or animal associated ecological niches where lack of iron limits bacterial growth [6]. LAB dominate fermentation microbiota in a majority of fermented foods (Fig. 1) but are also relevant as food spoilage organisms.

Metabolism of lactic acid bacteria: an overview

LAB have been classified as obligate homofermentative, facultative heterofermentative, and obligate heterofermentative [1, 2, 3]. The pentose phosphate pathway for homofermentative

fermentation of pentoses (Fig. 2) [7], however, is not accommodated in this classification. Moreover, major metabolic differences and branching points are dependent on the pathway employed for fermentation of hexoses rather than the ability to ferment pentoses (Table 1). In LAB fermenting glucose via the Emden Meyerhoff pathway (Fig. 2A), carbohydrates are preferentially transported by PTS systems, metabolism of sugars other than glucose is subject to carbon catabolite repression, pyruvate is the central branching point of metabolism, and fructose is exclusively used as carbon source (Table 1) [2, 8, 9]. In LAB fermenting glucose via the phosphoketolase pathway (Fig. 2B), PTS systems are not functional, metabolism of disaccharides is preferred over glucose fermentation, acetyl-phosphate is the central branching point of metabolism, and fructose is preferentially or exclusively reduced to mannitol (Table 1) [8, 10]. This communication aims to summarize recent advances related to lactic metabolism with emphasis on respiration, homolactic fermentation of pentoses, the utilization of lactate and diols, and their relevance for food quality.

Homolactic metabolism of hexoses and pentoses

Pyruvate is the key branching point of homolactic metabolism of hexoses (Fig. 2). The fate of pyruvate depends on the availability of oxygen and substrates. Anaerobic metabolism under substrate limitation is mediated mainly by pyruvate formate lyase (Fig. 3A) [7, 9]. Lactate is the main product of metabolism when the fermentable carbohydrates are abundant (Fig. 3B). Aeration allows the alternative regeneration of co-factors (Fig. 3C) but lactate generally remains the major metabolite of most LAB growing aerobically [11, 12, 13].

Many LAB are conditionally respiring [14]. LAB are auxotroph for heme (all LAB) and menaquinone (some LAB) but the availability of heme (and menaquinone) in the fermentation

79 substrate supports cofactor recycling and proton export by respiration (Fig. 3D) [15]. Respiration
80 shifts metabolism towards acetate and acetoin as major metabolites (Fig. 4) [6,16].

81 Homolactic LAB occur as sole fermentation microbiota in many in meat and dairy fermentations
82 and the fermentation of condiments at high salt concentrations; in vegetable and cereal
83 fermentations, they are found in association with heterolactic LAB (Fig. 1). Homofermentative
84 metabolism of carbohydrates in food yields lactate as sole or major product of metabolism (Fig.
85 1); exceptions include soy fermentations with *T. halophilus* where low concentrations of hexoses
86 favour metabolism by pyruvate formate lyase (Fig 1). *Carnobacterium* spp., which grow on
87 vacuum packaged meats and fish, preferentially metabolize hexoses via pyruvate formate lyase
88 [4].

89 Food fermentations with LAB are not aerated (Fig. 1) and thus do not support respiration. The
90 cytochrome oxidase of LAB, however, is active at low oxygen concentrations and may
91 contribute to oxygen elimination during initial stages of food fermentations [14]. Genes required
92 for respiratory metabolism are expressed even in the absence of heme and oxygen, suggesting a
93 preference of LAB for respiration whenever possible [12]. Respiration has become a valuable
94 tool in the production of starter cultures. Oxidative stress and the oxidation of membrane lipids is
95 a major factor limiting the shelf life of frozen or dried LAB for use as starter or probiotic
96 cultures. Respiratory metabolism increases the biomass yield as well as the resistance to
97 oxidative stress and thus improves the yield in large-scale culture production [14,17,18].

98 Acetoin formation impacts food quality even if it is only a minor metabolite. Chemical oxidation
99 of α-acetolactate, an intermediate of acetoin formation, yields diacetyl, which impacts the flavour
100 of beer, wine, bread, and dairy products. Diacetyl formation in beer constitutes a spoilage event

while the compound is a desired contributor to the flavour of wine and dairy products (Fig. 1). Diacetyl formation by *Lc. lactis* is supported by the availability of oxygen and citrate as alternative substrates to support cofactor regeneration [2, 9].

Homofermentative metabolism of pentoses has been initially observed in an isolate later classified as *Lactobacillus vini* [3]; the metabolic pathway was described in *Lc. lactis* and enterococci (Fig. 2C) [7]. The conversion of 3 mol pentoses through transketolase and transaldolase reactions yields 5 mol of triose phosphate; the net energy gain in the pathway (7 mol of ATP / 3 mol of pentose) is thus slightly higher when compared to pentose catabolism through the phosphoketolase pathway (Fig. 2D). During metabolism of pentoses through the pentose phosphate pathway by *Lc. lactis* and enterococci, a significant proportion of pyruvate is metabolised by pyruvate formate lyase (Fig. 3A) [7]. The occurrence of *L. vini* in wine or industrial fermentation of ethanol [19] implies that the metabolic pathway supports competitiveness in ecosystems where hexoses were depleted by yeast fermentation.

Heterofermentative metabolism of hexoses and pentoses.

Heterofermentative LAB employ the phosphoketolase pathway for carbohydrate metabolism (Figs. 2 and 5A). The energy yield of the pathway is only one ATP per glucose and most heterofermentative LAB grow poorly with glucose as sole carbon source [10]. Two metabolic strategies improve metabolic efficiency of the pathway; (i) phosphorolytic cleavage of disaccharides to eliminate the need phosphorylation at the expense of ATP [8]; (ii) the use of alternative electron acceptors to convert acetyl-phosphate to acetate instead of ethanol [10]. When combined, these metabolic shifts increase the yield of ATP per glucose to 2.5. Accordingly, metabolism of maltose sucrose and raffinose by disaccharide phosphorylases, and metabolism of pentoses is not repressed by glucose [8, 10].

Heterolactic metabolism generally converts pyruvate from hexoses and pentoses to lactate; however, alternative end products of pyruvate are observed in citrate and pyruvate metabolism of *Leuconostoc* spp and *Oenococcus oeni* [20,21**] and lactate utilization of *L. buchneri*. The use of alternative electron acceptors to oxidise reduced cofactors allows heterofermentative LAB to use acetyl-phosphate for ATP synthesis [10]. Some heterofermentative LAB do not harbour an alcohol dehydrogenase and do not ferment glucose in the absence of alternative electron acceptors [3, 22].

Oxygen and fructose are the most significant electron acceptors for recycling of reduced co-factors (Fig. 5B) [10] and many strains have the capacity for respiration [11, 21**]. However, some strain in the *L. reuteri* group do not grow aerobically and most *Weissella* spp. do not reduce fructose to mannitol [10, 23]. Other compounds that are reduced with concomitant oxidation of NAD(P)H include oxidized glutathione [10], a wide range of aldehydes and ketones including aldehydes originating from lipid oxidation [10], α-keto acids originating from amino acid transamination [24], and quinic acid [25]. Recent studies indicate that the reduction of hydroxycinnamic acids also contributes to cofactor recycling [26].

Heterofermentative LAB occur in most plant fermentations including wine, cider, cereal porridges and sourdough, and sauerkraut or kimchi (Fig. 1). Their competitiveness in plant substrates reflects the availability of maltose, sucrose, or raffinose, and alternative electron acceptors. The availability of alternative electron acceptors increases the growth rate of *L. reuteri* by 30 – 50% and hence contributes substantially to the competitiveness in food fermentations [27]. Cofactor recycling by heterofermentative LAB impacts food quality because acetate production is increased and the redox potential as well as the antioxidant capacity of fermented foods are strongly influenced. Acetate has antibacterial and antifungal activity, and impacts

147 flavour in addition to contributing to sour taste. Excessive acetate formation is considered a
148 spoilage event in the production of alcoholic beverages [28]; however, moderate levels of acetate
149 improve the flavour of baked goods (Fig. 1). Acetic acid formation in sourdoughs is readily
150 adjusted by supplementation with sucrose [10]. Sucrose addition to support production of
151 sufficient amounts of exopolysaccharides in sourdough, however, results in excessive acetate
152 production and the use of *Weissella* spp. that are unable to utilize fructose as electron acceptor is
153 preferred [23].

154 The requirement for co-factor regeneration to achieve efficient heterofermentative metabolism of
155 hexoses also influences the redox-potential of food fermentations [29*] and substantially alters
156 flavour formation in lipid oxidation pathways [30] as well as thiol exchange reactions [31].
157 Thiol-exchange reactions catalysed by heterofermentative LAB reduce allergenic proteins in
158 food fermentations [32].

159 **Utilization of lactate, glycerol, and diols.**

160 Anaerobic degradation of lactate (Fig. 6A) was described in silage and sourdough fermentations
161 [33] and as spoilage event in pickles [34]. In these fermentations, lactate utilizing lactobacilli are
162 associated with primary lactate producing fermentation organisms [34]. Growth of *L. buchneri* is
163 not supported by lactic acid as sole carbon source; however, co-fermentation of hexoses and
164 lactate yields acetate and 1,2 propanediol as main products [33]. With pyruvate as substrate, the
165 pathway produces equimolar amounts of acetate and lactate (Fig. 6B) [20].

166 Glycerol and 1,2 propanediol are metabolized through the same metabolic pathway (Fig. 6C)
167 [35,36]. Co-metabolism of glycerol or 1,2 propanediol and fermentable carbohydrates yields
168 mainly the reduced products 1,3 propanediol or propanol [33]. In the absence of fermentable
169 carbohydrates, the oxidising and reducing branches of the pathway operate simultaneously and

glycerol or 1,2 propanediol metabolism yields hydroxypropanoic acid or propanoic acid and 1,3 propanediol or propanol, respectively, in approximately equimolar amounts (Fig. 6C, [33,37*]. This metabolic pathway supports ATP generation and slow growth with glycerol or 1,2 propanediol as sole carbon source.

Metabolism of glycerol by homofermentative LAB also yields 1,3 propanediol [38] but in contrast to heterofermentative lactobacilli, co-factors regeneration by formation of 1,3 propanediol supports simultaneous glycerol catabolism by the glycerol kinase pathway (Fig. 6D) with propanediol, acetate and 2,3 butanediol as alternative end products [38].

