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Continuous Cultivation of Microorganisms

A Review

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INTRODUCTION

This review includes papers published in 1971 that reached us before the manuscript deadline, as well as those which appeared earlier but were not available in this country. Being aware of the incompleteness of this review, we hope that it is not far from the total number of publications brought out during the period followed. As in the preceding reviews, patents were not pursued on purpose but those on file were listed at the end of the references.

Compared with the year 1970, the number of publications is approximately by one fifth higher, which indicates an increasing interest in continuous processes. This trend was also apparent at the Fifth International Symposium and Study Group on Continuous Culture of Micro-organisms held from July 19 to 24, 1971, at Oxford. The symposium papers were originally published in the Journal of Applied Chemistry and Biotechnology, Vol. 22, Issues 1 to 4, and then (1972) reprinted as a book entitled Environmental Control of Cell Synthesis and Function; Eds. A. C. R. Dean, S. J. Pirt and D. W. Tempest, Academic Press 1972.

I. FURTHER DEVELOPMENT OF THE THEORY OF CONTINUOUS FERMENTATION

A. Reviews

A review of selected recent developments of the stoichiometry and kinetic reactions of important biological reactions

1. Andrews, J. F.: *Kinetic models of biological waste treatment.* In: 1971, Biol. Waste Treat. (ed. R. P. Canale), pp. 5—33, Interscience, New York, N.Y.

70th anniversary of the birth of N. D. Ierusalimskii, promotor of continuous cultivation in the USSR

2. Anonym: *70-th birth anniversary of N. D. Ierusalimskii.* (In Russian) Mikrobiologiya 40 : 581, 1971.

Lysine-rich food yeast from petroleum

3. Gatellier, C.: *Petroleum microbiology. Its scientific scope and its application to the creation of a new protein source.* (In French) Rev. Inst. Fr. Petrole Ann. Combust. Liquides 25 : 419, 1970.

Influence of continuous processes on British practice in the design of fermentors and auxiliary equipment; automation and computerization of operations

4. Hastings, J. J. H.: *Development of the fermentation industries in Great Britain.* In: 1971, Adv. Appl. Microbiol., Vol. 14 (ed. D. Perlman), pp. 1—45, Academic Press, New York and London.

A manual of continuous cultures providing an introduction to the theory and concepts and describing different culture techniques and their potential application

5. Kubitschek, H. E.: *Introduction to research with continuous cultures.* Prentice-Hall, Inc., Englewood Cliffs, 195 pp., 1970.

Historical development of continuous cultivations

6. Málek, I.: *Über kontinuierliche Züchtung von Mikroorganismen. Heutiger Stand und Bedeutung als Methode der experimentellen Forschung.* Leopoldina (3) 14 (1968) : 121, 1971.

Reluctance to use continuous cultivations in fermentation industry

7. Perlman, D.: *Some prospects for the fermentation industries.* Waller. Lab. Commun. 33 : 165, 1970.

A classification scheme dividing continuous beer fermentations into closed, partially closed, and open systems with respect to outflow of yeast cells, and further into homogenous, partially homogenous and heterogeneous with respect to the conditions or phases in the system

8. Portno, A. D.: *Theoretical and practical aspects of continuous fermentation.* Waller. Lab. Commun. 33 : 149, 1970.

Biological aspects in the control of normal and mixed populations, problems of the oscillatory phenomena

9. Rehm, H. J.: *Biologische Gesichtspunkte in biochemischen Industrien.* Chem.-Ing.-Techn. 43 : 56, 1971.

A review of publications dealing with continuous cultures

10. Řičica, J.: *Continuous cultivation of microorganisms. A review.* Folia Microbiol. 16 : 389, 1971.

Large-scale and small-scale continuous processes applied to production of pharmaceutical substances, organic chemicals, to drying and to treatment of sewage and trade wastes

11. Righelato, R. C., Elsworth, R.: *Industrial applications of continuous culture: pharmaceutical products and other products and processes.* In: 1970, Adv. Appl. Microbiol., Vol. 13 (ed. D. Perlman), pp. 399—417, Academic Press, New York and London.

Two classification groups: (a) main system types; (b) basic types of fermentation processes, used for the selection of the fermentation system and for the evaluation of the economic factors

12. Royston, M. G.: *Continuous fermentation.* Chem. and Industry (6) : 170, 1971.

Submersed cultivation of mammalian cells

13. Telling, R. C., Radlett, P. J.: *Large-scale cultivation of mammalian cells.* In: 1970, Adv. Appl. Microbiol., Vol. 13 (ed. D. Perlman), pp. 91—119, Academic Press, New York and London.

A monograph; kinetics and energetics of yeast growth, nutrition, physiology and biochemistry of yeasts

14. Van Uden, N.: *Kinetics and energetics of yeast growth.* In: 1971, The Yeasts, Vol. 2, (eds. A. H. Rose and J. S. Harrison), pp. 75—118, Academic Press, London and New York.

A review of enzyme production a short part of which deals with continuous processes

15. Zickler, F., Kupke, G.: *Enzyme und Lebensmittelproduktion. II. Enzymsynthese durch Mikroorganismen.* Ernährungsforschung 16 : 74, 1971.

B. Basic contributions and mathematical theory

Functional equations describing a population dynamics of bacteria; the individual cells are due to experience a cycle of growth and division during the proliferation period

16. Aiba, S., Endo, I.: *Statistical analysis of growth of microorganisms.* A.I.Ch.E. Journal 17 : 608, 1971.

The basic kinetic relationships of biological processes used for waste-water treatment

17. Andrews, J. F.: *Kinetic models of biological waste treatment processes.* In: 1971, Biol. Waste Treat. (ed. R. P. Canale), pp. 5—33, Interscience, New York, N.Y.

A dynamic model used for the prediction of the process performance during start-up operations of anaerobic digesters, other transient conditions and the frequency of digester failure

18. Andrews, J. F., Graef, S. P.: *Mathematical modeling and simulation of the anaerobic digestion process.* Amer. Chem. Soc., Div. Water, Air Waste Chem., Gen. Pap. 10 : 112, 1970.

A mathematical model for the production of gramicidin S based on the division of the age of a cell into two phases — an immature and a mature one

19. Blanch, H. W., Rogers, P. L.: *Production of gramicidin S in batch and continuous culture.* Biotechnol. Bioeng. 13 : 843, 1971.

A mathematical description of oxygen diffusion from flowing medium to microbial slime layer and description of the computer programme

20. Bungay, H. R., III, Harold, D. M., Jr.: *Simulation of oxygen transfer in microbial slimes.* Biotechnol. Bioeng. 13 : 569, 1971.

