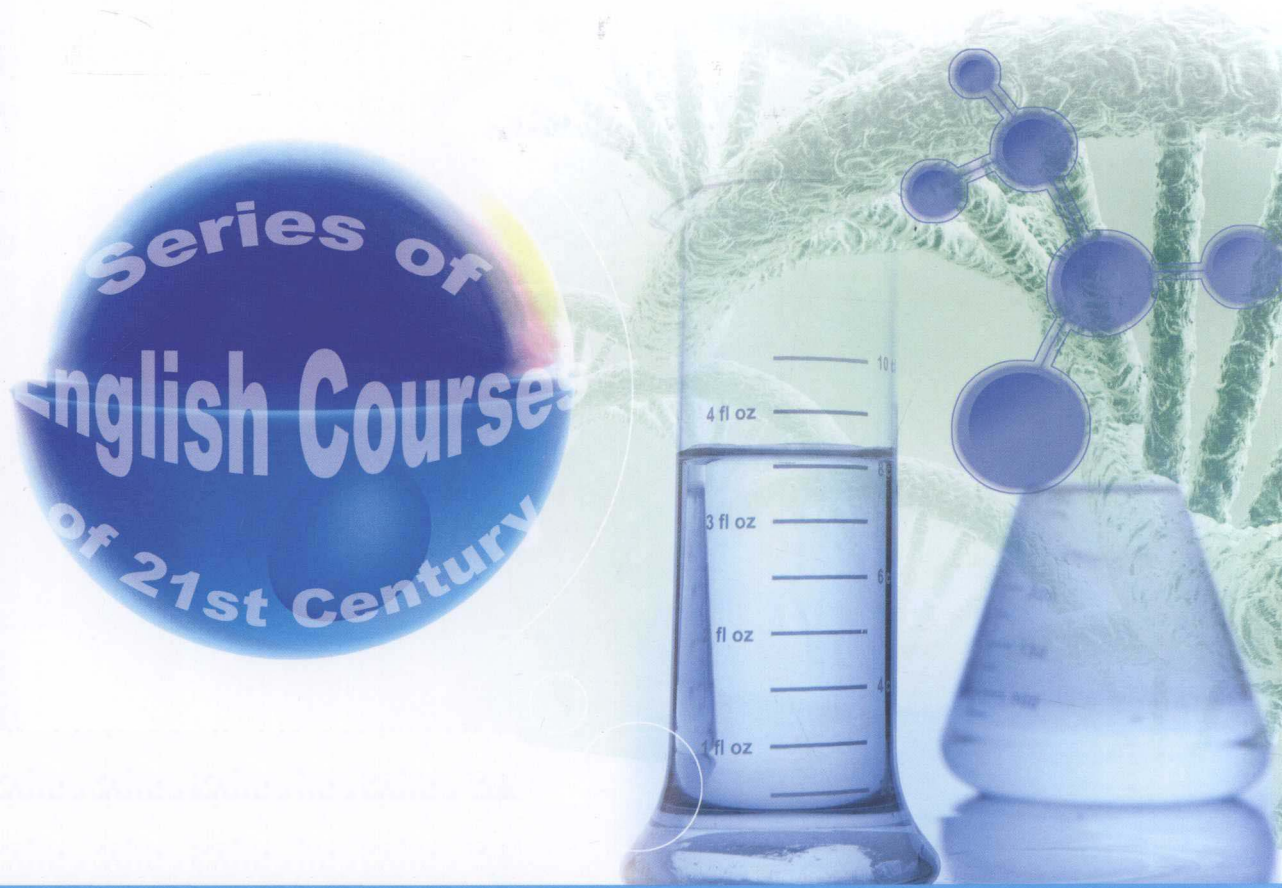
21世纪专业英语系列教程

生物工程专业英语

主编 姜 彦 田英华 张洪文

English Course for Biotechnology



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内容简介

生物工程技术专业的学生在完成基础英语的学习以后，随着专业基础课程和专业课程的学习，开始接触专业方面的英语资料了。本书在内容上主要选择了生物工程的原理、发展和应用等方面的专业知识，以生物工程学、生物化学、酶学等内容为主，力求使读者能够接触更多的专业词汇、形式多样的文体和更多实用句型。