Metabolism of glycerol and 1,2 propanediol constitutes spoilage in beer, wine, cider, and pickles. These ecosystems are characterized by paucity of fermentable carbohydrates and electron acceptors, which were consumed by primary fermentation organisms (Fig. 1). The metabolism of yeast and lactate metabolism by *L. buchneri* provide glycerol and 1,2-propanediol, respectively, as substrates. In pickles, lactate consumption and diol metabolism results in an increase of the pH and compromises the hygienic stability of the product [34]. The growth of a secondary lactic microbiota in cider and beer may result in off flavour [28]. 3-Hydroxypropionic aldehyde that is formed during maturation of cider and wine is chemically transformed to acrolein, which is responsible for undesirable peppery flavours in alcoholic beverages [39].

Glycerol metabolism generates several antimicrobial compounds contributing to food and feed preservation. The conversion of lactate to acetate and propionate by co-fermentation of primary lactate producers, lactate-utilizing *L. buchneri*, and propanediol-utilizing *L. diolivorans* delays the fungal spoilage of bread [33]. Hydroxypropionaldehyde or reuterin is a more potent antimicrobial compound than propionic or acetic acids, however, this intermediate accumulates only when glucose is limited and glycerol is present in excess. Supplementation of cheese milk

193 with glycerol and *L. reuteri* as adjunct culture allowed the generation of active levels of reuterin
194 and the reduction of spore counts of *Clostridium tyrobutyricum* [40*].

195 **Metabolism of citrate and malate.**

196 LAB produce succinate, lactate, acetate and ethanol, or acetoin as alternative end products from
197 citrate (Fig. 7). The conversion of citrate to succinate maximises the oxidation of reduced co-
198 factors (Fig. 7) [2, 10] but does not include a proton-consuming decarboxylation reaction.
199 *T. halophilus* converts citrate via pyruvate formate lyase to acetate and ethanol, thus combining
200 one proton-consuming decarboxylation reaction with ATP generation [41]; likewise, many
201 heterofermentative lactobacilli convert citrate to lactate, thus combining one proton-consuming
202 decarboxylation with regeneration of reduced NADH [10]. Citrate is converted to the alternative
203 end products acetoin and lactate by *Lc. lactis*, *Leuconostoc* spp. and *O. oeni* [2]. Citrate
204 conversion to acetoin proceeds via two proton consuming decarboxylation reactions, prevents
205 accumulation of an organic acid, and thus contributes to pmf generation and acid tolerance (Fig.
206 7) [42]. Product formation from citrate in *O. oeni* is dependent on the pH. Low pH favours
207 acetoin formation to maximise the contribution to pmf generation while neutral pH favours
208 lactate production to allow regeneration of reduced co-factors [42, 43].

209 The impact of acetoin formation on food flavour and quality was discussed above. Malolactic
210 fermentation by *O. oeni* not only reduces the acid level and hence the acid taste of wine,
211 particularly white wines, but also changes the concentration of flavour volatiles through
212 carbohydrate and citrate metabolism [55].

213 **Amino acid metabolism in response to acid stress**

Carbohydrate metabolism by LAB in food fermentations is often limited by acidification and low pH (Fig. 1). Low pH shifts lactic metabolism from hexose fermentation to utilization of amino acids. Glutamine, glutamate, and arginine play a major role in pH homeostasis and stationary phase survival of LAB (Fig. 8) [42]. Arginine catabolism via the arginine deiminase pathway generates metabolic energy by substrate level phosphorylation and increases intracellular and extracellular pH (Fig. 8B) [10]. The contribution of arginine conversion to acid resistance appears to be optimal at pH values higher than 3.5 while the protective effect of the glutamine / glutamate system extends to lower pH-values [44**]. Analysis of the expression of the arginine deiminase pathway also suggests that acid resistance by amino acid decarboxylation takes priority over the arginine deiminase pathway [44**, 45, 46]. Some LAB maintain an agmatine deiminase pathway that operates analogous to the arginine deiminase pathway and also increases acid resistance [47,48]. The use of agmatine by LAB indicates a trophic relationship between LAB and agmatine producing organisms such as *Enterobacteriaceae*.

Glutamine deamidation contributes to acid resistance in *L. reuteri* and other LAB [10, 44**]. The efficiency of the glutamate and glutamine systems to extrude protons is strongly dependent on the selection of ion species that are transported (Fig. 8A) [44**]. In *E. coli*, the ion selective antiporter GadC exchanges extracellular glutamate or glutamine with GABA [49*]. Import of uncharged glutamate or glutamine coupled to export of positively charged GABA couples glutamate decarboxylation to proton consumption, the net export of one positive charge, and hence pmf generation (Fig. 8A) [44**, 49*]. Expression of glutamate decarboxylase in lactobacilli is upregulated upon entry into the stationary phase of growth [44**] and by acid stress [44**, 50]. Moreover, glutamate decarboxylase of lactobacilli exhibits a sharp pH optimum at pH 4.5 and is essentially inactive at neutral pH [51]. Histidine decarboxylase and

tyrosine decarboxylase also contribute to pH homeostasis in LAB (Fig. 8C) [46]. Comparable to glutamate decarboxylation, intracellular consumption of protons and electrogenic antiport of histidine and histamine generate a proton motive force [42].

The metabolism of amino acids significantly impacts the quality of long-ripened fermented foods (Fig. 1). Glutaminase activity of LAB accumulates glutamate to levels exceeding the taste threshold and thus contributes to the umami, savoury taste of bread and long-ripened cheeses [52*,53]. Glutamate also accumulates to taste active concentrations in fish, meat and soy fermentations but meat-derived (meat) or fungal (soy) glutaminases may account for this accumulation. Strain specific glutamate decarboxylase activity of LAB has been described in dairy, meat, and in cereal fermentations and allows accumulation of γ-aminobutyrate (GABA) as bioactive ingredient. Particularly in East Asian countries, GABA is well-recognized for its relaxing and health-promoting properties and LAB are a major means of producing GABA or GABA-enriched foods [54].

Arginine conversion by LAB in food constitutes spoilage or contributes to flavour. Acid resistance in beer spoiling LAB is supported by arginine [50]. Citrulline, an intermediate of the arginine deiminase pathway (Fig. 8), is a precursor to the formation of toxic ethyl carbamate in wine and spirits and ADI-negative strains are preferred as starter cultures to initiate malolactic fermentation of wine [55]. In baked goods, arginine conversion by sourdough LAB provides ornithine as precursor to the character impact compound of wheat bread crust, 2-acetyl-1-pyrroline, and is thus a major contributor to crust odour [10].

Decarboxylation of amino acids other than glutamate generates biogenic amines with adverse implications for human health when consumed with alcohol or in combination with monoamine oxidase inhibitors. Histamine and tyramine are the major biogenic amines in fermented foods

and their formation is attributable to LAB [56]. Biogenic amine formation is controlled by selection of competitive and decarboxylase negative starter cultures that suppress decarboxylase positive microbiota throughout fermentation [57].

Conclusions

Lactic metabolism has been investigated for over a century but recent genomic analyses of LAB have allowed elucidation of several novel metabolic pathways that impact food quality [8, 7, 37, 44]. Current knowledge on major metabolic pathways of LAB provides a basis for the control of lactic metabolism in food but additional metabolic pathways that make only minor contributions to the overall metabolic flux but also impact food quality remain to be elucidated. Examples include the conversion of amino acids to flavour volatiles [24], esterases, decarboxylases, and hydratases involved in conversion of phenolic compounds [25], and enzymes involved in lipid metabolism. Moreover, awareness of the diversity of fermented foods (Fig. 1) and the development of starter cultures for fermented foods in emerging economies will lead to the discovery of LAB with novel metabolic properties.

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Figure legends

Figure 1. Periodic Table of Fermented Foods providing an overview on the diversity of products, fermentation organisms, and raw materials. Fermented foods are grouped by product category and ranked within a group by flavour intensity or ripening time where applicable. Colour coding of specific fields indicates the presence of specific groups of fermentation organisms (see key on top of table); typical organisms, typical concentration of metabolites, and characteristic ripening / fermentation times are indicated. Water activities are not presented for dry foods or alcoholic beverages. Food products are generally listed in the language of origin; translations are provided where possible. The figure is formatted for large scale (A0) printing.

Figure 2. Overview on carbohydrate fermentation lactic acid bacteria. Major end products of metabolism are printed in bold; branching points of metabolism or "metabolic switches" are underlined. The formation of reduced / oxidised co-factors (printed in white on blue background or blue, respectively) is indicated if it occurs upstream / downstream of relevant metabolic branching points; ATP synthesis (printed in red) is shown to indicate the net ATP yield of the metabolic pathway. **Panel A.** Homofermentative metabolism of hexoses via the Embden-Meyerhoff Pathway. **Panel B.** Heterofermentative metabolism of hexoses via the phosphoketolase pathway. **Panel C.** Homofermentative metabolism of pentoses via the pentose phosphate pathway. **Panel D.** Heterofermentative metabolism of pentoses via the phosphoketolase pathway. Drawn according to [2, 3, 7, 10].

Figure 3. Alternative fates of pyruvate in homofermentative lactic acid bacteria. Major end products of metabolism are printed in bold. The formation of reduced and oxidised co-factors is indicated as white font on blue background or as blue font, respectively; ATP synthesis in red font. Dashed arrows indicate chemical conversions.

Panel A. Metabolism by pyruvate formate lyase. Equal proportions of pyruvate are reduced to ethanol to regenerate reduced co-factors, or oxidised to acetate to synthesise ATP. Pyruvate formate lyase is inhibited by an abundant substrate supply and by low pH, and is inactivated by oxygen [3, 7, 9]. In *Lc. lactis*, sugars that are imported by PTS systems favour pyruvate conversion to lactate while non-PTS sugars favour metabolism via pyruvate formate lyase [9].

Panel B. Metabolism by lactate dehydrogenase. This metabolic route is dominant at anaerobic or aerobic conditions when fermentable carbohydrates are abundant, i.e. in most food fermentations.

Panel C. Metabolism by pyruvate oxidase or α-acetolactate synthase. Acetate and acetoin are minor products of most organisms at aerobic conditions; however, lactate may be converted to acetate during the stationary phase of growth [11, 12] and *Tetragenococcus halophilus* produces acetate as main product at aerobic conditions [13]. Acetate is formed by pyruvate oxidase and acetate kinase activities [11].