Growth kinetics of heterogeneous microbial populations of sewage origin

21. Chiu, S. Y., Fan, L. T., Kao, I. C., Erickson, L. E.: *Kinetic behavior of mixed populations of activated sludge.* In: 1971, Amer. Chem. Soc., Div. Microbial Chem. and Technol., 162nd ACS Nat. Meet., Washington, D.C., Sept. 13—16, 1971.

Interaction of macromixing and micromixing in microbial flow stirred reactors in series; a series combination of a plug-flow reactor and a stirred tank reactor

22. Fan, L. T., Tsai, B. I., Erickson, L. E.: *Simultaneous effect of macromixing and micromixing on growth processes.* A.I.Ch.E. Journal 17 : 689, 1971.

The renewal equation describing the periodic change of the growth rate in an externally synchronized cell population

23. Franke, E. K.: *Mathematical model of synchronized periodic growth of cell populations.* J. Theoret. Biol. 26 : 373, 1970.

Classification of fermentations and fermentors and formulation of models for the growth of pure cultures of both the unicellular and filamentous organisms

24. Fredrickson, A. G., Megee, R. D., Tsuchiya, H. M.: *Mathematical models for fermentation processes.* In: 1970, Adv. Appl. Microbiol., Vol. 13 (ed. D. Perlman), pp. 419—465, Academic Press, New York and London.

Perspectiyes of the application of structured models

25. Fredrickson, A. G., Ramkrishna, D., Tsuchiya, H. M.: *The necessity of including structure in mathematical models of unbalanced microbial growth.* Chem. Eng. Progr., Symp. Ser. 67 : 53, 1971.

Cell yield of heterogeneous populations of sewage origin acclimated to glucose was subjected to statistical analysis; equations were developed to show the effect of different parameters on the stability

26. Gaudy, A. F., Jr., Ramanathan, M.: *Variability in cell yield for heterogeneous microbial populations of sewage origin grown on glucose.* Biotechnol. Bioeng. 13 : 113, 1971.

27. Ramanathan, M., Gaudy, A. F., Jr.: *Steady-state model for activated sludge with constant recycle sludge concentration.* Biotechnol. Bioeng. 13 : 125, 1971.

Mathematical models describing variations of specific growth rates, generation times, concentrations of substrates and products in anaerobic mixed digester populations

28. Ghosh, S.: *Kinetics of substrate assimilation and product formation in anaerobic mixed culture systems.* In: 1971, Amer. Chem. Soc., Div. Microbial Chem. and Technol., 162nd ACS Nat. Meet., Washington, D.C., Sept. 13—16, 1971.

An approximate prediction of the steady-state bacterial density, glucose and lactate concentrations using either a graphical technique or a method based on the kinetic model of the batch culture

29. Hanson, T. P.: *Steady state and transient behavior of a continuous fermentor.* Diss. Abstr. B 31 : 650-B, 1970.

From a graphical analysis a mathematical model is derived relating growth, glucose utilization and lactic acid formation

30. Hanson, T. P., Tsao, G. T.: *Kinetic studies of the lactic acid fermentation in batch and continuous cultures.* In: 1971, Amer. Chem. Soc., Div. Microbial Chem. and Technol., 162nd ACS Nat. Meet., Washington, D.C., Sept. 13—16, 1971.

Methods for predicting substrate utilization rates of urea, CO_2 production rates of extracellular metabolites, photosynthetic quotients as functions of specific growth rate and growth limiting conditions obtained from variables of an algae propagator

31. Hanson, D. T., Fredrickson, A. G., Tsuchiya, H. M.: *Continuous propagation of microalgae. III. Material balance relations.* Chem. Eng. Progr., Symp. Ser. 67 : 151, 1971.

Microbial growth rate equations for theoretical systems deficient in or having an excess of substrate

32. Irvine, R. L., Schaezler, D. J.: *Kinetic analysis of data from biological systems.* J. Sanit. Eng. Div., Amer. Soc. Civil Eng. 97 (SA4) : 409, 1971.

Kinetic studies of relationship between productivity of cell mass and dilution rate and the effect of operating conditions

33. Kono, T., Asai, T.: *Studies on fermentation kinetics. Kinetic analysis of productivity of cell mass in continuous fermentation.* J. Ferment. Technol. (Japan) 49 : 133, 1971.

Analogue computer modelling of microbial inhibitor interrelations

34. Kožešník, J.: *Dynamic modelling of microbiological production processes.* (In Russian) Biofizika 17:270, I971.

Steady-state kinetic models of waste treatment employing suspended or fluidized cultures of microorganisms for two completely mixed biological process configurations and for a plug flow modification with and without microorganism recycle are presented

35. Lawrence, A. W.: *Application of process kinetics to design of anaerobic processes.* Amer. Chem. Soc., Div. Water, Air Waste Chem., Gen. Pap. 10 : 115, 1970.

36. Lawrence, A. W., Milnes, T. R.: *Biokinetic approach to activated sludge system design.* In: 1971, Amer. Chem. Soc., Div. Microbial Chem. and Technol., 162nd ACS Nat. Meet., Washington, D.C., Sept. 13—16, 1971.

A model considering the anaerobic decomposition of organic wastes as a series of bacterially mediated reactions. The yield of organisms is a function of the reaction energetics and the concentration of all components is a function of the cellular retention time

37. McCarty, P. L.: *Energetics and kinetics of anaerobic treatment.* Adv. Chem. Ser. (Anaerobic Biol. Treat. Process.) 105 : 91, 1971.

A mechanistic model of the growth kinetics of yeast utilizing a liquid hydrocarbon as sole carbon source

38. Moo-Young, M., Shimizu, T.: *Hydrocarbon fermentations using Candida lipolytica. II. A model for growth kinetics.* Biotechnol. Bioeng. 13 : 761, 1971.

Numerical solutions of the appropriate transient equation for the enzymatic reaction inhibited by substrate; it is shown how the system approaches stable steady-state in instances where there are three possible steady-state points

39. O'Neill, S. P.: *Steady-state stability of substrate inhibited enzyme catalysis in open reaction systems.* Biotechnol. Bioeng. 13 : 493, 1971.

40. O'Neill, S. P., Lilly, M. D., Rowe, P. N.: *Multiple steady states in continuous-flow, stirred-tank enzyme reactors.* Chem. Eng. Sci. 26 : 173, 1971.