本书第1单元介绍了氨基酸的生产方法、用途和前景，以及各种氨基酸的生产工艺；第2单元概述了酶学的发展史，并以纤维素酶为例分析了酶的应用；第3单元介绍了奥地利生物工程的发展史和酶的某些特性的利用等；第4单元介绍了抗体生产的发展、方法、未来趋势及生化工程的研究进展；第5单元介绍了固定化细胞和酶的原则、方法、稳定性及应用。第6单元介绍了乳酸菌的抗菌肽及生物工程中固态发酵的应用和方法等；第7单元介绍了生物工程下游技术中的利用反向微团技术提取蛋白质，以植物细胞培养中次级代谢产物的提取。

本书的各个单元都分为A、B两个部分，可以根据实际情况对全部或部分内容进行讲授。

本书可作为生物工程专业的英语教材，也可作为生物工程技术人员学习英语的参考书。

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PREFACE

本专业英语的编写原则是:(1)有利于学生通过专业知识学习英语;(2)教材内容取材于国内外权威资料,涉及当前经典领域,且覆盖面广,包括生物工程概论及基础、酶学、生物工程技术、发酵工程及生物化学理论与实验技术等,代表性强,便于学生通过专业知识学习英语,了解当前生物工程发展的状况及趋势;(3)课文难度略难于科普读物,便于学习和教授。把英语与专业知识结合起来,以专业为背景,分析科技英语的各种表示方法。

该教材的特点是:(1)均选自英文原版书籍;(2)提高阅读理解能力;(3)包含了科技英语中主要的语法,词与词组的用法;(4)重视词汇;(5)重视写作能力的培养。

本书可作为生物工程专业的英语教材,内容涉及整个生物工程领域,相当于专业概论,也可作为生物工程技术人员学习英语或其他科技人员了解生物工程的参考书。

本书第1~3单元由姜彦编写;第4~5单元由田英华编写;第6~7单元由张洪文编写。

由于编者水平有限,书中疏漏之处再所难免,敬请有关同行和读者提出宝贵意见。

编　者

2012年7月

English Course for Biotechnology

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Unit 1

··· Part A ···

Amino acid

1 Introduction

The story of amino acid production started in 1908 when the chemist, Dr K. Ikeda, was working on the **flavouring** components of **kelp**. Kelp is traditionally very popular with the Japanese due to the specific taste of its preparations, kombu and katauobushi (Fig. 1.1). After acid **hydrolysis** and **fractionation** of kelp, Dr K. Ikeda discovered that one specific fraction he had isolated consisted of **glutamic acid**, which after **neutralization** with **caustic soda**, developed an entirely new, delicious taste. This was the birth of the use of **monosodium glutamate** (**MSG**) as a flavour-enhancing compound, the production of monosodium glutamate was soon commercialized by the Ajinomoto company based on its isolation from vegetable proteins such as **soy** or wheat protein. Since less than 1 kg MSG could be isolated from 10 kg of raw material. The waste fraction was high. The chemical synthesis of D, L-Glutamate, which had been partially successful, was also of little use since the **sodium salt** of the D-**Isomer** is tasteless.

