APPLIED BIOCHEMISTRY AND BIOTECHNOLOGY 6, 179–188 (1981)

Patents and Literature

The objective of this section is to keep readers aware of significant inventions and trends in industrial research as well as to highlight those areas of research that may lead to new biotechnological opportunities. Four major areas of biochemistry will be covered corresponding to enzymes, cells, bioproducts, and nucleic acids. The patent section will briefly cover each area every issue of the journal. The literature section will focus on one area per issue.

Patents

This section will identify patents and published patent applications from the international patent literature. The title, name(s) of the inventor(s), the patent number, the date of filing, the assignee, and a short description of the invention will be given. Copies of US patents can be obtained for 50¢ each from the Commissioner of Patents and Trademarks, Washington, DC 20231.

Enzymes

Carrier-Bound Acylases

H. L. Hulsmann; G. Renckhoff
US 4,188,263 (Jan. 25, 1978)
Dynamit Nobel Aktiengesellschaft

Acylases are immobilized to a cellulose derivative using the hydroxyl groups of the cellulose and a reagent containing two reactive functional groups. The reaction of the hydroxyl groups with the bifunctional reagent is performed with the cellulose dissolved in dimethylsulfoxide containing polyhydroxymethylene.

Process for the Production of Immobilized Glucose Isomerase

M. Yoshikazu; S. Kazumasa; M. Tsuyoshi
US 4,191,810 (Dec. 1, 1977)
Mitsui Sugar Co., Ltd.

Glucose isomerase from Actinomycetes cells is immobilized by mixing free-thawed cells with gelatin or caseinate and treating the resulting paste with a glutaraldehyde solution in acetone. The solid that forms is separated from the acetone solution by filtration and then dried.

Support Matrices for Immobilization

R. P. Rohrbach; J. Levy
US 4,206,259 (Oct. 16, 1978)
UOP Inc.

A matrix is prepared by depositing a salt of amino-polystyrene in a solid, inorganic, water insoluble, support material. The composite is then reacted with an excess of a bifunctional reactive monomer, which results in the formation of a co-polymeric organic material with free groups to which an enzyme may be coupled to.

Immobilization of Glucose Isomerase

I. Ehrenthal; K. E. Miner
US 4,208,482 (April 23, 1976)
Anheuser-Busch, Incorporated

Microbial cells containing glucose isomerase are mixed with agar and combined with an organic solvent; discrete particles of agar gel containing entrapped whole microbial cells are recovered.

Xanthine Oxidase

J. P. Zikakis
US 4,238,566 (Jan. 21, 1980)
University of Delaware

A xanthine oxidase was isolated from milk and used for the production of uric acid; the enzyme has two pH optima, one at pH 8.3 and the other at pH 8.7.

Enzyme Electrode Provided with Immobilized Enzyme Membrane

K. Yoda; R. Urakabe; T. Tsuchida
US 4,240,889 (Jan. 24, 1979)
Toyo Boseki Kabushiki Kaisha

An enzyme electrode useful for polarographic determinations comprised of an immobilized enzyme membrane with a dense skin layer and a porous layer; the en-

zyme is immobilized onto the porous layer which is permeable to hydrogen peroxide.

Secondary Alcohol Dehydrogenase Enzyme and Use Thereof

C. Hou; R. Patel; A. Laskin
US 4,241,184 (Mar. 27, 1979)
Exxon Research & Engineering Co.

A process for converting a C_3–C_6 secondary alcohol to the corresponding methyl ketone using cells or enzymes derived from microorganisms cultured on methyl-containing substrate.

Novel Enzyme Particles and Their Preparation

P. K. Bogerman; P. J. Eygermans; A. G. van Velzen
US 4,242,219 (June 26, 1978)
Gist-Brocades N.V.

A process for preparing enzyme-containing particles that do not dust when subjected to external mechanical pressure. The particles are composed of the enzyme, a hydrophilic organic cohesive, a building agent, a polyol, and an external coating with a water repellent material such as linseed oil or lanolin.

Production of Increased Yields of Cellulolytic Enzymes from Thielaria Terrestris and Separating Methods Therefore

W. A. Skinner; S. Takenishi
US 4,243,752 (April 9, 1979)
SRI International

A method for increasing the yields of cellulolytic enzymes by the addition of 0.5–5% glycerol to the culture medium.