Panel D. Oxidation of reduced co-factors at aerobic conditions and at aerobic conditions supporting respiration. LAB are conditionally respiring dependent on the availability of heme; many organisms also require menaquinone supplementation for respiration. Cofactor recycling and proton extrusion by the respiratory chain allow energy generation by the F_0F_1ATPase [12, 15] and shifts metabolism towards acetate and acetoin as major products. Acetate formation with concomitant ATP generation by acetate kinase is energetically favourable, however, acetoin formation prevents acidification of the growth medium and thus contributes to pH homeostasis [16].

Enzymes are indicated by numbers as follows: **1,** pyruvate formate lyase; **2,** acetaldehyde dehydrogenase; **3,** alcohol dehydrogenase; **4,** phosphotransacetylase; **5,** acetate kinase; **6,** lactate

dehydrogenase; **7,** pyruvate oxidase; **8,** pyruvate dehydrogenase; **9,** acetolactate synthase; **10,** acetolactate dehydrogenase, **11,** NADH oxidase or NADH peroxidase. MQ and MQH_2, menaquinone / menaquinol couple; NoxAB, type II NADH dehydrogenase complex; CydAB, respiratory cytochromes.

Figure 4. Metabolism of *Lc. lactis* MG1363 at anaerobic conditions (black symbols), aerobic conditions (gray symbols), and aerobic conditions supporting respiration (open symbols). Shown are the concentrations of glucose (▲), lactate (●), acetate (▼), and acetoin (■). Data are re-plotted from [6].

Figure 5. Alternative fates of acetyl phosphate and pyruvate in hexose metabolism by heterofermentative lactic acid bacteria. Major end products of metabolism are printed in bold. The formation of reduced and oxidised co-factors is indicated as white font on blue background or as blue font, respectively; ATP synthesis in red font; proton consuming decarboxylation reactions are indicated in gray. Note that the ATP yield does not account for the phosphorylation of glucose because disaccharide phosphorylases produce glucose-1-P without expending ATP. **Panel A.** Anaerobic metabolism in the absence of alternative electron acceptors.

Panel B. Metabolism in the presence of alternative electron acceptors.

Enzymes are indicated by numbers as follows: **1,** phosphoketolase; **2,** phosphotransacetylase, acetaldehyde dehydrogenase, and alcohol dehydrogenase; **3,** Emden-Meyerhoff pathway and lactate dehydrogenase; **4**, acetate kinase; **5,** NADH oxidase, NADH peroxidase or respiratory chain; **6**, NAD(P)H dependent dehydrogenases reducing organic substrates including fructose, oxidised glutathione, and a wide range of aldehydes and ketones including aldehydes originating from lipid oxidation and α-keto acids originating from amino acid transamination, quinic acid, and hydroxycinnamic acids. Drawn with information from [10, 24, 25, 26, 30, 31].

Figure 6. Catabolism of lactate, pyruvate, diols, and glycerol by lactic acid bacteria. Major end products of metabolism are printed in bold. The formation of reduced and oxidised co-factors is indicated as white font on blue background or as blue font, respectively; ATP synthesis in red font.

Panel A. Lactate metabolism by *Lactobacillus buchneri*. In the oxidising branch of the pathway, lactate is oxidised to acetate with concomitant formation of ATP. The reducing branch of the pathway yields 1,2 propanediol to regenerate reduced co-factors. Homologues of lactaldehyde dehydrogenase and propanediol dehydrogenase in *L. buchneri* are found in genomes of many lactobacilli but this metabolism has been described only for *L. buchneri, L. parabuchneri,* and *L. parafarraginis* [33, 34].

Panel B. Pyruvate metabolism in *Leuconostoc* spp. and *Oenococcus oeni* [20].

Panel C. Conversion of glycerol and diols. Diol metabolism in *L. reuteri* occurs in a proteinaceous microcompartment, likely to protect against the toxic intermediate reuterin [35]. The oxidative and ATP-generating branch of the metabolic pathway generates 3-hydroxypropionate and propionate, respectively, from glycerol and 1,2-propanediol while the reducing branch regenerates the reduced co-factors and produces 1,3 propanediol and propanol, respectively. In co-fermentation with hexoses, only the reducing branch of the pathway is used to support ATP-generation from acetyl-P. This pathway or parts of this pathway were shown to be operating in *Lactobacillus diolivorans*, *Lactobacillus reuteri*, and *Lactobacillus collinoides*. Drawn with information from [33, 36, 37].

Panel D. Glycerol kinase pathway. This pathway is used for glycerol catabolism by *Pediococcus pentosaceus*; enzymes of this pathway may also result in glycerol formation from pyruvate by heterofermentative LAB under stress conditions [38].

Enzymes are indicated by numbers as follows: **1,** lactate dehydrogenase; **2,** pyruvate dehydrogenase; **3,** phosphotransacetylase and acetate kinase; **4,** lactaldehyde dehydrogenase / glycolaldehyde dehydrogenase; **5,** propanediol dehydrogenase; **6;** glycerol / propanediol dehydratase; **7,** phosphotransacylase; **8,** propionate kinase; **9,** propane(di)ol oxidoreductase; **10 – 11,** glycerol kinase pathway; glycerol kinase and glycerol phosphate dehydrogenase to dihydroxyacetone-3-phosphate; further conversion by the Emden-Meyerhoff pathway and pyruvate dehydrogenase or α-acetolactate synthase yields acetate and 2,3 butanediol as end products. The enzymes related to lactate metabolism by *L. buchneri* are designated as per annotation of the *L. buchneri* genome sequence (Accession No. NC_015428.1).

Figure 7. Alternative fates of citrate and malate in heterofermentative lactic acid bacteria to support pH homeostasis or cofactor regeneration. Major end products of metabolism are printed in bold. The formation of reduced and oxidised co-factors is indicated as white font on blue background or as blue font, respectively; ATP synthesis in red font; proton consuming decarboxylation reactions are indicated in gray. Dashed arrows indicate chemical conversions. Citrate is converted to succinate to achieve regeneration of two reduced cofactors, or to acetoin to achieve proton consumption and pmf generation by two decarboxylation reactions. Citrate conversion to lactate or acetate and ethanol combined oxidation of one mole NADH and one decarboxylation reaction. Lactobacilli convert citrate to succinate or lactate [2, 10]; *T. halophilus* converts citrate preferentially via pyruvate formate lyase acetate and ethanol [13, 41]; *Lc. lactis*, *Leuconostoc* spp. and *O. oeni* convert citrate to the alternative end products acetoin or lactate [2, 42, 43].

Enzymes are indicated by numbers as follows: **1,** citrate lyase; **2,** malate dehydrogenase; 3**,** fumarate hydratase, **5,** succinate dehydrogenase; **6,** oxaloacetate decarboxylase; **7,** malolactic

enzyme; **8**, lactate dehydrogenase; **9,** acetolactate synthase; **10,** acetolactate dehydrogenase; **11,** pyruvate formate lyase; **12,** acetaldehyde dehydrogenase; **13,** alcohol dehydrogenase; **14,** phosphotransacetylase; **15,** acetate kinase

Figure 8. Acid resistance that are mechanisms based on the conversion of amino acids. Protons that are consumed in enzymatic reactions are printed in bold red font.

Panel A. Conversion of glutamine to glutamate and γ-aminobutyrate (GABA). Charges of substrates and metabolites are drawn to reflect an intracellular and extracellular pH of 4.25. Drawn with information from [42, 44**, 49*].

Panel B. Conversion of arginine to ornithine [10]. The agmatine deiminase pathway in *Lc. lactis* and *L. brevis* operates analogously to convert agmatine to putrescine [47, 48].

Panel C. Decarboxylation of histidine, phenylalanine, or tyrosine, shown at the example of histidine. Charges of substrates and metabolites are drawn to reflect an intracellular and extracellular pH of 4.25. [46, 48]

Table 1. Comparison of metabolic properties of homolactic and heterolactic metabolism.

	Homolactic metabolism	**Heterolactic metabolism[a)]**
Metabolism of glucose	Emden-Meyerhoff pathway	Phosphoketolase pathway[b)]
Metabolism of galactose	Tagatose pathway and / or Leloir pathway	Leloir pathway
Metabolism of fructose	Emden Meyerhoff pathway	Mannitol-dehydrogenase[c)], phosphoketolase pathway
Metabolism of pentoses	Phosphoketolase pathway or pentose phosphate pathway; sequential metabolism of hexoses and pentoses	Phosphoketolase pathway; simultaneous metabolism of hexoses and pentoses
Preferred substrate	Glucose	Fructose[c,d)], sucrose and / or maltose
Alternative products from pyruvate	Formate, ethanol, and acetate; lactate, or acetoin	Lactate, acetate, (acetoin)[e)]
Alternative end products from acetyl-phosphate	Acetate	Ethanol or acetate[e)]
Products of lactate metabolism	Acetate, formed by stationary cultures at aerobic conditions, or acetoin	1,2 Propanediol and acetate[f)]

[a)] All species in the *Lactobacillus vaccinostercus,* and *L. collinoides* groups, most species in the *L. reuteri, L. brevis, L. buchneri* and *L. fructivorans* groups, *L. rossiae, L. siliginis*, *L. floricola;* and all *Leuconostococaceae* (Genera *Fructobacillus*, *Leuconostoc, Oenococcus*, and *Weissella*).

[b)] not all heterofermentative LAB grow with glucose as sole carbon source.

[c)] Mannitol dehydrogenase is absent in most strains of *Weissella*

[d)] *Fructobacillus* spp. preferentially ferment fructose. Several *Fructobacillus* species do not produce ethanol from fructose as they apparently lack an alcohol dehydrogenase.

[e)] Acetoin formation during co-metabolism of hexoses or pentoses and citrate is observed in *Lu. mesenteroides* and *Oenococcus* spp. but not in heterofermentative lactobacilli. Diacetyl results from chemical oxidation of α-acetolactate, an intermediate of acetoin formation.

[f)] This pathway is found only in *L. buchneri* and few other species.