Fig. 1.1 The ideogram for kombu as it appears on kelp preparation used as a food component

The **breakthrough** in the production of MSG was the isolation of a specific **bacterium** by Dr S. Udaka and Dr S. Kinoshita at Kyowa Hakko kogyo in 1957. They screened for **amino acid**-excreting **microorganisms** and

discovered that their isolate, No. 534, had grown on a **mineral salt** medium excreted L-Glutamate. It soon became apparent that the isolated organism needed **biotin** and that L-Glutamate Excretion was triggered by an insufficient supply of biotin. A number of **bacteria** with similar properties were also isolated, which are today all known by the species name **corynebacterium glutamicum** (Fig. 1.2). **c. glutamicum** is a **gram-positive** bacterium, which can be isolated from soil. Together with genera like **Streptomycetes**, **propionibacterium** or **Arthrobacter**, it belongs to the **actinomycetes** subdivision of gram-positive bacteria. The successful commercialization of MSG production with this bacterium provided a big boost for amino acid production with c. glutamicum and later with other bacteria like **e. coli** as well. **Nucleotide** production for use as **flavour enhancers** also developed rapidly in the 1970s with **c. ammonia genes**, which is closely related to **c. glutamicum**. The production **mutants** and the processed developed also resulted in a demand for sophisticated fermentation devices. Consequently, the development of amino acid technology was an incentive for the fermentation industry in general.

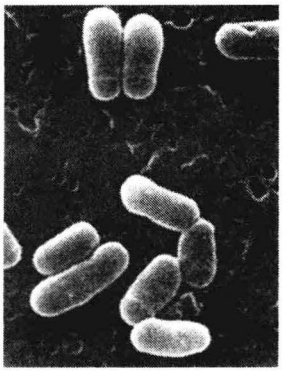

Fig. 1.2 Electron micrograph of corynebacterium glutamicum showing the typical V-shape of two cells as a consequence of cell division

New Words

flavouring	调味料
kelp	海藻,海藻灰(可提取碘的)
hydrolysis	水解
fractionation	分馏法
glutamic acid	谷氨酸
neutralization	中和
caustic soda	苛性钠
monosodium glutamate (MSG)	味精,味素;谷氨酸一钠(味精的化学成分)
soy	酱油,大豆
sodium salt	钠盐;(专指)氯化钠
isomer	异构体

breakthrough	突破
bacterium (bacteria)	细菌
amino acid	氨基酸
microorganism	微生物,微小动植物
mineral salt	天然盐
biotin	维生素 H,生物素
bacteria	细菌
corynebacterium	棒状杆菌
corynebacterium glutamicum	谷氨酸棒杆菌
gram-positive	革兰氏(染色)阳性
genera	类,属
streptomycete	链霉菌
propionibacterium	丙酸杆菌
arthrobacter	节杆菌属
actinomycete	放射菌类
e. coli	大肠杆菌
nucleotide	核苷
flavour enhancer	香味增强剂,风味增强剂,鲜味增强剂(如味精等)
mutant	突变体

Notes

After acid hydrolysis and fractionation of kelp, Dr K. Ikeda discovered that one specific fraction he had isolated consisted of glutamic acid, which after neutralization with caustic soda, developed an entirely new, delicious taste. 海藻经酸水解和分馏后,Ikeda 博士发现他所分离的包含谷氨酸的特定馏分经过苛性钠中和后,逐渐形成了全新的可口的味道。

2 Commerical Use of Amino Acids

Amino acids are used for a variety of purposes. The food industry requires L-Glutamate as a flavour enhancer, and **glycine** as a **sweetener** in juice, for instance (Table 1.1). The chemical industry requires amino acids as building blocks for a diversity of compounds. The

pharmaceutical industry requires the amino acids themselves in **infusions** in particular the essential amino acidsor in special dietary food. And last but not least, a large market for amino acids is their use as animal feed **additive**. The reason is that typical **feedstuffs**, such as **soybean meal** for pigs, are poor in some essential amino acids, like **methionine**, for instance. This is illustrated in Fig. 1.3 where the nutritive value of soybean meal is given by the barrel but the use of the total barrel is limited by the stave representing methionine. Methionine is added for this reason, and considerably increases the **effectiveness** of the feed. The addition of as little as 10 kg methionine per tonne increase the protein quality of the feed just as effectively as adding 160 kg soybean meal or 56 kg fish meal. The first limiting amino acid in feed based on crops and **oil seed** is usually L-Methionine, followed by L-**Lysine**, and L-**Threonine**. Another aspect of feed **supplementation** is that with a balanced amino acid content the manure contains less **nitrogen** thus reducing environmental pollution.