Theory of a chemostat with feedback extended to include concentration of the biomass outside or inside the culture vessel by some mechanical means

41. Pirt, S. J., Kurowski, W. M.: *An extension of the theory of the chemostat with feedback of organisms. Its experimental realization with a yeast culture.* J. Gen. Microbiol. 63 : 357, 1970.

A theory of diffusion control within hollow fiber catalysts for insolubilized enzymes is derived; effectiveness factors are calculated and formulas for reactant conversion in both a fixed-bed and a continuous-feed stirred reactor are derived

42. Rony, P. R.: *Multiphase catalysis. II. Hollow fiber catalysts.* Biotechnol. Bioeng. 13 : 431, 1971.

A nonlinear mathematical model solved by a perturbation technique describes the rate of diffusion-coupled biochemical reactions of the cellulose conversion to protein

43. Ross, L. W., Updegraff, D. M.: *Kinetics of diffusion-coupled fermentation processes: the conversion of cellulose to protein.* Biotechnol. Bioeng. 13 : 99, 1971.

Mathematical modelling of bacterial reactions concerned with the effect of substrate concentration on growth rate, with the segregation effects, with the prediction of steady states and transient responses to changes in substrate concentration and dilution rate

44. Schaezler, D. J.: *Mixing and segregation in pure and heterogeneous bacterial cultures.* Diss. Abstr. B 32 : 2139-B, 1971.

Mathematical modelling of microbial reactions in batch, steady-state and transient experiments

45. Schaezler, D. J., McHarg, W. H., Busch, A. W.: *Effect of the growth rate on the transient responses of batch and continuous microbial cultures.* In: 1971, Biol. Waste Treat. (ed. R. P. Canale), pp. 107—129, Interscience, New York, N.Y.

Two kinetic models used for cell production and for biological waste treatment

46. Shah, P. S., Fan, L. T., Erickson, L. E.: *Optimal control theory applied to growth processes.* In: 1971, Amer. Chem. Soc., Div. Microbial Chem. and Technol., 162nd ACS Nat. Meet., Washington, D.C., Sept. 13—16, 1971.

A variant of the Monod's model modified for endogenous metabolism and used for prediction of transient behaviour under certain conditions

47. Sinclair, C. G., Topiwala, H. H., Brown, D. E.: *Experimental investigation of a growth model for Aerobacter aerogenes in continuous culture.* Chem. Eng. (London) (249) : 198, 1971.

Some of the sources of error in dynamic models of experimental transient responses of continuous culture

48. Sinclair, C. G., King, W. R., Ryder, D. H., Topiwala, H. H.: *Some difficulties in fitting dynamic models to experimental transient data in continuous culture.* Biotechnol. Bioeng. 13 : 451, 1971.

Deterministic mathematical models considering important variables, such as the distributed concentration of substrates, phenotypes and the total biomass of microbial systems possessing two growth-

49. Standing, C. N.: *Microbial growth in two-substrate systems.* Diss. Abstr. B 31 : 5519-B.

limiting substrates; these models were solved with the aid of a digital computer

Stabilization of a cultivator with feedback of the population solved by means of phase space methods and optimal control

50. Stepanova, N. V., Fedorova, T. A.: *Optimization of transient processes in continuous cultivation of microorganisms (a model considering the inhibition with products of secondary metabolism).* (In Russian) Biofizika 16 : 841, 1971.

Examination of a statistical model for growth by solving the partial differential integral equations

51. Subramanian, G., Ramkrishna, D., Fredrickson, A. G.: *On the mass distribution model for microbial cell populations.* Bull. Math. Biophys. 32 : 521, 1970.

The importance of wall growth below the surface of the culture in evaluating continuous culture data

52. Topiwala, H. H., Hamer, G.: *Effect of wall growth in steady-state continuous cultures.* Biotechnol. Bioeng. 13 : 919, 1971.

Determination of kinetic parameters of the fitted steady-state model which are strong functions of temperature; the transient response of the culture and the dynamic lag depend on the nature and direction of the temperature step change

53. Topiwala, H. H., Sinclair, C. G.: *Temperature relationship in continuous culture.* Biotechnol. Bioeng. 13 : 795, 1971.

Importance of micromixing in growth processes and the influence of segregation on the rate of cell production

54. Tsai, B. I., Fan, L. T., Erickson, L. E., Chen, M. S. K.: *Reversed two-environment model of micromixing and growth processes.* J. Appl. Chem. Biotechnol. 21 : 307, 1971.

Equations of the transfer rates of substrates and products into and out of cells, the rates of heat production and of biomass production, and the exchange rates of heat and matter

55. Van Uden, N.: *Thermodynamics of the chemostat.* Zeitschr. Allg. Mikrobiol. 11 : 541, 1971.

Economy of mathematical models, reaction kinetics and flow pattern of the enzymatic reactions and of the production of enzymes

56. Yuh-shu Ho L.: *Optimization studies of processes for enzymatic reactions and microbial enzyme production.* Diss. Abstr. B 31 : 3352-B, 1970.

Dynamics models for anaerobic digestion of organic wastes

(see IA/1)

A model for the performance of algal population using a mathematical expression for the high response curve of photosynthesis

(see IIA/68)

Product feedback repression model used for analog computer simulation of cytochrome oscillations

(see IIA/88)

Parameters for individual cell growth obtained by use of an integral-differential equation based on limitation caused by slow flux through the cell surface

(see IIA/102)

A mathematical model based on a theoretical and experimental understanding of bacterial growth on heptane

(see IIA/165)

II. PHYSIOLOGY OF MICROORGANISMS AND PRODUCT FORMATION

A. Physiology and metabolic studies

A logarithmic loss of viability due to unbalanced growth of a part of the population at the beginning of each cycle during an induced synchronization of cell division in a semicontinuous culture system

57. Anagnostopoulos, G. D.: *Unbalanced growth in a semicontinuous culture system designed for the synchronization of cell division.* J. Gen. Microbiol. 65 : 23, 1971.

Cultivation of yeast on methanol

58. Asthana, H., Humphrey, A. E.: Moritz, V.: *Growth of yeast on methanol as the sole carbon substrate.* Biotechnol. Bioeng. 13 : 923, 1971.

Sensitivity of algae to temperature resulting in changes of cell number, mean cell size and dry weight per wet cell volume in nitrate limited cultures

59. Blaug, M.: *The effect of temperature on continuously cultured algae.* Diss. Abstr. B 31 : 6151-B, 1971.

Influence of formic acid and of temperature treatment of milk on the growth of lactobacilli and on the formation of acetaldehyde, acetoin and diacetyl

60. Bottazzi, V., Battistotti, B., Vescovo, M.: *Continuous production of yoghurt cultures and stimulations of Lactobacillus bulgaricus by formic acid.* Milchwissenschaft 26 : 214, 1971.