Key to description of fermented foods

Yeasts
Other organisms
Bacilli
Staphylococci
Moulds

Lactic acid bacteria (Lactobacillales)
Propionibacteria
Actinobacteria
Acetic acid bact.

number → 109 Westphalia, D ← Typical Origin
Name → Pumper-nickel
Main ingredient → rye
pH → 5.0
aw → 0.96
Fermentation time → 1 d
L. sanfrancisc. C. humilis ← Fermentation organisms
L: 0.15; A: 0.01; G ← Selected metabolites

L	Lactate (mol / L)	2Ac	Diacetyl above flavour threshold
A	Acetate (mol / L)	G	Glutamate above taste threshold
E	Ethanol (%)	N	Ammonia above flavor theshold
P	Propionate (mol / L)	Ac	Acetaldehyde above flavor threshold

h:	hour	m:	month
d:	day	y:	year
w	week	c:	century

Period

1 White wines

1 Feder-weisser
Germany, Austria
grapes 3.5-4.0 n/a 2 - 8 d
S. cerevisiae E: 4 - 10

3 White wine
worldwide
grapes 3.5-4.0 n/a 1 - 5 y
S. cerevisiae *O. oeni* E: 8 - 10; L: <0.04

11 Champagne, Prosecco
Champagne (F), Italy
grapes 3.5-4.0 n/a 1 - 5 y
S. cerevisiae *O. oeni* E: 8 - 12

19 Vermouth
Italy
grapes 3.5-4.0 n/a 1 - 5 y
S. cerevisiae E: 16 - 18

37 Sherry
Spain
grapes 3.5-4.0 n/a >5 y
S. cerevisiae *Debaromyces* *L. plantarum* E: 15

55 Eiswein / Ice Wine
Germany, Canada
grapes 3.5-4.0 n/a 0.5 - 1 y
S. cerevisiae E: 12 - 16

87 Sake (清酒)
Japan
rice 3.1-4.4 *S. cerevisiae* n/a *L. plantarum* 6 - 12 m
A. oryzae *S. cerevisiae* E: 15 L: 0.02

2 Red wines

4 Red Wine
worldwide
grapes 3.5-4.0 n/a 1 y - 1c
S. cerevisiae (*O. oeni*) E: 12

12 Fruit wines
worldwide
fruits 3.5 - >5 n/a var.
S. cerevisiae (variable) E: >5

20 Botrytised wine
Germany
grapes 3.5-4.0 n/a 1 - 10 y
S. cerevisiae *B. cinerea* E: 8 - 12

38 Port wine
Duoro (Portugal)
grapes 3.5-4.0 n/a 1 y - 1c
S. cerevisiae E: 19 - 23

56 Eiswein / Ice Wine
Germany, Canada
grapes 3.5-4.0 n/a 0.5 - 1 y
S. cerevisiae E: 12 - 16

88 Shaoxing wine
Zhejiang (China)
rice 3.5-4.5 n/a 6 - 12 m
A. oryzae *S. cerevisiae* *M. purpureus* E: >14

3 Ciders

21 Cider
U.K., U.S.A
apples 3.5-4.0 n/a 4 d
S. cerevisiae E: 8

39 Cidre / Most
France, Spain, Suebia (D)
apples 3.5-4.0 n/a 2 - 4 w
S. cerevisiae *L. brevis* *Ac aceti* E: 5-8; L: 0.05

71 Ice Cider
Quebec (CAD)
apples 3.5-4.0 n/a 2 - 4 m
S. cerevisiae Lactic and acetic acid bact E: 8-11

103 Meijiu (梅酒).
China, Korea
prunes ? n/a ?
S. cerevisiae lactic acid baceria E: >12

4 Light Beer

22 American light
U.S.A.
corn 4.0 n/a 4 w
S. cerevisiae E: 5

40 Helles / Pilsner
Belgium, Bavaria (D), Pilsen (CZ)
barley 3.5-4.0 n/a 4 w
S. cerevisiae NSLAB E: 5; L: 0.1

72 Wheat / Weizen
Bavaria, Berlin
wheat 3.5-4.0 n/a 4 w
S. cerevisiae E: 5; L: 0.1

104 Chibuku
Botswana, Zimbabwe
sorghum 4.0 n/a 1 - 2 d
S. cerevisiae lactic acid bacteria E: 5; L: 0.1

5 Dark Beer

23 Dark Ale
U.K., Belgium
barley 3.5-4.0 n/a 4 w
S. cerevisiae E: 5

41 Munich Dunkel
Munich (D)
barley 3.5-4.0 n/a 4 w
S. cerevisiae E: 5

73 Stout
U.K.
barley 3.5-4.0 n/a 4 w
S. cerevisiae E: 5-6

105 Eisbock
Germany
barley 4.0 n/a 4 w
S. cerevisiae E: 8-14

6 Cereal beverages

24 Boza
Turkey, Bulgaria
wheat 3.5 0.98 24 h
Lu.mesenteroi *L. sanfrancisc* *Candida spp.* E: 1; L: 0.15

42 Mahewu
South Africa
corn 3.5 Malt 3.5 0.98 12 h
Lc. lactis *L. delbrueckii* *Sc. thermophil.* L: 0.12 *S. cerevisiae* *L. casei* E: 0.5; L: 0.01

74 Kvas (квас)
Russia, Ukraine
S. cerevisiae *Lu.mesenteroi* *L. casei* E: 0.5; L: 0.01

106 Bushera
Uganda
sorghum 3.5 - 4.5 0.98 1 - 4 d
L. fermentum *L. brevis* *L. plantarum* L: 0.12; A: 0.01

7 Cereal porridges

25 Koko
Ghana
millet 3.5 - 4.2 0.98 1 - 3 d
W. confusa *L. fermentum* *Pc. pentosaceus* L: 0.12

43 Mawe / Ogi
West Africa (Benin, Nigeria)
corn 3.8 - 4.2 0.98 1 - 3 d
L. fermentum *Pc. acidilactici* *Candida spp.* L: 0.12

75 Idli
India
rice 3.5 - 4.0 0.98 1 d
Lu *L. plantarum* *P. pentosaceus* L: 0.1 - 0.2

107 Ting
Botswana
sorghum 4.0 0.98 1 - 2 d
L. reuteri *L. fermentum* *L. plantarum* L: 0.12; A: 0.01

8 Bread (wheat)

26 Baguette
France
wheat 5.5-6.0 0.97 8 - 16 h
S. cerevisiae *L. sakei* *Pc. pentosaceus* L: 0.1; E: 0.5

44 Pannettone
Italy
wheat, egg 5.0 0.95 2 d
L. sanfrancisc. *L. pontis* *C. humilis* L: 0.1; A: 0.01

76 Mutschel
Reutlingen, D
wheat egg 5.5 0.96 1 d
L. sanfrancisc. *C. humilis* L: 0.1; A: 0.01

108 Sourdough Bread
Bay Area (U.S.)
San Francisco
wheat 4.5 0.96 1 d
L. sanfrancisc. *C. humilis* L: 0.12; A: 0.01

9 Bread (rye)

27 Light rye
Europe
wheat / rye 5.5-6.0 0.96 8 - 24 h
S. cerevisiae *L. pontis* *L. panis* L: 0.1; A: 0.02

45 Vollkornbrot
Germany
rye 4.5-5.5 0.96 1 d
L. sanfrancisc. *L. mindensis* *C. humilis* L: 0.1; A: 0.01

77 Ruisleipä
Finland
rye 4.5-5.0 0.97 1 d
L. sanfrancisc. *L. crispatus* *S. cerevisiae* L: 0.15; A: 0.02

109 Pumper-nickel
Westphalia, D
rye 5.0 0.96 1 d
L. sanfrancisc. *C. humilis* L: 0.15; A: 0.01; G

10 Soy and bean

28 Tempe
Indonesia
soy ~4.5 0.98 1 d
R. stolonifer *A. oryzae* phytase

46 豆腐乳 (fermented tofu)
China
soy ~6.0 0.98 2 - 3 d
Mucor spp. *Bc. subtilis* *M. purpureus* Monascur ubr anis