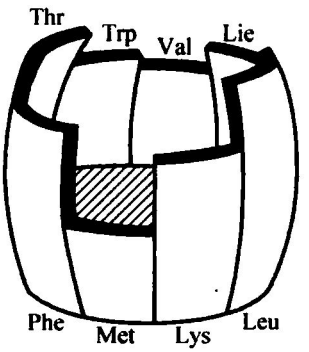

Fig. 1.3 The barrel represents the nutritive value of soybean meal, which is first limited by its methionine content

Table 1.1 Current amounts of amino acids produced

Production scale (tonnes y^{-1})	Amino Acid	Preferred production method	Main use
800,000	L-Glutamic acid	Fermentation	Flavour enhancer
350,000	L-Lysine	Fermentation	Feed additive
350,000	D,L-Methionine	Chemical synthesis	Feed additive
10,000	L-Aspartate	Enzymatic catalysis	Aspartame
10,000	L-Phenylalanine	Fermentation	Aspartame
15,000	L-Threonine	Fermentation	Feed additive
10,000	Glycine	Chemical synthesis	Feed additive, sweetener
3,000	L-Cysteine	Reduction of cystine	Feed additive, pharmaceutical
1,000	L-Arginine	Fermentation, extraction	Pharmaceutical
500	L-Leucine	Fermentation, extraction	Pharmaceutical
500	L-Valine	Fermentation, extraction	Pesticides, pharmaceutical
300	L-Tryptophan	Whole cell process	Pharmaceutical
300	L-Isoleucine	Fermentation, extraction	Pharmaceutical

Over the years the demand for amino acids has increase dramatically. The market is growing steadily by about 5 to 10 per cent per year. Thus, within 10 years the total market has approximately doubled (Fig. 1.4). Some amino acids, such as L-Lysine, which is required as a feed additive, display a particularly great increase. The world market for this amino acid has increased more than 20-fold in the past two decades. Other amino acids have appeared on the market, like L-Threonine, L-**Aspartate** or L-**Phenylalanine**, the latter two being required for the synthesis of the newly developed sweetener **aspartame**.

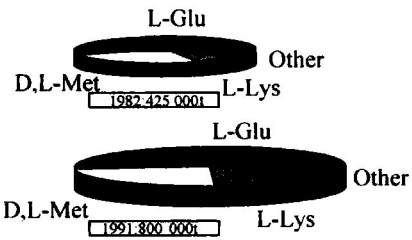

Fig. 1.4 The amino acid market doubles about every ten years

(t = tonnes)

Estimates for current worldwide demand for the most relevant amino acids are given in Table 1.1. L-**Glutamate** continues to occupy the top position followed by L-Lysine together with D, L-Methionine, while the other amino acids trail behind at a considerable distance.

There is a close interaction between the prices of the amino acids and the **dynamics** of the market. More efficient fermentation technology can provide cheaper products and hence boost demand. This in turn will lead to production on a larger scale with a further **reduction of costs**. However, since the supply of some amino acids, e. g. L-Lysine, as a feed additive is directly competitive with soybean meal (the **natural** L-Lysine **source**) there are considerable fluctuations in the amino acid demand depending on the crop yields. The amino acids produced in the largest quantities are also the cheapest (Fig. 1.5). The low prices in turn dictate the location of the production plants. The main factors governing the location of production plants are the price of the **carbon source** and the local market. Large L-Glutamate production plants are spreading all over the world, with a significant presence in the Far East, e. g. Thailand and Indonesia. For L-Lysine the situation is different. Since one-third of the world market is in North America and there is convenient access to **maize** as a feedstock material for the fermentation process, about one-third of the L-Lysine production capacity is located there. In almost all cases, the companies producing