Increase in glucose concentration has a marked effect on fatty-acid composition of some yeasts; these changes correlate with a decrease in the oxidative degradation of glucose and therefore indicate a possible decrease in mitochondrial lipid

61. Brown, C. M., Johnson, B.: *Influence of glucose concentration on the lipid content of some yeasts.* (In: Soc. Gen. Microbiol., 62nd Meet. at Trinity College, Dublin, 16—17 Sept. 1971, pp. i—xxv.) J. Gen. Microbiol. 68 (3) : vii, 1971.

Fatty-acid content, repression of mitochondrial structures, amino acid pool, aerobic and fermentative metabolism of yeast cells grown at increasing concentrations of glucose and galactose and at decreasing oxygen tensions

62. Brown, C. M., Johnson, B.: *Influence of the concentration of glucose and galactose on the physiology of Saccharomyces cerevisiae in continuous culture.* J. Gen. Microbiol. 64 : 279, 1971.

63. Brown, C. M., Johnson, B.: *Influence of oxygen tension on the physiology of Saccharomyces cerevisiae in continuous culture.* Antonie van Leeuwenhoek 37 : 477, 1971.

Maintenance coefficient for glucose and for oxygen, nonlinear relationship between growth rate and glucose utilization rate and the effect of oxygen tension on the morphology

64. Carter, B. L. A., Bull, A. T., Pirt, S. J., Rowley, B. I.: *Relationship between energy substrate utilization and specific growth rate in Aspergillus nidulans.* J. Bacteriol. 108 : 309, 1971.

65. Carter, B. L. A., Bull, A. T.: *The effect of oxygen tension in the medium on the morphology and growth kinetics of Aspergillus nidulans.* J. Gen. Microbiol. 65 : 265, 1971.

A mode of death acceleration by glycerol, glucose and pyruvate of cells limited by glycerol; prevention of this effect by 3′—5′ cyclic AMP

66. Calcott, P. H., Postgate, J. R.: *Substrate-accelerated death: role of recovery medium and prevention by 3′—5′ cyclic AMP.* (In: 1971, 61st Gen. Meet. Soc. Gen. Microbiol. at the Univ. Coll. London, 5—7 April 1971, pp. i—viii.) J. Gen. Microbiol. 66 (3) : i.

The growth of microorganisms in media where oil had been maintained as the continuous phase

67. Coty, V. F., Corring, R. L., Heilweil, I. J., Leavitt, R. I., Srinivasan, S.: *Growth of microbes in an oil-continuous environment.* Biotechnol. Bioeng. 13 : 825, 1971.

Effects of the specific growth rate and of the incident light intensity on algal biomass productivity and algal physiology

68. Dabes, J. N.: *The behavior of Chlorella pyrenoidosa in steady state continuous culture.* Diss. Abstr. B 32 : 902-B, 1971.

Independent control of nuclear and plastid ploidy by growth conditions in normal medium and under phosphate starvation

69. Davis, E. A., Epstein, H. T.: *Some factors controlling step-wise variation of organelle number in Euglena gracilis.* Exp. Cell Res. 65 : 273, 1971.

Sensitivity of yeasts to oxygen supply during different stages of the cell cycle in a cyclone column apparatus

70. Dawson, P. S. S.: *A pilot plant apparatus for continuous phased culture — some observations on oxygen usage by Candida utilis during the cell cycle.* Biotechnol. Bioeng. 13 : 877, 1971.

Effect of drugs on bacteria and their metabolism

71. Dean, A. C. R.: *Adaptive drug resistance in gram-negative bacteria.* Proc. Roy. Soc. Med. 64 : 534, 1971.

72. Dean, A. C. R., Moss, D. A.: *Barbitone induced oscillatory responses in Klebsiella (Aerobacter) aerogenes.* Biochem. Pharmacol. 20 : 1, 1971.

73. Dean, A. C. R., Moss, D. A.: *Interaction of nalidixic acid with Klebsiella (Aerobacter) aerogenes growing in continuous culture.* Chem.-Biol. Interactions 2 : 281, 1970.

Sustained oscillations in light absorption when bacteria are allowed to respire in a non-growing state in a system open to oxygen

74. Degn, H., Harrison, D. E. F.: *Undamped short period oscillations of flavin in respiring non-growing bacteria.* Biochem. Biophys. Res. Commun. 45 : 1554, 1971.

Dependence of two pathways of pyruvate conversion: a reduction to lactate and phosphoroelastic cleavage on the dilution rate; requirement of lactate dehydrogenase for fructose-1,6-diphosphate and manganous ions

75. De Vries, W., Kapteijn, W. M. C., Van der Beek, E. G., Stouthamer, A. H.: *Molar growth yields and fermentation balances of Lactobacillus casei L 3 in batch cultures and in continuous cultures.* J. Gen. Microbiol. 63 : 333, 1970.

Anaerobic cultivation of pure strains of methanogenic bacteria growing on a mixture of hydrogen and carbon dioxide

76. Dework, F. M., Paynter, M. J. B.: *Continuous cultivation of methanogenic bacteria.* In: 1971, Amer. Chem. Soc., Div. Microbial Chem. and Technol., 162nd ACS Nat. Meet., Washington, D.C., Sept. 13—16, 1971.

White light induction of β-carotene formation in streptomycin-bleached algae influenced by the type of carbon source and aeration

77. Dolphin, W. D.: *Photoinduced carotenogenesis in chlorotic Euglena gracilis.* Plant Physiol. 46 : 685, 1970.

Microbial degradation of aliphatic and branched hydrocarbons, metabolic mechanisms, transport, role of oxygen, metabolic products, cultivation, growth kinetics, yield, productivity and separation

78. Einsele, A., Fiechter, A.: *B. Liquid and solid hydrocarbons.* In: 1971, Adv. Biochem. Eng., Vol. 1, (eds. T. K. Ghose and A. Fiechter), pp. 169—194, Springer-Verlag.

The ionic polymer composition of the cell walls of bacilli

79. Ellwood, D. C.: *The anionic polymers in the cell wall of Bacillus subtilis var. niger grown in phosphorus-limiting environments supplemented with increasing concentrations of sodium chloride.* Biochem. J. 121 : 349, 1971.