78 Black beans (豆豉)
China
beans ~6.0 0.94 6 m
Mucor spp. *M. purpureus* *Bc. subtilis* Monascur ubr anis

110 Natto (納豆)
Japan
soy 5.5-6.0 0.97 1 d
Bc. subtilis Polyglutamate

11 Condiments (soy and fish sauces)

29 Miso (味噌)
Japan
soy 4.0-5.0 0.90 1 - 2 y
A. oryzae *Z. rouxii* *T. halophilus* G

47 Gochujang (고추장)
Korea
pepper ? 1 - 3 y
A. oryzae *Z. rouxii* *Bc. subtilis* G

79 Fish sauce
South-East Asia
fish 4.0-4.5 0.85 1y - 1c
T. halophilus *T. muriaticus* *Lt. salicampi* E: 44 L: 0.1; G

111 Soy Sauce (醤油)
East Asia
soy 3.5-4.5 0.83 6 - 9 m
A. sojae *T. halophilus* *Z. rouxii* L: 0.1; G

12 Vegetables products

30 Sauerkraut Kimchi
Germany, Korea
cabbage 3.5-4.0 0.97 2 - 4 w
Lukimchi *L. plantarum* *L. brevis* L: 0.15; A: 0.02

48 Pickles
worldwide
cucumber 3.5-4.0 0.96 2 - 4 w
Lu.mesenteroi *L. brevis* *L. plantarum* L: 0.1

80 Olives
Spain, Greece
olives 3.5-4.2 0.96 2 - 4 d
L. plantarum *L. pentosus* *Candida spp.* L: 0.2

112 Sinki (raddish)
India, Nepal
raddish 4.0-4.5 <0.4 2 - 3 w
L. fermentum *L. brevis* *L. plantarum* L: 0.2

13 Dairy products

5 Buttermilk
Europe and others
bovine 4.5 0.99 12 h
Lc. lactis *Lc. cremoris* *Lu. cremoris* L: 0.1; 2Ac; Ac

13 Yoghurt
Bulgaria
bovine 4.0-4.5 0.98 3 h
L. delbrueckii ssp. bulgaricus *Sc. thermophil.* L: 0.1; Ac

31 Sour cream / cultured
worldwide
bovine 4.5 0.98 6 h
Lc. lactis *Lu.mesenteroi* *Lc. lactis* L: 0.1; 2Ac; Ac

49 Viili
Finland Scandinavia
bovine 4.5 0.98 16 h
Lc. lactic *Lc. cremoris* *G. candidum* L: 0.1; 2Ac

81 Koumiss
Central Asia
mare 4.0-4.5 0.98 24 h
L. acidophilus *K. marxianus* *S. lactis* L: 0.15; E: 1.5

113 Kefir
Caucasus region
bovine 4.0 0.98 24 h
Lactobacillus *Leuconostoc* *K. marxianus* L: 0.08; E: 1.2Ac

14 Soft cheese

6 Cottage Cheese
U.K.
bovine 4.5 0.97 1 - 3 d
Lc. lactis *Lc. cremoris* L: 0.1

14 Quark
Germany
bovine 4.4-4.8 0.97 1 d
Lc. lactis L: 0.1

32 Cream Cheese
worldwide
bovine 4.4-4.9 0.95 1 - 2 d
Lc. lactis *Lu.mesenteroi* L: 0.1

50 Feta
Greece
ovine 4.4-4.6 0.95 2 - 4 m
Lc. lactis L: 0.1

82 Mozzarella
South-Central Italy
buffal 4.7-5.2 0.97 1 d
L. helveticus L: 0.1

114 Caciotta
Tuscany (Italy)
ovine 5.0-5.5 0.98 1 - 4 w
Lc. lactis *Lu.mesenteroid* L: 0.1

15 Hard cheese

7 Cheddar
U.K. and U.S.A.
bovine 4.8-5.8 <0.97 4w-4y
Lc. lactis *Lu.mesenteroi* (NSLAB) L: 0.1; (G)

15 Gouda
Holland
31.0 4.8-5.8 <0.97 4w-4y
Lc. lactis *Lu.mesenteroi* (NSLAB) L: 0.1; (G)

33 Emmental (CH) Emmentaler (Swiss)
Emmental (CH)
raw 5.1-5.3 0.96 4 - 14m
Sc. thermophil. *L. helveticus* *Pr. jensenii* L: 0.1; P: 0.1

51 Tilsit (D, CH)
Tilsit (D, CH)
bovine 5.0-5.5 0.97 2 - 4 w
Lc. lactis *Lu.mesenteroi* *Lc. lactis* L: 0.1; 2Ac

83 Parmigiano
Parma (I)
raw bov 6.0 0.90 1 - 5 y
L. helveticus *Sc. thermophil* NSLAB L: 0.1; G

115 Pecorino
Italy
rawov 5.5-6.0 0.90 0.5 - 5 y
L. helveticus *Sc. thermophil.* NSLAB L: 0.1; G

16 Surface ripened cheeses

8 Gruyere
Gruyere (CH)
raw 5.2-5.4 0.96 5 - 18 m
L. helveticus *Sc. thermophil.* *Br. linens* L: 0.1

Gruyère
raw 5.2-5.4 0.96 6 - 8 m
L. helveticus *Sc. thermophil.* *Br. linens* L: 0.1; 2Ac; Ac

34 Oka
Quebec (CAD)
bovine 5.0-5.5 0.97 1 - 3 m
Lc. lactis *Br. linens* *G. candidum* L: 0.1

52 Limburger
Limburg (D, B, NL)
bovine 5.2-5.4 0.97 1 - 3 m
Lc. lactis *Br. linens* *D. hansenii* L: 0.1; N

84 Bern (CH)
Bern (CH)
raw 5.2-5.4 0.97 3 - 6 m
L. helveticus *Sc. thermophil.* *Micrococcus* L: 0.1

116 Münster
Muenster Valley (Alsace)
raw 5.2-5.4 0.97 1 - 3 m
Lc. lactis *Br. linens* *G. candidum* L: 0.1; N

Tête de Moine
raw 5.2-5.4 0.97 3 - 6 m
L. helveticus *Sc. thermophil.* *Micrococcus* L: 0.1

17 Mould ripened cheeses

9 Brie
Brie (F)
raw 5.0-6.0 0.97 2 - 4 m
Lc. lactis *Lc. cremoris* *P. camenberti* L: 0.1

17 Camembert
Normandie (F)
raw 5.5-6.0 0.97 1 - 4 m
Lc. lactis *Lc. cremoris* *P. camenberti* L: 0.1; N

35 Allgäu (D)
Allgäu (D)
bovine 5.5-6.0 0.97 1 - 4 m
Lc. lactis *P. camenberti* *P. roqueforti* L: 0.1

53 Blue Stilton
Leicestershire, Nottinghamshire
bovine 5.5-6.0 0.97 1 - 4 m
Lc. lactis *P. roqueforti* L: 0.1; N

85 North Italy
North Italy
bovine 5.5-6.0 0.96 3 - 6 m
Lc. lactis *P. roqueforti* L: 0.1; N

117 Roquefort (F)
Roquefort (F)
rawov 5.5-6.5 0.97 3 - 6 m
Lc. lactis *P. roqueforti* L: 0.1; N

18 Meats and fish

2 Summer Sausage
U.S.
meats 4.5-5.0 0.95 2 w
Pc. acidilactici L: 0.1

10 Cervelat
Central Europe
meats 3.0-5.5 0.92 - 4 w
L. sakei *L. curvatus* *St. carnosus* L: 0.1

18 Salami
Italy, Hungary
meats 5.5-6.0 0.89-94 4 - 8 w
L. plantarum *St. carnosus* *P. nalgiovense* L: 0.1; G

36 Chorizo
Spain
pork 5.0-5.5 0.96 1 - 8 w
E. faecium *St. xylosus* *D. hansenii* L: 0.1; G

54 Prosciutto / Jamón
Italy, Spain
pork 5.0-7.0 0.90 0.5 - 2 y
staphylococci G

Narezushi
Japan
fish, rice 4.0-4.5 0.90 2 - 12m
L. plantarum *L. brevis* *D. hansenii* L: 0.05; G

Rakfisk
Norway
trout 5.5-6.5 0.96 2-4m
NSLAB? enzymatic hydrolysis N; G

Spirits and vinegar

57 Vodka (водка)
Russia
potatoes 6.0 n/a 2 d
S. cerevisiae E: 40

58 Rum
Carribean
sug cane 4.0-5.0 n/a 0.5-2 y
S. cerevisiae E: 40-80

59 Kirsch-wasser
Black Forest (D)
cherries 3.5 - 4.0 n/a 2 - 12 m
S. cerevisiae *L. suebicus* E: 44 A: 0.01

60 Calvados
Normandie (F)
apples 4.5 - 5 n/a 12 m
S. cerevisiae Lactic and acidbacteria E: 40; A: 0.02

61 Cognac
Cognac (F)
wine 4.5 - 5 n/a 2 - 50 y
S. cerevisiae E: 40

62 Grappa
Italy
pomace 4.5 - 5 n/a 2 - 4 d
S. cerevisiae lactic acid bacteria E: >40

63 Tequila, Mezcal
Mexico
agave 4.5-5.0 n/a 0.5 - 4
S. cerevisiae *C. humilis* *W. cibaria* E: 44

64 Baijou (白酒)
China
sorghum 4.5 - 5 n/a 2 - 50 y
A. oryzae *S. cerevisiae* *L. parabuchneri* E: 35-53

65 Whiskey / Whisky
U.K., Ireland, U.S.A.
barley 3.5-4.5 n/a 1 - 2 y
S. cerevisiae *L. fermentum* *L. acidophilus* E: 44

66 White vinegar
worldwide
grains 2.5 n/a 2d
S. cerevisiae Acetobacter A: 0.8-3

67 Wine vinegar
worldwide
grapes 2.5 n/a 4w / 1d
S cerevisiae *Acetobacter* A: 0.8 - 1

68 Fruit Vinegar
worldwide
fruits 2.5-3.0 n/a 4w / 1d
S cerevisiae *Acetobacter* A: 0.8 - 1

69 Vinegar (醋)
China
grains 2.5 n/a 3 - 6m
A. oryzae *S. cerevisiae* *Acetobacter* A: 1; L: 0.1

70 Aceto Balsamico di Modena
Modena (I)
grapes 2.5 n/a 12 y
S. cerevisiae *Acetobacter* *Zygosaccharomyces* A: 1; L: 0.01

Tea, coffee and chocolate

89 Green Tea (绿茶)
China
tea - n/a
enzymatic fermentation

90 Pu-erh Tea (普洱茶)
China
tea ? n/a 2m
A. niger *S. cerevisiae* *Bl. adeninivorans* volatiles

91 Black tea
India
tea - n/a
enzymatic fermentation

92 Oolong tea (乌龙)
China
tea - n/a
enzymatic fermentation

93 Kombucha
East Asia
tea 3.5 0.99 1d
Gl. xylinum *Z. bailii* *Lactobacillus* E: 0.5 A: 0.1 L: 0.1

94 Water kefir
unknown
sucrose 3.3-3.5 n/a 1d
L. hordei *S. cerevisiae* *Acetobacter* E: 3; L: 0.2; A: 0.1

95 Coffee arabica
Ethiopia
coffee 5.0 n/a 2 d
Pichia spp. *Bwinia spp.* *Lu.mesenteroid* volatiles

96 Coffee robusta
Brazil
coffee 5.0 n/a -
fungi none

97 Kopi Luwak (Civet coffee)
Indonesia
coffee 5.5 n/a 2 d
Paradoxurus *Thermophiodi* (Civet cat) volatiles

98 Vanilla
Mexico, Madagascar
Vanilla 5.5 n/a 2 d
Bc. subtilis beta-glycosidase Vanillin

99 cocoa
tropical countries
cocoa 5.0-5.5 0.30 7d
Candida spp. *Lactobacillus* *A. aceti* volatiles