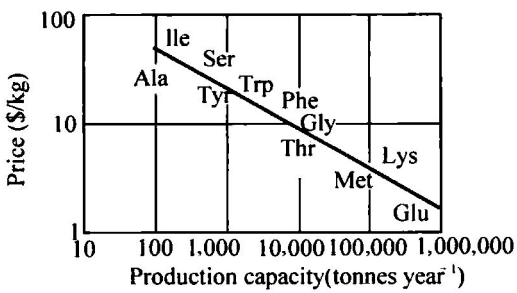

Fig. 1.5 The amino acids with the largest market are the cheapest

L-Lysine are associated with the maize **milling** industry, either as producers, in joint ventures or as suppliers of cheap sugar. This illustrates the fact that the commercial production of amino acids is a vigorously growing and changing field with many global interactions.

New Words

glycine	甘氨酸,氨基乙酸
sweetener	(调味用)甜料,甜味佐料
pharmaceutical	药物;制药(学)上的
infusion	溶液;注射
additive	添加剂
feedstuff	饲料,饲料中的营养成分
soybean	大豆
methionine	蛋氨酸,甲硫氨酸
meal	粗磨粉,颗粒物
effectiveness	效力
oil seed	含油种子
lysine	赖氨酸
threonine	苏氨酸
supplementation	增补,补充,追加
nitrogen	氮
aspartate	天(门)冬氨酸盐(或酯)
phenylalanine	苯基丙氨酸
aspartame	天(门)冬氨酰苯丙氨酸甲酯(一种约比蔗糖甜200倍的甜味剂)
dynamic	动态
reduction of cost	降低成本
natural source	天然源
carbon source	碳源
maize	玉米
milling	磨,制粉

3 Production Methods and Tools

Some amino acids are chemically synthesized, such as glycine, which has no **stereochemical** centre, or D, L-Methionine. This latter **sulphur**-containing amino acid can be added to feed as a **racemic mixture**, since animals contain a D-Amino acid **oxidase**, which together with a **transaminase** activity, converts D-Methionine to the nutritively effective L-Form. The classical procedure of amino acid isolation from acid **hydrolysates** of proteins is still in use for selected amino acids with a low market volume, e. g. L-**Cysteine** (Table 1. 1). Other methods in use are those of precursor conversion with bacteria, or enzymatic synthesis. However, for L-Amino acids required in large volumes, fermentation production with bacteria is the method of choice.

1 Classical strain development

However, bacteria do not normally excrete amino acids in significant amounts because **regulatory mechanisms** control the amino acid synthesis in an economical way. Therefore, mutants have to be generated which over-synthesis the respective amino acid. A large number of amino acid—producing bacteria have been derived by **mutagenesis** and screening programmes. This has involved the consecutive application of:

undirected mutagenesis;
selection for a specific phenotype;
selection of the mutant with the best amino acid accumulation.

Taking the best resulting strain, the entire procedure was repeated over several additional rounds to increase the productivity each time, and, eventually, resulted in an industrial producer (see Table 1.2 as an example). Due to this **optimization** over several decades, together with the accompanying process adaptation excellent high-performance strains are now available. The certainly carry a variety of unknown mutations also decisive for their production properties, as will become evident from the examples described below.

Table 1.2 A genealogy of strains obtained by classical mutagenesis and screening, showing the yield improvement obtained and some phenotypic characters known

Strain	Character	Yield of L-Lysine (%)
AJ 1511	Wild type	0
AJ 3445	AECr	16
AJ 3424	AECr Ala-	33
AJ 3796	AECr Ala-CCLr	39
AJ 3990	AECr Ala-CCLr MLr	43
AJ 1204	AECr Ala- CCLr MLr FPs	50

2 Application of recombinant techniques

In conjunction with this classical technique for strain development, **recombinant** DNA techniques are also applied. They serve

to rapidly develop new producers by increasing limiting enzyme activities;

to analysis mechanisms of flux control;

to combine this knowledge with classically obtained stains for their further development.