Assimilation of NO_3^- and NH_4^+ during light-dark cycles with cultures of the phytoplankton; measurement of the activities of N-assimilating enzymes in cell-free extracts

80. Eppley, R. W., Rogers, J. N., McCarthy, J. J., Sournia, A.: *Light/dark periodicity in nitrogen assimilation of the marine phytoplankters Skeletonema costatum and Coccolithus huxleyi in nitrogen-limited chemostat culture.* J. Phycol. 7 : 150, 1971.

A method embodying some features of batch and continuous cultivation for the selective production of heat resistant spores

81. Evans, C. G. T., Harris-Smith, R.: *A novel selective method for the production of Bacillus subtilis var. niger spores.* J. Appl. Bacteriol. 34 : 215, 1971.

Anomalous growth yields, energy of maintenance, and energetic uncoupling

82. Forrest, W. W., Walker, D. J.: *The generation and utilization of energy during growth.* In: 1971, Adv. Microbial Physiol., Vol. 5 (eds. A. H. Rose and J. F. Wilkinson), pp. 213—274, Academic Press, London and New York.

Relationship between specific growth rate and substrate concentration, evaluation of the saturation constant

83. Gaudy, A. F., Jr., Obayashi, A., Gaudy, E. T.: *Control of growth rate by initial substrate concentration at values below maximum rate.* Appl. Microbiol. 22 : 1041, 1971.

The rate of sulphur oxidation as a function of surface area of the sulphur globules

84. Van Gemerden H., Jannasch, H. W.: *Continuous culture of Thiorhodaceae. Sulfide and sulfur limited growth of Chromatium vinosum.* Arch. Mikrobiol. 79 : 345, 1971.

Phosphorus content (lipid, cold water extractable, RNA, and DNA fractions) in yeast cells limited by glucose

85. Glättli, H., Dawson, P. S. S.: *Changes in phosphorus composition of Candida utilis during the cell cycle and postcycle period.* Can. J. Microbiol. 17 : 339, 1971.

Inhibitory effect of cycloheximide on the growth rate and activity of the cytochrome C group of yeast cells; chloramphenicol stimulation of fermentation and reduction of the efficiency of glucose utilization

86. Gray, P. P., Rogers, P. L.: *Action of chloramphenicol and cycloheximide on Saccharomyces carlsbergensis. Batch and continuous studies.* Aust. J. Biol. Sci. 24 : 487 1971.

87. Gray, P. P., Rogers, P. L.: *I. Cytochrome oscillations in continuous culture. Action of chloramphenicol on Saccharomyces carlsbergensis and Candida utilis.* Biochim. Biophys. Acta 230 : 393, 1971.

88. Gray, P. P., Rogers, P. L.: *II. Mathematical simulation of cytochrome oscillations.* Biochim. Biophys. Acta 230 : 401, 1971.

Effect of external conditions on yield coefficient and both potential and *in situ* respiration rates of facultative anaerobes

89. Harrison, D. E. F., Loveless, J. E.: *The effect of growth conditions on respiratory activity and growth efficiency in facultative anaerobes grown in chemostat culture.* J. Gen. Microbiol. 68 : 35, 1971.

90. Harrison, D. E. F., Loveless, J. E.: *Transient responses of facultatively anaerobic bacteria growing in chemostat culture to a change from anaerobic to aerobic conditions.* J. Gen. Microbiol. 68 : 45, 1971.

Inhibition of acetylene-reducing activity and nitrogen-fixing capacity by oxygen and dimorphism of colonies

91. Hill, S.: *Influence of oxygen concentration on the colony type of Derxia gummosa grown on nitrogen-free media.* J. Gen. Microbiol. 67 : 77, 1971.

Examination of the initiation of morphogenesis in the sporulating organisms during vegetative growth

92. Hsu, E. J., Younger, L., Barns, W., Burger, A.: *Phase contrast and scanning-beam electron microscopy of sporulation of Clostridium thermosaccharolyticum.* In: 1971, Bacteriol. Proc. 1971, Abstr. 71st Ann. Meet., Minneapolis, Minn., 2—7 May 1971, Amer. Soc. Microbiol., p. 58.

Cultivation of bacteria in a dialysis fermentor with aeration by dialysis transfer of oxygen

93. Humphrey, H. E. B.: *Dialysis culture of bacteria: dialyzer design, nutrient transfer, growth and dialysis aeration.* Diss. Abstr. B 31 : 6775-B, 1971.

Effect of phosphate, arginine or Na acetate limitation on growth and chlorosis of algae

94. Hudock, G. A., Gring, D. M., Bart, C.: *Responses of Chlamydomonas reinhardii to specific nutritional limitation in continuous culture.* J. Protozool. 18 : 128, 1971.

Indirect proportionality between growth inhibition by pH and stimulation of organic acid formation in lactate-containing media

95. Ibragimova, S. I., Neronova, N. M., Rabotnova, I. L.: *The effect of hydrogen ions on some properties of Propionibacterium shermanii.* (In Russian) Mikrobiologiya 40 : 833, 1971.

Limitation of marine bacteria by glucose, lactate, and glycerol

96. Jannasch, H. W.: *Threshold concentrations of carbon sources limiting bacterial growth in sea water.* In: 1970, Symp. Org. Matter Natur. Waters, pp. 321—330, (ed. by D. W. Hood), Inst. of Mar. Sci. Univ. of Alaska: College Alaska.

Fermentation of some amino acids via pyruvate to acetate in which more acetate than could be accounted for from the metabolized glucose is formed

97. Johnson, M. G.: *Effect of variations in pyruvate metabolism on molar growth yields of Streptococcus faecalis.* Diss. Abstr. B 32 : 1097-B, 1971.