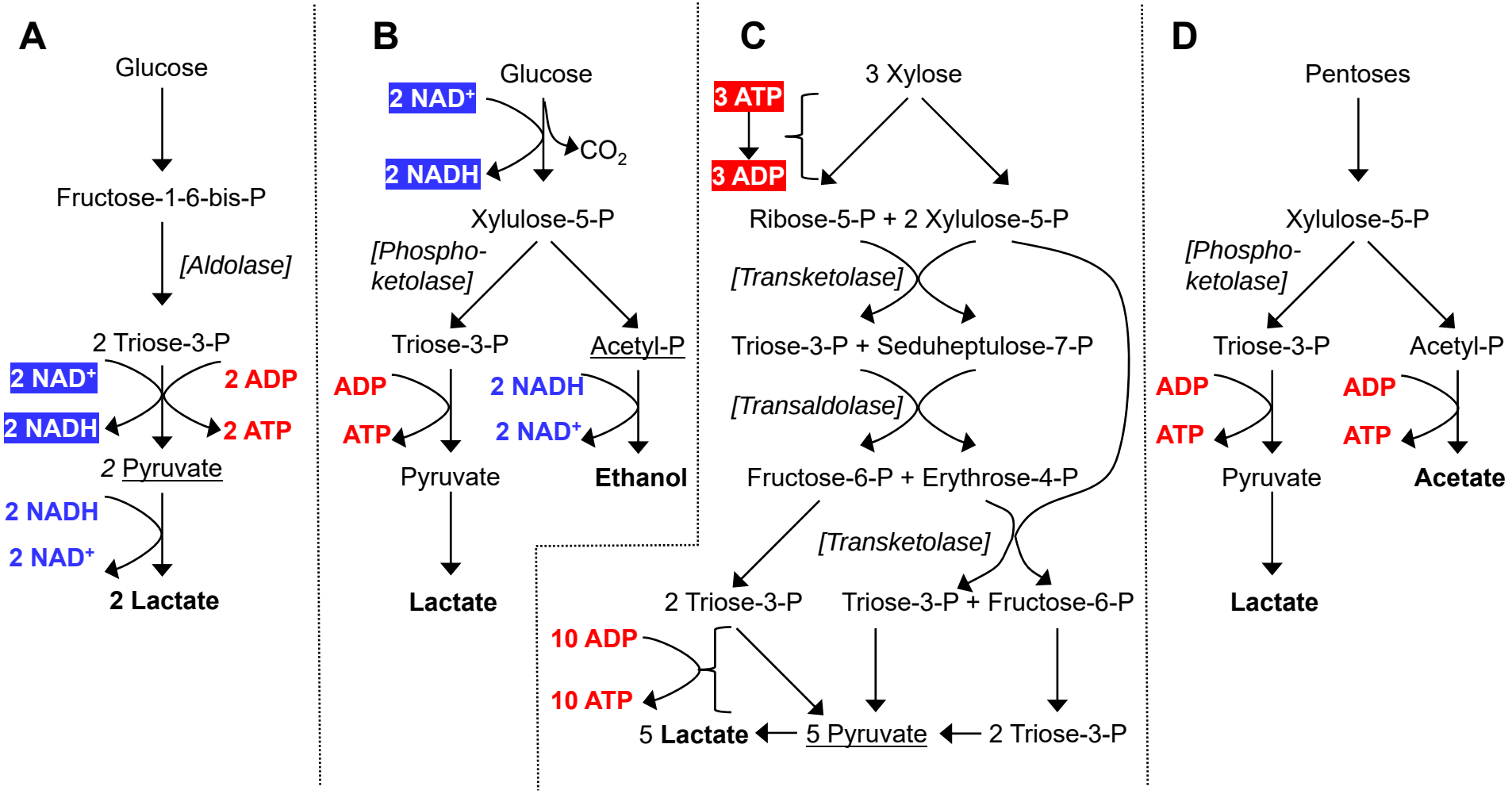
100 Milk chocolate
tropical countries
cocoa 5.5-6.5 0.40 7d
Candida spp. *Lactobacillus* *A. aceti* volatiles

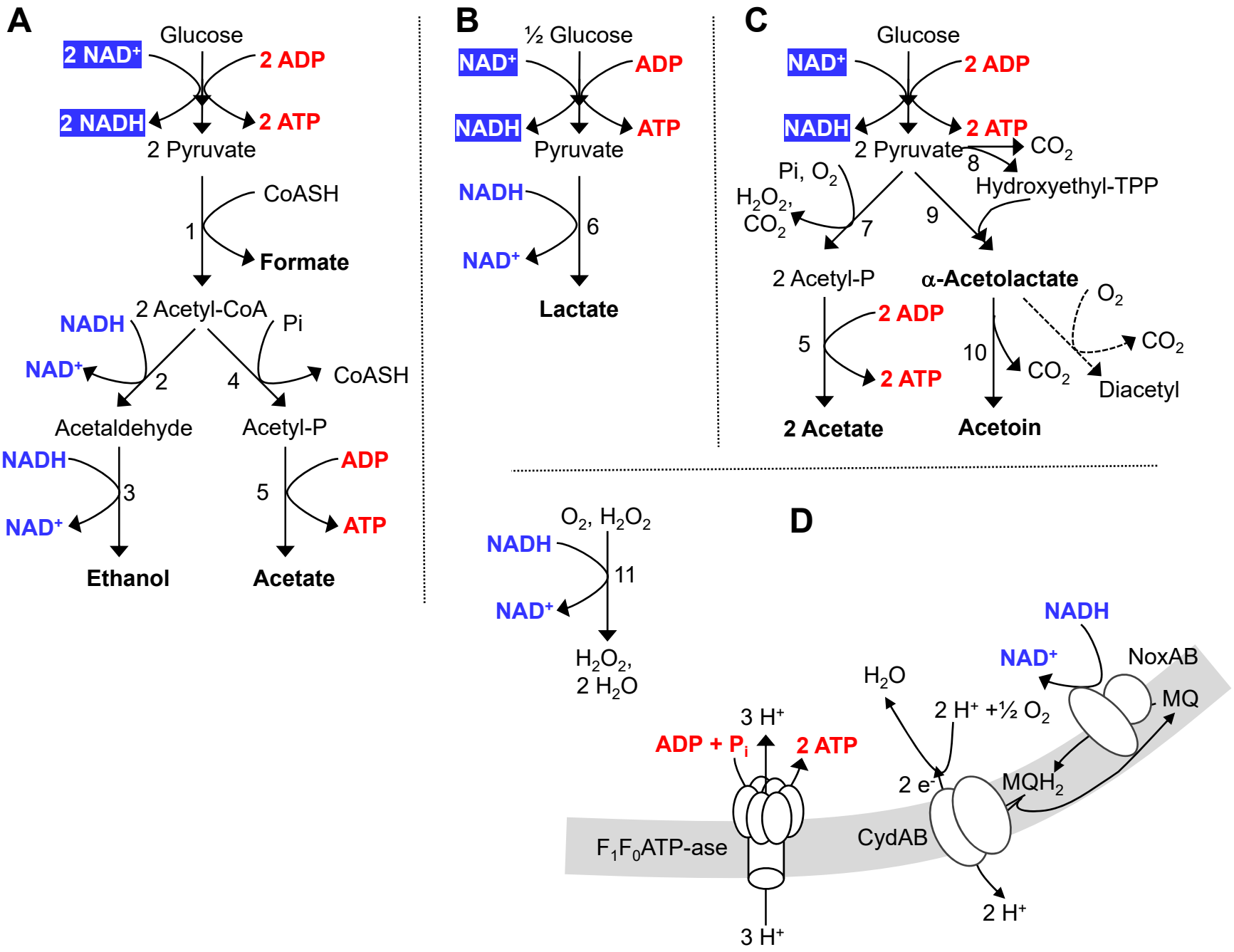
101 Dark chocolate
tropical countries
cocoa 5.0-5.5 0.40 7d
Candida spp. *Lactobacillus* *A. aceti* volatiles

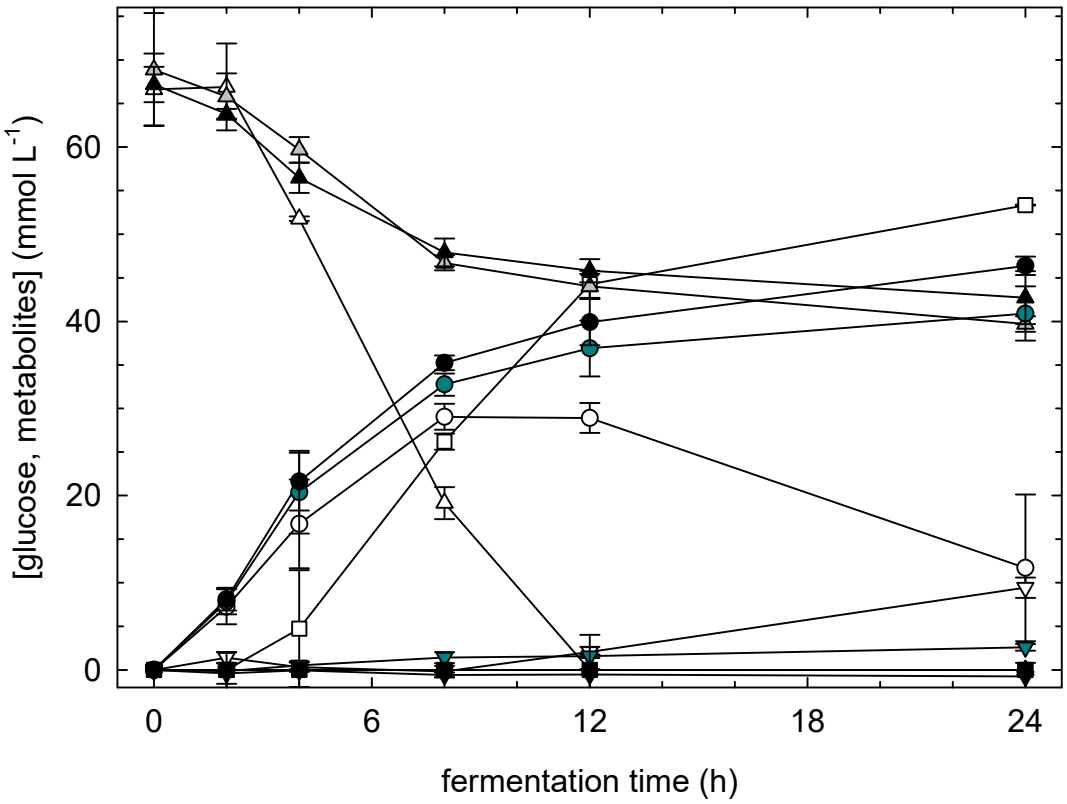
102 Filled chocolate
tropical countries
cocoa 5.0-5.5 n/a 7d
Candida spp. *Lactobacillus* *A. aceti* E: 5