3 Intracellular flux analysis

An exciting new approach in strain development combining both the genetic and classical procedure is the reliable **quantification** of the carbon **fluxes** in the living cell. A great deal of progress has been made here recently in developing to a high level of sophistication the old **isotope** labeling technique. In particular, with ^{13}C-**NMR spectroscopy** the **intracellular** fluxes were quantified to extreme high resolution. For instance, in c. glutamicum it has even been possible to quantify the exchange flux rates as are present in the **pentose phosphate** pathway. Such flux identifications are of major assistance in selecting the reactions in the central **metabolism** to be modified by genetic engineering.

4 Functional genomics

Another tool whose potential is only now being exploited is the **genome** analysis of producer

strain. The availability of the entire sequence of the **chromosomes** from c. glutamicum and e. Coli opens up exciting possibilities to compare mutants and to uncover new mutations essential for high **overproduction** of metabolites. For instance, RNA analysis using chip technology will make it possible to detect whether a specific gene is altered in its expression for producers of different efficiency. New mutations and genes might thus be discovered which are not directly concerned with carbon fluxes, but rather with total cell control, or are involved in **energy metabolism.** Chip technology will also make it possible to use genome analysis as a tool to qualify individual fermentations, thus resulting in still further improvements and consolidations of the production processes.

New Words

stereochemical	立体化学的
sulphur	硫,硫磺
racemic mixture	外消旋混合物
oxidase	氧化酶
transaminase	(=aminotransferase)转氨酶
hydrolysate	水解产物
cysteine	半胱氨酸,巯基丙氨酸
enzymatic synthesis	酶催化合成
strain	品系
regulatory mechanism	调节机制
mutagenesis	突变形成,变异发生
phenotype	显型,表现型
optimization	最佳化,最优化
recombinant	重组,重组体;重组的
quantification	流量,通量
flux	量(化)
isotope	同位素
NMR	(=nuclear magnetic resonance) 核磁共振
spectroscopy	光谱学,波谱学,分光镜使用
intracellular	戊糖

pentose	细胞内的
phosphate	磷酸盐
metabolism	新陈代谢
genomics	基因组学
genome	基因组,染色体组
chromosome	染色体
overproduction	生产过剩
energy metabolism	能量代谢

4 Outlook

Although amino acids are now among the classical products in **biotechnology**, their constant development means that processes must be improved, new processed established and our understanding of the exceptional capabilities of producer strains deepened. Just one example of **molecular** research is the recent discovery of the L-Lysine export carrier, which opens up an entirely new field in the metabolism of amino acids in bacteria in general. Moreover, much information has been gathered from strain development in conjunction with fermentation technology, with the new science of **metabolic engineering** at the interface between them. In fact, amino acid production is an outstanding example of the integration of many different techniques. In this way, the early Japanese activities on the taste of kelp laid the foundation for the continuing very successful and flourishing production of amino acids.