Process for the Production of Choline Oxidase by Fermentation

T. Nakanishi; Y. Machida
US 4,245,050 (July 25, 1979)
Kyowa Hakko Kogyo Co., Ltd.

A choline oxidase was isolated from *Brevibacterium album*, *Brevibacterium cerinun*, or *Corynebacterium murisepticum*, and its biochemical characteristics were defined.

Cells

Method for Immobilizing Enzymes and Microbial Cells

S. Fukui; T. Yamamoto; T. Iida
US 4,195,129 (Dec. 29, 1977)
Kansai Paint Co., Ltd.

A method for immobilizing enzymes or microbial cells that employs a photocurable resin, photopolymerizable unsaturated groups, and hydrophilic groups.

Microbial Desulfurization of Coal

C. Detz; G. Barvinchak
US 4,206,288 (May 5, 1978)
Union Carbide Corporation

An aqueous slurry containing finely divided coal particles is subjected to the action of iron- and sulfur-oxidizing microorganism selected from the *Thiobacillus ferrooxidans* group.

Process for Culturing Methanol-Utilizing Yeasts

K. Tonomura; T. Urakami
US 4,229,543 (Sept. 12, 1978)
Agency of Industrial Science & Technology
Ministry of International Trade and Industry
Mitsubishi Gas Chemical Company, Inc.

A process by which yeasts are cultured in a medium containing methanol as the main carbon source.

Method of Magnetic Separation of Cells and the Like, and Microspheres for Use Therein

A. E. Senyei; K. J. Widder
US 4,230,685 (Feb. 28, 1979)
Northwestern University

Magnetically-responsive microspheres having Protein A associated with their outer surface are reacted with antibodies selective to cells, bacteria, or viruses that are to be separated from a mixed population. Following binding of antibody, the desired population is removed in a magnetic separation.

Process for Producing Food Proteins from Trichoderma Album

T. J. Staron
US 4,238,567 (June 2, 1978)
Institut National de la Recherche Agronomique

Process for producing food protein from the fungus *Trichoderma album* in liquid medium at a temperature below 28°C. The culture is stirred in such a way as to not cause lysis and foaming.

Biosynthesis of Protein by Fermentation of Methanol Obtained from the Gasification of Coal or Residual Oil

E. T. Child; R. M. Suggitt
US 4,242,458 (Oct. 25, 1978)
Texaco Development Corporation

A process for the production of single cell protein from liquid hydrocarbon fuel by first converting the fuel to carbon monoxide and hydrogen, which are subsequently converted to methanol; the methanol is added to a nutrient solution used for growing *Hansanula polymorpha* DL yeast.

Bioproducts

High Mannitol Process (Enzymatic Isomerization)

W. M. Kruse
US 4,173,514 (June 2, 1977)

Mannitol-rich solutions of sorbitol and mannitol are prepared by empimerizing glucose to mannose, contacting this solution with glucose isomerase to produce a glucose—fructose—mannose solution, and then hydrogenating this solution to produce sorbitol and mannitol.

Process for the Production of L-Serine

K. Nakayama; K. Araki; Y. Tanaka
US 4,183,786 (Nov. 28, 1977)
Kyowa Hakko Kogyo Co. Ltd.

A process for converting glycine to L-serine by a mutant from the genus Nocardia that cannot decompose L-serine.

Process for Converting Biodegradable Wastes into Industrial Gases

P. Morel; Y. Ortega; C. Jullien; A. Jullien
US 4,204,842 (Jan. 10, 1979)

Biodegradable wastes are crushed and fed through a four cell treatment unit by gravity and methane gas is recovered.

Process for the Production of Coenzyme Q

K. Aida; K. Uchida; I. Kawada
US 4,205,125 (Jan. 25, 1979)
Ko Aida

Coenzyme Q is produced by culturing a Pseudomonas organism in a medium containing an alcohol (e.g., isopentenyl), an acetate (e.g., geranyl), or β-methyl crotonic acid.

Novolak Resins Containing Lactose and or Galactose

A. Richards; R. A. Khan
US 4,239,665 (May 30,1979)
Talres Developmet (N.A.) N.V.

A method for preparing a novolak resin wherein a phenol, a formaldehyde, and a reducing sugar selected from the group lactose, galactose, and mixtures thereof are condensed in an acid catalyzed reaction.