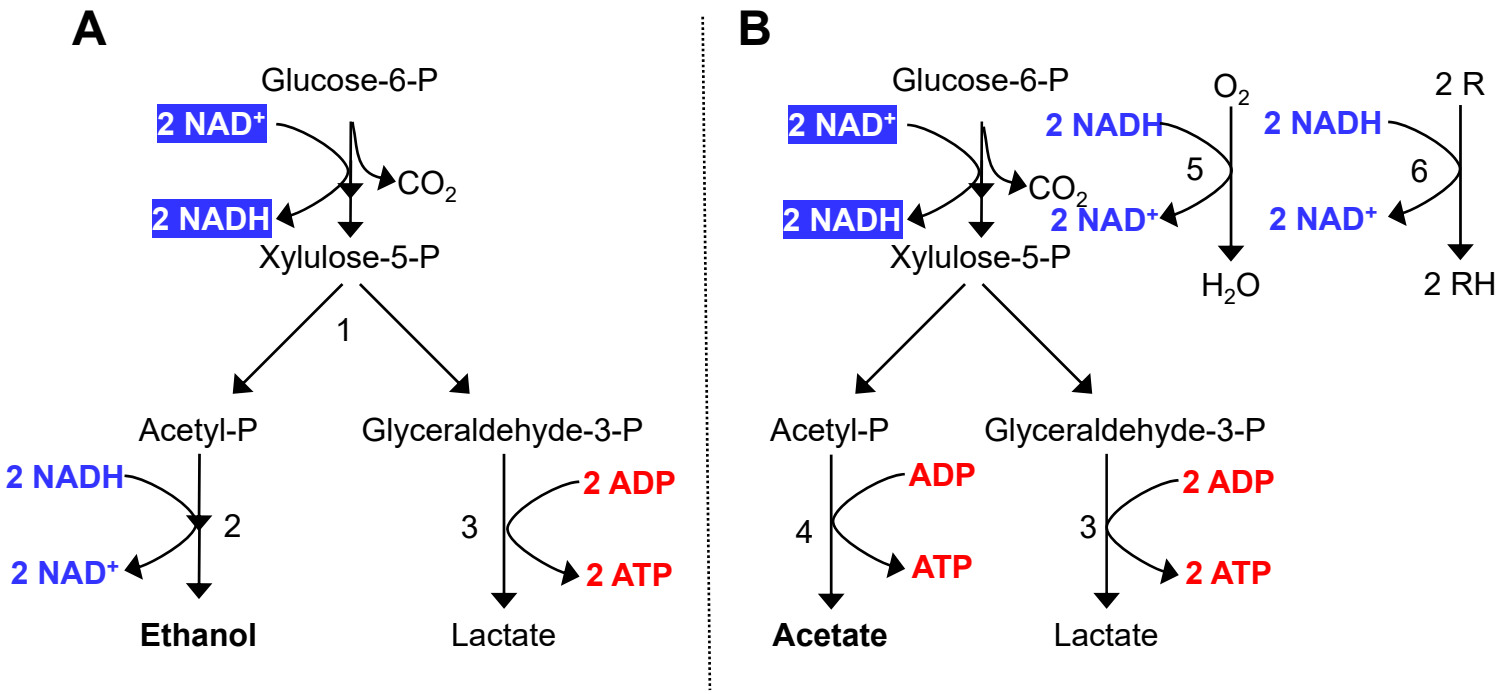
Common Fermentation Organisms in Food

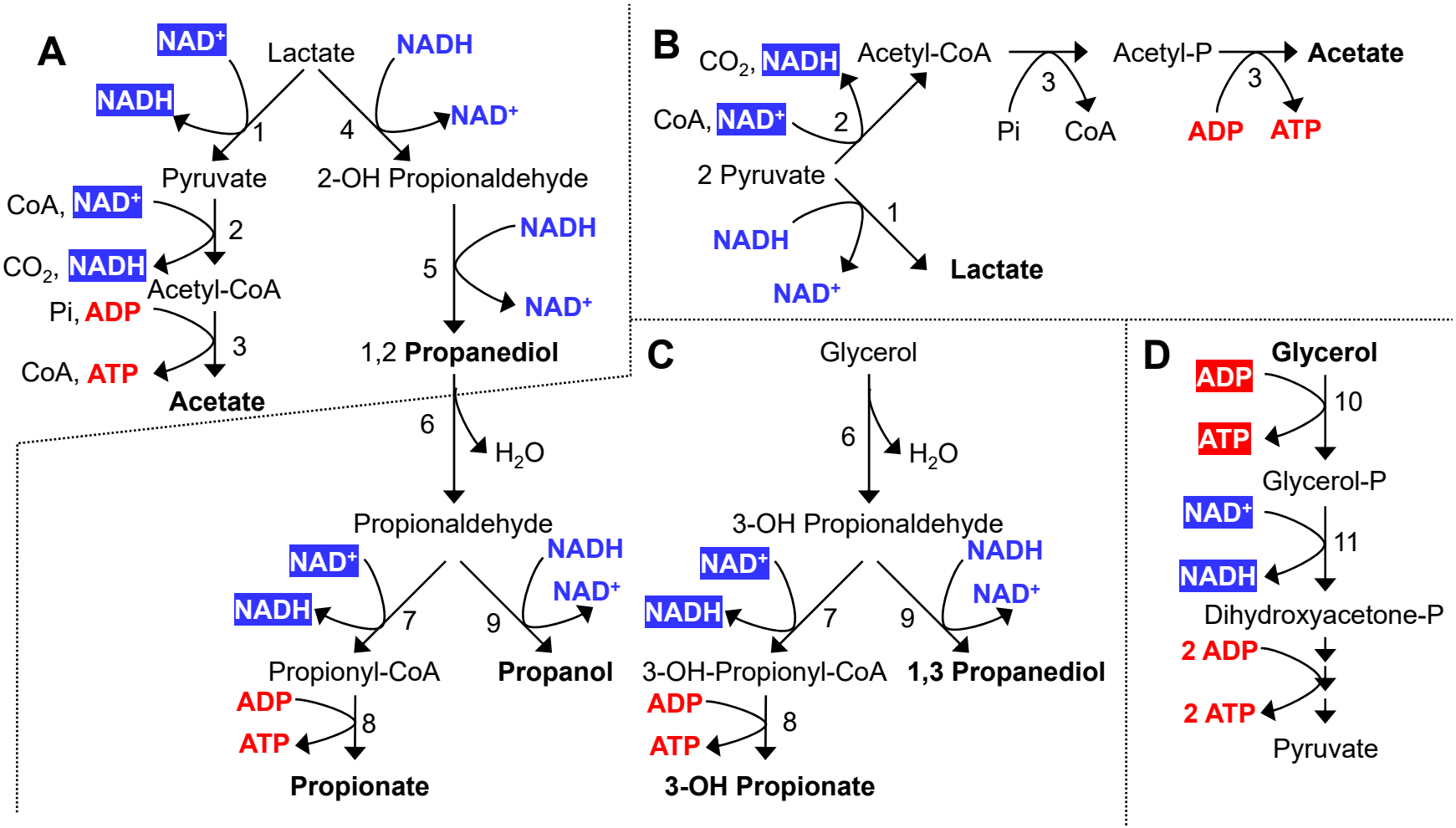
Lactobacillaceae		*Streptococcaceae, Enterococcaceae*		Other bacteria		Fungi		Yeasts	
Lactobacillus	*L.*	*Lactococcus*	*Lc.*	*Acetobacter*	*Ac.*	*Aspergillus*	*A.*	*Saccharomyces*	*S.*
Leuconostoc	*Lu.*	*Streptococcus*	*Sc.*	*Staphylococcus*	*St.*	*Penicillium*	*P.*	*Candida*	*C.*
Weissella	*W.*	*Tetragenococcus*	*T.*	*Gluconacetobacter*	*Gl.*	*Geotrichum*	*G.*	*Debaromyces*	*D.*
Pediococcus	*Pc.*	*Enterococcus*	*E.*	*Bacillus; Lentibacillus*	*Bc.; Lt*	*Monascus*	*M.*	*Kluyveromyces*	*K.*
Oenococcus	*O.*	Non starter lactic acid bacteria	NSLAB	*Brevibacterium*	*Br.*	*Rhizopus*	*R.*	*Zygosaccharomyces*	*Z.*
				Propionibacterium	*Pr.*	*Botrytis*	*B.*	*Blastobotrys*	*Bl.*