Growth energy obtained from pyruvate metabolism by a lipoic acid-dependent mechanism of streptococci grown anaerobically on glucose

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(see IB/38)

A model of endogenous metabolism predicting the transient behaviour and discussing both the steady-state and dynamic character of such culture systems

(see IB/47)

Changes in growth rate and in galactose phenotype initiation in microbial systems possessing two growth-limiting substrates (glucose and galactose or glucose and xylose)

(see IB/49)

Characterization of different types of cell growth on the wall of the cultivator, importance of the surface growth in evaluating the culture data

(see IB/52)

Dependence of the steady-state and of the transient values of growth rate and yield on temperature

(see IB/53)

Nitrogen metabolism in blue-green algae grown on nitrate or under phosphate and urea limitations

(see IIB/160)

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(see IIF/209)

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Production of enzymes; a review

(see IA/15)

Substrate inhibited enzyme reactions displaying multiple steady-state behaviour

(see IB/39, 40)

The analogy between biological cells and encapsulated enzymes: hollow fibers are attractive alternatives to spherical microcapsules for attaining enzymes insolubilized but not immobilized

(see IB/42)

Production of α-amylase by a combination of a logistic growth model and an enzyme-synthesis model

(see IB/56)

C. Alcohols, solvents and gases

Fermentation of molasses with a higher sugar content in two-stage and three-stage systems results in higher yields of ethanol

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(see IIIA/237)

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Lactic acid production in a glucose-yeast extract medium under controlled pH		(see IB/29)
Effect of pH, feed concentration of glucose and residence time on the production of lactic acid		(see IB/30)
Conversion of 9α-fluoro-16α-hydrocortisol to 9α-fluoro-16α-prednisolone by intracellular dehydrogenase; conversion of glucose to gluconic acid		(see IB/56)
Continuous production of yoghurt seed		(see IIA/60)
Production of methane		(see IIA/76)
Formation of β-carotene in chlorotic algae		(see IIA/77)
Increase of acid production rate by selection of lactic streptococci in a chemostat or by treatment of the cells with a mutagen		(see IIB/184)
Lactic acid fermentation of sour milk		(see IIIA/237)

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Cultivation of cells of higher organisms in large quantities		(see IIIA/228)

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(see IB/21)

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(see IB/26, 27)

Mixed digester cultures fed with a soluble substrate

(see IB/28)

Growth differences of wild type and mutant strains to algae in competitive cultures with phosphate limitation under continuous light, continuous dark or alternating periods of light and darkness

(see IIA/94)

Replication of rubella virus in host BHK cells

(see IIA/100)

Interaction between non-hydrocarbon utilizing and hydrocarbon-utilizing organisms; a mathematical model of the process

(see IIA/165)

Coexistence of resistant and sensitive cells in a bacterium-phage population

(see IIB/183)

A mixed culture of two types of gram-negative nonsporulating rod-like methane-oxidizing bacteria

(see IVA/262)

Symbiotic algal-bacterial system for nutrient removal from waste water

(see IVC/287, 288)

Application of a mixed fungal and bacterial population for treatment of waste waters containing saccharides

(see IVC/291)

Growth of heterogeneous populations on various carbon sources from initial inocula of sewage

(see IVC/298, 298)

III. CONTINUOUS CULTIVATION EQUIPMENT

A. Cultivation devices

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(see IA/12)

Continuous flow laboratory reactors and batch reactors for aerobic biological waste water treatment seeded from continuous flow unit

(see IB/35)

A small-scale automatic apparatus for induction of synchronized cell division

(see IIA/57)

Scheme of yoghurt production

(see IIA/60)

Large scale cyclone column fermentor for phased culture

(see IIA/70)

Aparatus for cultivation of pure strains of methanogenic bacteria

(see IIA/76)

A dialyser-dialysis culture system composed of a fermentor and a separate medium reservoir with culture aeration by dialysis gas transfer

(see IIA/93)

Schematic flowsheet of 5-litre fermentor

(see IIA/126)

Apparatus for the accumulation of heterotrophic algae exposed to light

(see IIA/130)

An apparatus for quantitative measuring and recording of the phototopotactic response

(see IIA/131)

A turbidostat with measuring of pH, aeration rate, dilution rate, absorbance, culture volume, light intensity, input and output of carbon dioxide

(see IIA/138)

A diagram of a culture system monitoring cell concentration changes in autotrophic

(see IIA/141)

algae cultures exposed to clock-controlled cycles

Design of a small laboratory chemostat (see IIB/174)

Cultivation equipment for anaerobes and pathogenes (see IIB/187, 170)

Automated bioassay of antibiotics (see IID/198)

Schematic outline of a process to produce quarg in a system composed of a stirred fermentor, a plug-flow fermentor and a separator in series (see IID/200)

Diagram of chemostat and of the auxiliary equipment for the cultivation of plant cells in suspension culture (see IIE/204)

A versatile glass apparatus for cultivation of plant cells equipped with fully automatic sampling device and regulation of the optical density (see IIE/206, 207)

A two-stage apparatus for cultivation of protozoa utilizing bacteria (see IIF/210)

Diagram of an artificial rumen (see IIF/219)

A tower-type fermentor for beer production (see IVB/269)

An experimental apparatus for increasing the oxidation capacity of activated sludge (see IVC/302)

B. Bioengineering problems

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effects of dispersion and mass transfer resistance on the degree of conversion in an immobilized-enzyme reactor

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A dynamic model describing the interactions between the solution and gas phases, rates of change in volatile acid concentration, gas production rate, pH and other parameters. The effectiveness of different control techniques in preventing digester failure is presented

(see IB/18)

A model based on diffusion mechanisms accounts for oxygen transfer from flowing nutrient medium into a film of organisms in slime; parameter sensitivity tests for flow rate, oxygen concentration in the medium, and mass transfer coefficients

(see IB/20)

Additional effect of micromixing in different types of microbial flow reactors

(see IB/22)

Temperature control of wine fermentation in a metal, single-tower VICO fermentor fitted with a cooling system

(see IVB/264)

Chemical engineering aspects of tower-fermentation systems and their application in microbiological industry

(see IV/269)

IV. APPLICATION OF THE CONTINUOUS CULTIVATION METHODS

A. Production of cell mass and protein

Production of yeast cells on normal $C_{12}H_{26}$ - $C_{15}H_{32}$ alkanes

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Two complementary processes for the yeast protein production using gas oil and *n*-paraffin feeds

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Effect of pH on the yield of cell mass in relation to *n*-alkanes, wood hydrolyzates and glucose

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Utilization of C_{12}—C_{18} *n*-paraffins from petroleum by lysine-rich food yeast

(see IA/3)

Conversion of cellulose to protein — (see IB/43)

Production of yeast on cheap methanol from natural gas — a new potential source for single-cell protein — (see IIA/58)

Increase in the cell concentration in the aqueous phase where oil is maintained as the continuous phase — (see IIA/67)

Optimum algal biomass productivity and the prediction of the performance of algal systems — (see IIA/68)

Cultivation and metabolism of organisms producing protein from hydrocarbons — (see IIA/78)

Growth of yeast cells on a simple defined medium with *n*-dodecane as sole carbon source — (see IIA/126; IB/38)

Fractionation of microbial protein — (see IIA/144)

Production of algae — (see IIA/146, 155)

A sewage oxidation pond producing reusable water effluent and also an algal protein for feeding animals — (see IVC/294)