Fermentation Process

W. C. Muller; F. D. Miller
US 4,242,454 (May 29, 1979)
National Distillers and Chemical Corp.

A process to make ethanol by carrying out the fermentation in a series of vessels in which the ethanol content is progressively increased as the fermentable sugar is consumed. The reaction employs at least two strains of ethanol-producing yeasts, one that produces best in low-ethanol, high-sugar concentrations, and another that produces best in high-ethanol, low-sugar concentrations.

Novel Glycoproteins from Bovine Cartilage

C. A. Spillburg; J. M. Scheid
US 4,234,582 (April 26, 1979)
Monsanto Company

A high purity glycoprotein was isolated from bovine cartilage; it has a molecular weight of 65,000 an isoelectric point of 3.8, and can act as a trypsin inhibitor and as an inhibitor of endothelial cell growth.

Process for the Fermentative Production of Xanthan Gum with Organic Acids

A. L. Demain; P. Souw
US 4,245,046 (March 23, 1979)
Massachusetts Institute of Technology

The addition of α-ketoglutaric acid and pyruvic acid to the nutrient medium used in growing *Xanthomonas campestris* NRRL B-1459 results in the stimulation of xanthum gum production.

Process for Producing Coenzyme Q_{10}

K. Hata; K. Ohshima, I. Kano; M. Matsui; T. Sato
US 4,245,048 (Sept. 20, 1979)
Jujo Paper Co., Ltd.

A process to produce coenzyme Q_{10} by cultivating an organism belonging to the genus *Trichosporon* in a media containing sulfite waste liquid as the carbon source.

Process for the Production of Fructose

S. L. Neidleman; W. F. Aman; J. Geigert
US 4,246,347 (Oct. 24, 1979)
Cetus Corporation

A method for making fructose from glucose that involves the conversion of D-glucose to D-glucosone by enzymatic oxidation and then hydrogenating the D-glucosone to D-fructose.

Nucleic Acids

A Plasmid and Its Microbiological Preparation

J. J. Manis
UK Patent Application GB 2 043 652 A (Mar. 3, 1980)
The Upjohn Company

The plasmid pUC6 can be obtained from the *Streptomyces espinosus* biotype 23724a, NRRL 11439 and used as a cloning vehicle in recombinant DNA work.

Literature Survey

The objective of the literature survey is to make a thorough, recent review of publications in one specific area. This issue's survey will be on cells. Future surveys will be on bioproducts, nucleic acids, and enzymes. The articles will be chosen for their impact on current biotechnology processes and for their potential to break new ground that may lead to new applications. The entries are listed in alphabetical order by the first author's name.