New Words

biotechnology	生物工艺学
molecular	分子的,由分子组成的
metabolic engineering	代谢工程

··· Part B ···

Production of Amino acid

1 L-Glutamate

As already mentioned, L-Glutamate was the first amino acid to be produced. The very successful production still exclusively uses the original bacterium c. glutamicum. As metabolic pathways c. glutamicum uses glycolysis, the pentose phosphate pathway and the citric acid cycle to generate precursor metabolites and reduced pyridine nucleotides. However, this bacterium displays a special feature in the anaplerotic reactions of the citric acid cycle (Fig. 1.6). Since L-Glutamate is directly derived from α-ketoglutarate, a high capability for replenishing the citric acid cycle is, of course, a prerequisite for high glutamate production. It was originally assumed that only the phosphoenol pyruvate carboxylase is present as a carboxylating enzyme within the anaplerotic reactions. However, molecular research in close conjunction with ^{13}C-labelling studies and flux analysis showed that an additional carboxylating reaction must be present. The pursuit of this enzyme activity resulted in the detection of pyruvate carboxylase activity, (PyrC), and the cloning of its gene. This carboxylase was not detected by the original enzyme measurements since it is very unstable in crude extracts. Its detection requires an in situ enzyme assay using carefully permeabilised cells. Therefore, c. glutamicum has the pyruvate dehydrogenase (PyrDH) shuffling acetyl-CoA into the citric acid cycle but two enzymes supplying oxaloacetate: pyruvate carboxylase (PyrC) together with a phosphoenol pyruvate carboxylase (PEPC) (Fig. 1.6). The successful cloning of both genes together with mutant studies showed that both carboxylases can basically replace each other to ensure conversion of glucose-derived C3-units to oxaloacetate. This is different from e. coli, which has exclusively the phosphoenol pyruvate carboxylase serving this purpose, or Bacillus subtilis, where only the pyruvate carboxylase is present. Since c. glutamicum possesses both enzymes, it has an enormous flexibility for replenishing citric acid cycle

intermediates upon their withdrawal.

The reductive amination of α-ketoglutarate to yield L-Glutamate is catalysed by glutamate dehydrogenase. The enzyme is a multimer, each subunite having a molecular weight of 49, 100. It has a high specific activity of 1.8 mmol min^{-1} · mg protein, and L-Glutamate is present in the cell in a rather high concentration of about 150 mmol L^{-1}. In case of other amino acids, in contrast, the intracellular concentra-tions are usually below 10 mmol L^{-1}. The high concentration serves to ensure the supply of L-Glutamate directly required for cell synthesis and also for the supply of amino groups via transaminase reactions for a variety of cellular reactions. As much as 70% of the amino groups in cell material stems from L-Glutamate.

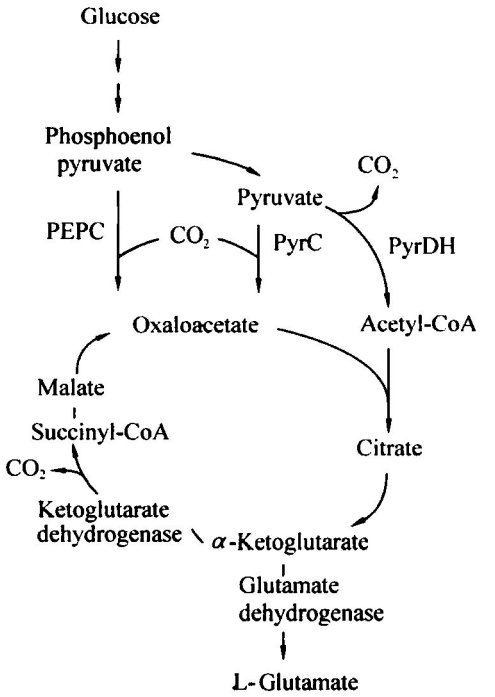

Fig. 1.6 Sketch of main reaction in c. glutamicum connected with the citric acid cycle and of relevance for L-Glutamate production. Abbreviations: PyrDH, pyruvate dehydrogenase; PyrC, pyruvate carboxylase; PEPC, phosphoenol pyruvate carboxylase

1 Production strains

For the biotechnological production of L-Glutamate the intracellularly synthesized amino acid must be released from the cell. This is, of course, usually not the case since the charged L-Glutamate is retained by the cytoplasmic membrane, otherwise the cell would not be viable. However, as shown by the special circumstances in discovering c. glutamicum, L-Glutamate is already excreted when biotin is limiting. This striking fact is based on two essential characteristics:

A carrier is present mediating the active excretion of L-Glutamate;

The lipid environment of this carrier triggers its activity.

A specific carrier is required since otherwise, in addition to the charged L-Glutamate, other metabolites and ions would also leak from the cell, Moreover, only an active export enables the energy-dependent "uphill" transport of L-Glutamate from inside the cell (0.15 M) towards the