B. Fermented beverages

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Changes in populations of sewage origin due to different dilution rates	(see IB/21, 46)
Yield of cell mass of mixed population of sewage origin adapted to glucose using recycle for stabilization	(see IB/26, 27)
Growth rate equations used for the design and for the prediction of performance characteristics of waste water treatment systems	(see IB/32)
A rational approach to design of a biological waste treatment process. Using the rate limiting step concept, methane formation is identified as the process controlling step in anaerobic fermentation of complex organic waste	(see IB/35, 36; IVC/277, 292, 293)
Anaerobic treatment of wastes	(see IB/37)
Conditions necessary for the design of a denitrification treatment plant	(see IIA/123)
Utilization of a mixture of various carbon sources dissolved in synthetic waste water; growth rate, natural fluctuations in the concentration of biological solids, accumulation of metabolic intermediates, and acclimation period were examined	(see IIA/140)
Decomposition of domestic sewage by means of symbiotic culture of microalgae and sewage bacteria	(see IIF/217)
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Waste treatment in a tower-type activated sludge system	(see IIIB/246)

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LIST OF ORGANISMS

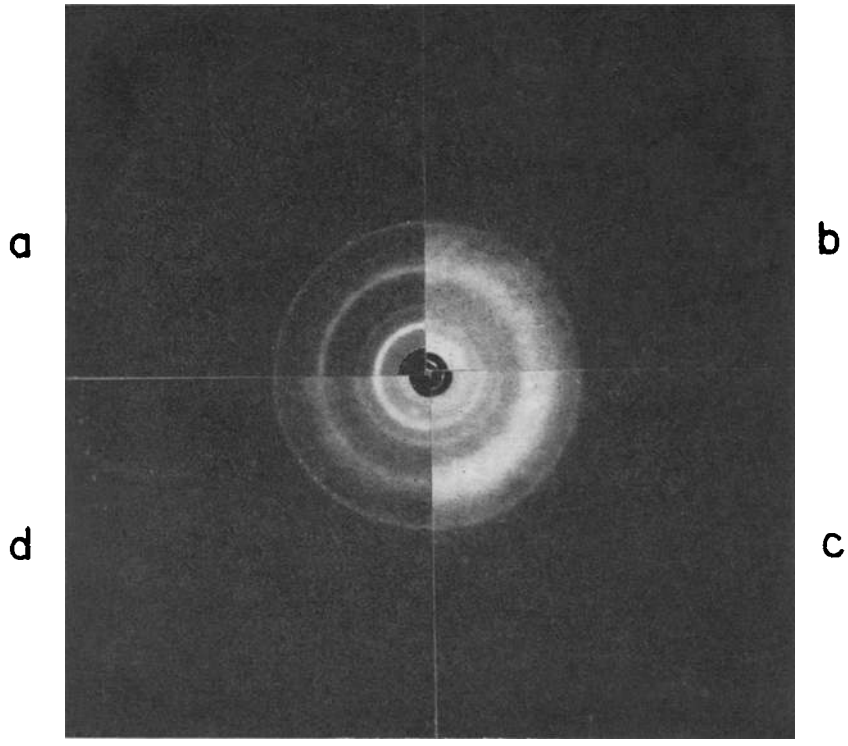

PLATE 1. X-Ray diffraction patterns of chitin (a) and fractions A (b), B (c), C (d).

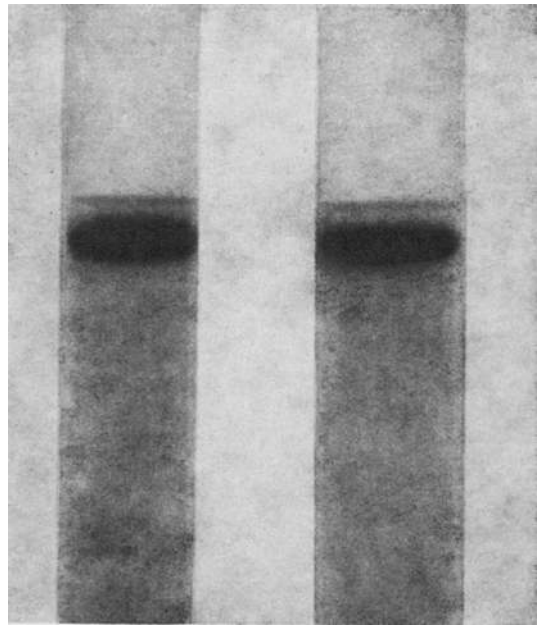

PLATE 1. Acrylamide gel electrophoresis of megaterioproteinase A (right) and S (left). Samples of 100 μg of enzyme protein. Reservoir buffer: Tris-glycine (pH 8.3) without Ca^{2+}. Anode top, cathode at bottom.