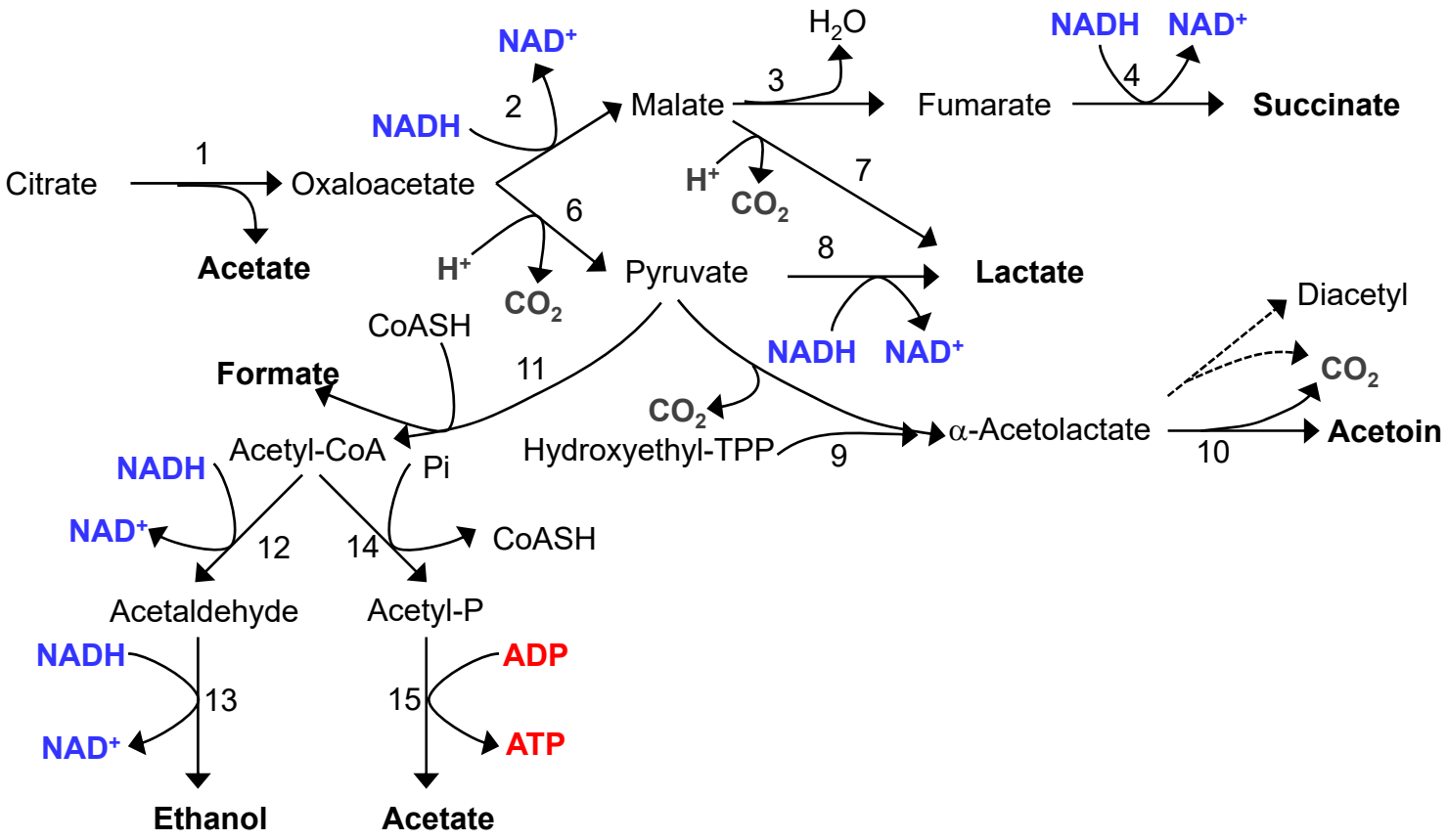

A
Glucose
Fructose-1-6-bis-P
[Aldolase]
2 Triose-3-P
2 NAD+
2 NADH
2 ADP
2 ATP
2 Pyruvate
2 NADH
2 NAD+
2 Lactate
B
Glucose
2 NAD+
2 NADH
CO2
Xylulose-5-P
[Phospho-ketolase]
Triose-3-P
Acetyl-P
ADP
ATP
2 NADH
2 NAD+
Pyruvate
Ethanol
Lactate
C
3 Xylose
3 ATP
3 ADP
Ribose-5-P + 2 Xylulose-5-P
[Transketolase]
Triose-3-P + Seduheptulose-7-P
[Transaldolase]
Fructose-6-P + Erythrose-4-P
[Transketolase]
2 Triose-3-P
Triose-3-P + Fructose-6-P
10 ADP
10 ATP
5 Lactate
5 Pyruvate
2 Triose-3-P
D
Pentoses
Xylulose-5-P
[Phospho-ketolase]
Triose-3-P
Acetyl-P
ADP
ATP
ADP
ATP
Pyruvate
Acetate
Lactate

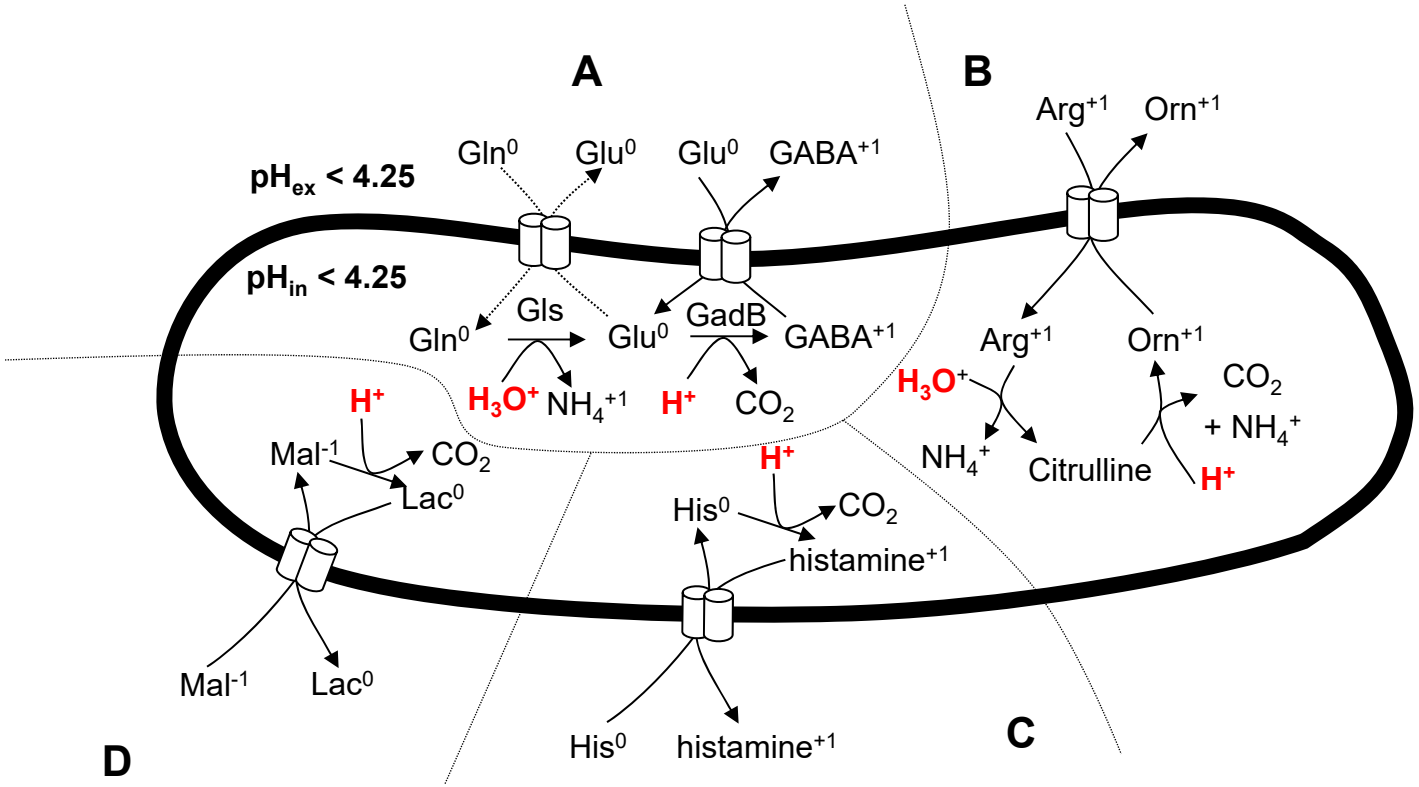

A
Glucose
2 NAD+
2 ADP
2 NADH
2 ATP
2 Pyruvate
CoASH
1
Formate
2 Acetyl-CoA
NADH
Pi
NAD+
2
4
CoASH
Acetaldehyde
Acetyl-P
NADH
3
ADP
5
NAD+
ATP
Ethanol
Acetate
B
½ Glucose
NAD+
ADP
NADH
ATP
Pyruvate
NADH
6
NAD+
Lactate
C
Glucose
NAD+
2 ADP
NADH
2 ATP
2 Pyruvate
CO2
8
Pi, O2
H2O2,
CO2
7
9
Hydroxyethyl-TPP
2 Acetyl-P
α-Acetolactate
O2
5
2 ADP
10
CO2
CO2
2 ATP
Diacetyl
2 Acetate
Acetoin
D
O2, H2O2
NADH
11
NAD+
H2O2,
2 H2O
NADH
NAD+
NoxAB
H2O
MQ
2 H+ +½ O2
3 H+
ADP + Pi
2 ATP
2 e-
MQH2
F1F0ATP-ase
CydAB
2 H+
3 H+


[glucose, metabolites] (mmol L-1)
0
20
40
60
0
6
12
18
24
fermentation time (h)


A
Glucose-6-P
2 NAD+
CO2
2 NADH
Xylulose-5-P
1
Acetyl-P
Glyceraldehyde-3-P
2 NADH
2
2 NAD+
3
2 ADP
2 ATP
Ethanol
Lactate
B
Glucose-6-P
2 NAD+
CO2
2 NADH
Xylulose-5-P
O2
2 NADH
5
2 NAD+
H2O
2 R
2 NADH
6
2 NAD+
2 RH
Acetyl-P
Glyceraldehyde-3-P
4
ADP
ATP
3
2 ADP
2 ATP
Acetate
Lactate


A
NAD+
Lactate
NADH
NADH
1
4
NAD+
Pyruvate
2-OH Propionaldehyde
CoA, NAD+
2
NADH
5
CO2, NADH
Acetyl-CoA
NAD+
Pi, ADP
3
1,2 Propanediol
CoA, ATP
Acetate
6
H2O
Propionaldehyde
NAD+
NADH
NADH
7
9
NAD+
Propionyl-CoA
Propanol
ADP
8
ATP
Propionate
B
CO2, NADH
Acetyl-CoA
3
Acetyl-P
Acetate
CoA, NAD+
2
Pi
CoA
3
ADP
ATP
2 Pyruvate
1
NADH
NAD+
Lactate
C
Glycerol
6
H2O
3-OH Propionaldehyde
NAD+
NADH
NADH
7
9
NAD+
3-OH-Propionyl-CoA
1,3 Propanediol
ADP
8
ATP
3-OH Propionate
D
ADP
Glycerol
10
ATP
Glycerol-P
NAD+
11
NADH
Dihydroxyacetone-P
2 ADP
2 ATP
Pyruvate


NAD+
H2O
NADH
NAD+
NADH
2
3
4
Malate
Fumarate
Succinate
1
Citrate
Oxaloacetate
H+
CO2
7
6
Acetate
H+
CO2
Pyruvate
8
Lactate
Diacetyl
CoASH
NADH
NAD+
CO2
Formate
11
CO2
Acetyl-CoA
Pi
Hydroxyethyl-TPP
9
α-Acetolactate
10
Acetoin
NADH
NAD+
12
14
CoASH
Acetaldehyde
Acetyl-P
NADH
ADP
13
15
NAD+
ATP
Ethanol
Acetate


A
B
C
D
pH_ex < 4.25
pH_in < 4.25
Gln0
Glu0
Glu0
GABA+1
Gls
GadB
Gln0
Glu0
GABA+1
H3O+
NH4+1
H+
CO2
Arg+1
Orn+1
Arg+1
Orn+1
H3O+
NH4+
Citrulline
CO2
+ NH4+
H+
H+
Mal-1
CO2
Lac0
H+
His0
CO2
histamine+1
Mal-1
Lac0
His0
histamine+1