Cells

1. Regeneration of ATP by Immobilized Microbial Cells and Its Utilization for the Synthesis of ATP and CDP-Choline, Y. Ado, Y. Suzuki, T. Tadokoro, K. Kimura, and H. Samejima, *Appl Biochem. Biotechnol.* **4,** 43–55 (1979).
2. Production of L-Tryptophan by Immobilized Bacteria, R. Azerad, R. Calderon-Seguin, and P. Decottignies-Le Mareohal, *Bull. Soc. Chim. Fr.* **1–2,** 83—86 (1980).
3. Hydrolysis of Lactose in Whey Milk by Immobilized Whole Microbial Cells, M. Banerjee, *Proc. Natl. Semin. Immobilized Enzyme Eng.* **1,** 90–93 (1979).
4. Steroid Transformation at High Substrate Concentrations Using Immobilized Corynebacterium Simplex Cells, A. Constantinides, *Biotechnol. Bioeng.* **22,** 119–136 (1980).
5. Immobilized Yeast Cells with Methanol Oxidase Activity: Preparation and Enzymatic Properties, R. Couderc and J. Baratti, *Biotechnol. Bioeng.* **22,** 1155–1173 (1980).
6. Immobilized Bacterial Cells Containing A Thermostable Beta-Galactosidase, M. De Rosa, A. Gamabacorta, B. Nicholaus, V. Buonocore, and E. Poerio, *Biotechnol. Lett.* **2,** 29–34 (1980).
7. Continuous Conversion of Sucrose to Fructose and Gluconic Acid by Immobilized Yeast Cell Multienzyme Complex, S. F. D'Souza and G. B. Nadkarni, *Biotechnol. Bioeng.* **22,** 2179–2189 (1980).
8. Immobilized Catalase-Containing Yeast Cells: Preparation and Enzymic Properties, S. F. D'Souza and G. B. Nadkarni, *Biotechnol. Bioeng.* **22,** 2191–2205 (1980).
9. Rapid Ethanol Fermentation in Immobilized Yeast Cell Reactor, T. K. Ghose and K. K. Bandyopadhyay, *Biotechnol. Bioeng.* **22,** 1489–1496 (1980).
10. Calcium Alginate Immobilized Cells of Clostridium Acetobutylicum for Solvent Production, L. Haeggstroem and N. Molin, *Biotechnol. Lett.* **2,** 241–246 (1980).
11. Ammonia Electrode with Immobilized Nitrifying Bacteria, M. Hikuma, T. Kubo, T. Yasuda, I. Karube, and S. Suzuki, *Anal. Chem.* **52,** 1020–1024 (1980).
12. Amperometric Determination of Total Assimilable Sugars in Fermentation Broths with Use of Immobilized Whole Cells, M. Hikuma, H. Obana, T. Yasuda, I. Karube, and S. Suzuki, *Enzyme Microb. Technol.* **2,** 234–238 (1980).
13. Amperometric Estimation of BOD Using Living Immobilized Yeasts, M. Hikuma, H. Suzuki, T. Yasuda, I. Karube, and S. Suzuki, *Eur. J. Appl. Microbiol. Biotechnol.* **8,** 289–297 (1980).
14. Glucose Sensor Using Immobilized Whole Cells of Pseudomonas Fluorescens, I. Karube, S. Mitsuda, and S. Suzuki, *Eur. J. Appl. Microbiol. Biotechnol.* **7,** 343–350 (1979).
15. Methane Production from Wastewaters by Immobilized Methanogenic Bacteria, I. Karube, S. Kuriyama, T. Matsunaga, and S. Suzuki, *Biotechnol. Bioeng.* **22,** 847–857 (1980).

16. Immobilized Whole Cells: Methods for Immobilization: Survey, K. Klein and K. D. Vorlop, *DECHEMA-Monogr.* **84,** 266–273 (1979).
17. Redox Reactions in the Transformation of Hydrocortisone and Prednisolone by Adsorbed Cells of Mycobacterium Globiforme 193, K. A. Koshcheenko, A. Yu Arinbasarova, and G. K. Skryabin, *Prinkl. Biokhim. Mikrobiol.* **15,** 645–653 (1979).
18. Production of Ethanol by Immobilized Yeasts, P. G. Krouwel, *Antonie van Leeuwenhoek* **45,** 646 (1979).
19. Continuous Production of *N*-Butanol And Isopropanol by Immobilized, Growing Clostridium Butylicum Cells, P. G. Krouwel, W. F. M. Van der Laan, and N. W. F. Kossen, *Biotechnol. Lett.* **2,** 253–258 (1980).
20. Alcohol Production by Magnetically Immobilized Yeasts, P. O. Larsson and K. Mosbach, *Biotechnol. Lett.* **1,** 501–506 (1979).
21. Alanine Acylase Activity of Encapsulated Yeasts, E. N. Makarova, A. B. Melkonyan, and L. S. Markosyan, *Biol. Zh. Arm.* **32,** 860–864 (1979).
22. Preparation of Luminous Materials Containing Immobilized Luminous Bacterial Cells, N. Makiguchi, M. Arita, and Y. Asai, *J. Ferment. Technol.* **58,** 167–169 (1980).
23. Current Status and Future of Immobilized Enzyme and Immobilized Microbial Cells, T. Miyauchi, *Kagaku Kogaku* **44,** 91–94 (1980).
24. Continuous Production of Bacitracin by Immobilized Living Whole Cells of Bacillus SP, Y. Morikawa, I. Karube, and S. Suzuki, *Biotechnol. Bioeng.* **22,** 1015–1023 (1980).
25. Continuous Production of Glutathione Using Immobilized Microbial Cells Containing ATP Generating System, K. Murata, K. Tani, K. Kato, and I. Chibata, *Biochimie* **62,** 347–352 (1980).
26. Conversion of Glycerol to Dihydroxyacetone by Immobilized Whole Cells of *Acetobacter Xylinum*, K. Nabe, N. Izuo, S. Yamada, and I. Chibata, *Appl. Environ. Microbiol.* **38,** 1056–1060 (1979).
27. Preparation of Immobilized Animal Cells, K. Nilsson and K. Mosbach, *Fed. Lett.* **118,** 145–150 (1980).
28. "Living Electrode" as a Long-Lived Photoconverter for Biophotolysis of Water, H. Ochiai, H. Shibata, Y. Sawa, and T. Katoh, *Proc. Natl. Acad. Sci. USA* **77,** 2442–2444 (1980).
29. Immobilization of Yeast Cells by Entrapment and Adhesion Using Siliceous Materials, P. G. Rouxhet, J. L. VanHaecht, J. Didelez, P. Gerard, and M. Briquet, *Enzyme Microb. Technol.* **3,** 49–54 (1981).
30. Ethanol Production in an Immobilized-Cell Reactor, C. O. Sitton and J. L. Gaddy, *Eur. J. Biochem.* **110,** 1735–1748 (1980).
31. Continuous Citric Acid Synthesis within Polyacrylamid Gel Immobilized *Candida lipolytica* Cells, U. Stottmeister, *Z. Allg. Mikrobiol.* **19,** 763–765 (1979).
32. Kinetics of Production of L-Aspartic Acid by Aspartase of Immobilized *Escherichia coli* Cells, S. Takamatsu, K. Yamashita, and A. Sumi, *J. Ferment. Technol.* **58,** 129–133 (1980).
33. Entrapment of Microbial Cells and Organelles with Hydrophilic Urethane Prepolymers, A. Tanaka, I. Jin, S. Kawamoto, and S. Fukui, *Eur. J. Appl. Microbiol. Biotechnol.* **7,** 351–354 (1979).
34. Stereospecific Hydrogenations with Immobilized Microbial Cells or Enzymes, W. Tischer, W. Tiemeyer, and H. Simon, *Biochimie* **62,** 331–339 (1980).
35. Xanthine Oxidase Activity of Arthrobacter X-4 Cells Immobilized in Glutaraldehyde-Crosslinked Gelatin, J. Tramper, H. C. Van der Plas, A. Van der Kaaden, F. Mueller, and W. J. Middelhoven, *Biotechnol. Lett.* **1,** 397–402 (1979).

36. Immobilized Microbial Cells, K. Venkatasubramanian and W. R. Vieth, *Prog. Ind. Microbiol.* **15,** 61–86 (1979).
37. Pellets of Immobilized Yeast Cells as Biocatalysts for Transforming Bioomass, R. Villet, J. Dillon, and G. Manderson, *Sun 2, Proc. Int. Sol. Energy Soc.* **1,** 78–82 (1979).
38. Immobilized Whole Cells as Industrial Biocatalysts, V. Vojtisek, R. Zeman, M. Barta, K. Culik, J. Drobnik, and F. Svec, *Biol. Listy* **44,** 192–211 (1979).
39. A New Immobilization of Microbial Cells. Immobilized Growing Cells Using Carrageenan Gel and Their Properties, M. Wada, J. Kato, and I. Chibata, *Eur. J. Appl. Microbiol. Biotechnol.* **8,** 241–247 (1980).
40. Continuous Production of L-Isoleucine Using Immobilized Growing Serratia Marcescens Cells, M. Wada, T. Uchida, J. Kato, and I. Chibata, *Biotechnol. Bioeng.* **22,** 1175–1188 (1980).
41. Production of D-Phenylglycine-Related Amino Acids by Immobilized Microbial Cells, H. Yamada, S. Shimizu, H. Shimmda, Y. Tani, S. Takahaski, and T. Ohashi, *Biochimie* **62,** 395–399 (1980).
42. Continuous Production of L-Alanine Using *Pseudomonas dacunhae* Immobilized with Car rageenan, K. Yamamoto, T. Tosa, and I. Chibata, *Biotechnol. Bioeng.* **10,** 2045–2054 (1980).

Hugh C. McDonald
Corning Glass Works