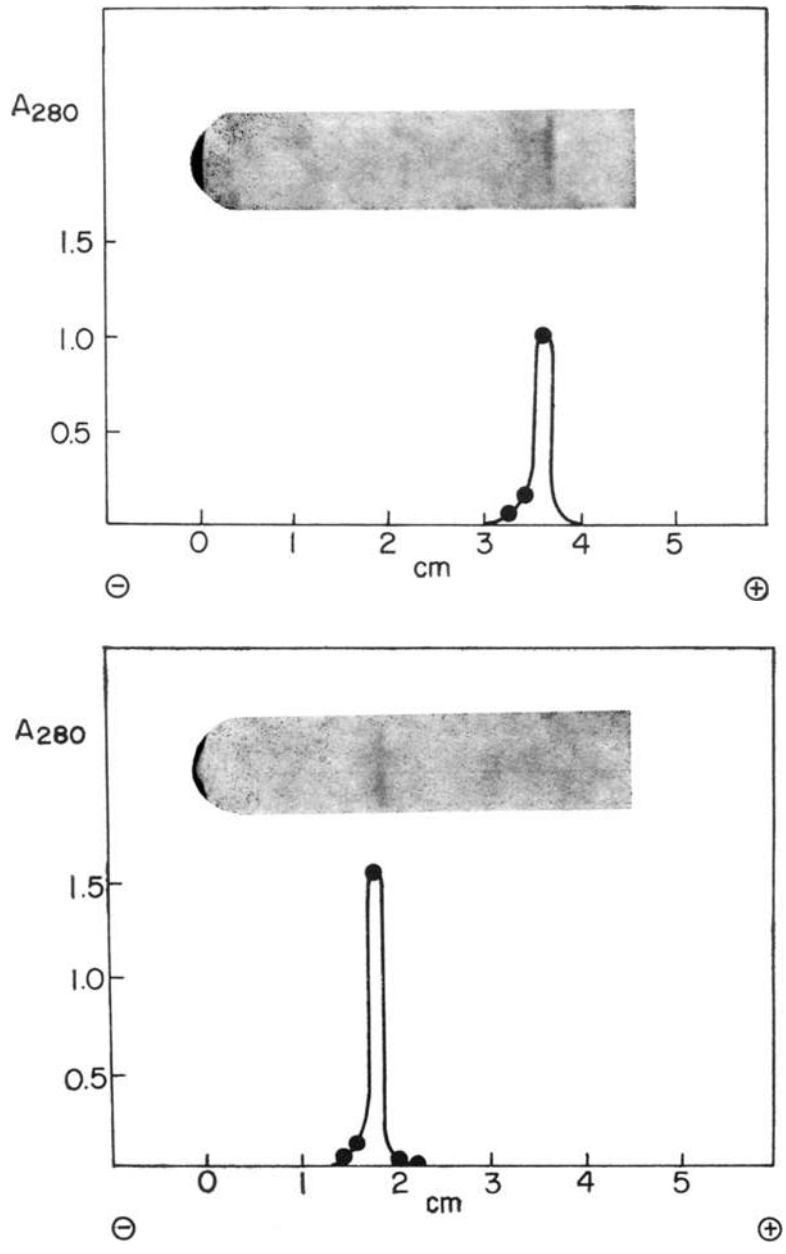

PLATE 2A, B. Acrylamide gel electrophoresis of megaterioproteinase A (a) and S (b). Samples of 50 μg of enzyme protein. Reservoir buffer: Tris-glycine (pH 8.3) containing 2mM $CaCl_2$. Proteolytic activity is expressed as the increase of absorbance at 280 nm in the TCA filtrate.

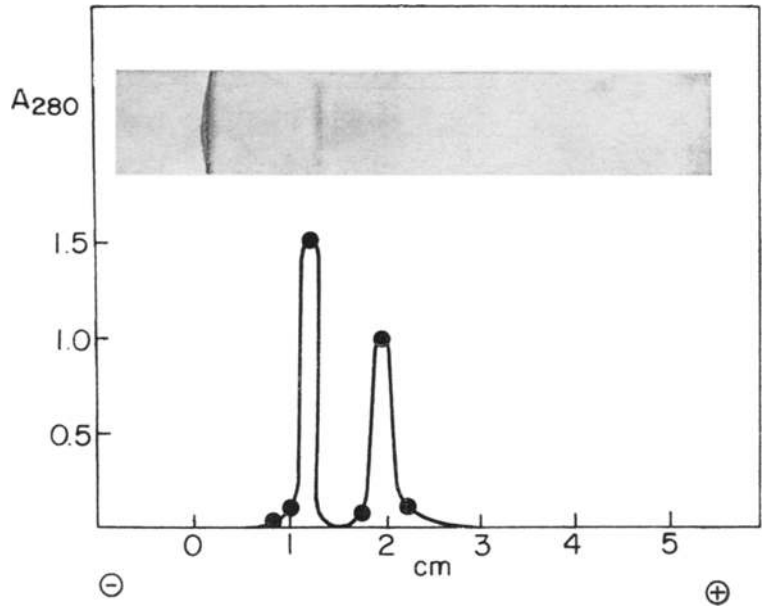

PLATE 3. Acrylamide gel electrophoresis of a mixture of megaterioproteinases A and S. 50 μg of megaterioproteinase A were mixed with 50 μg of megaterioproteinase S before applying to the gel column. Reservoir buffer and enzyme activity were as described in Plate 2.

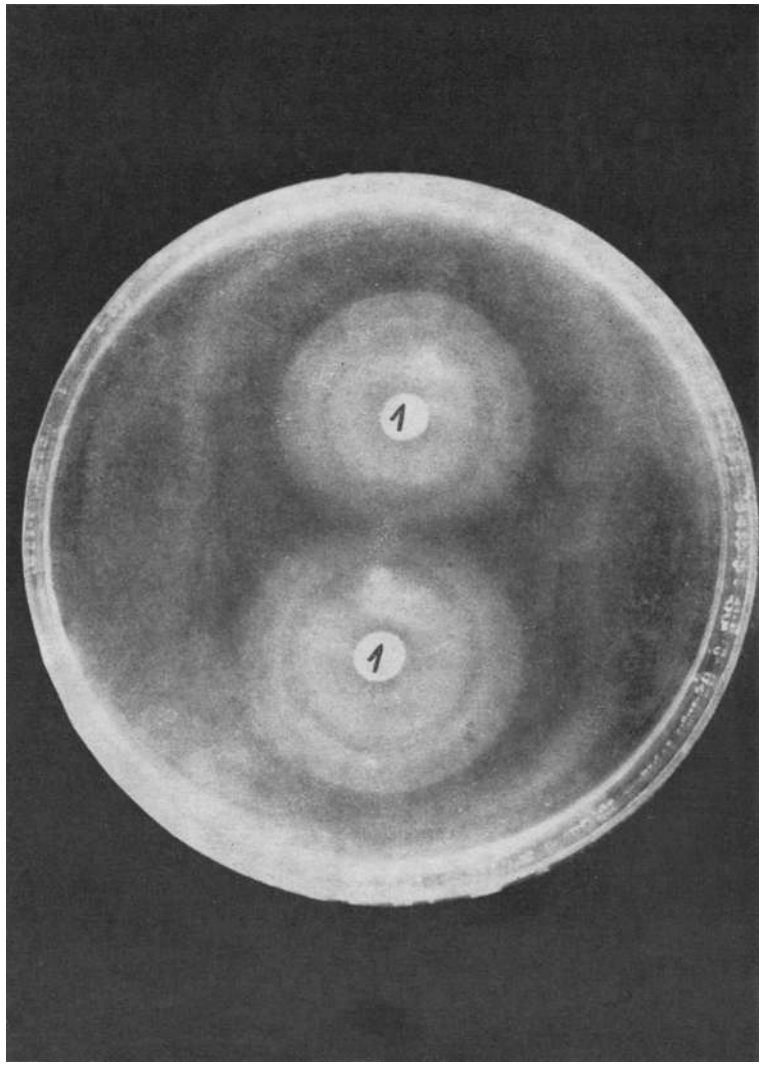

PLATE 1. Movement of LT2 cells in a tryptone medium with 0.3% agar. 1, LT2 SU 86 F^-.

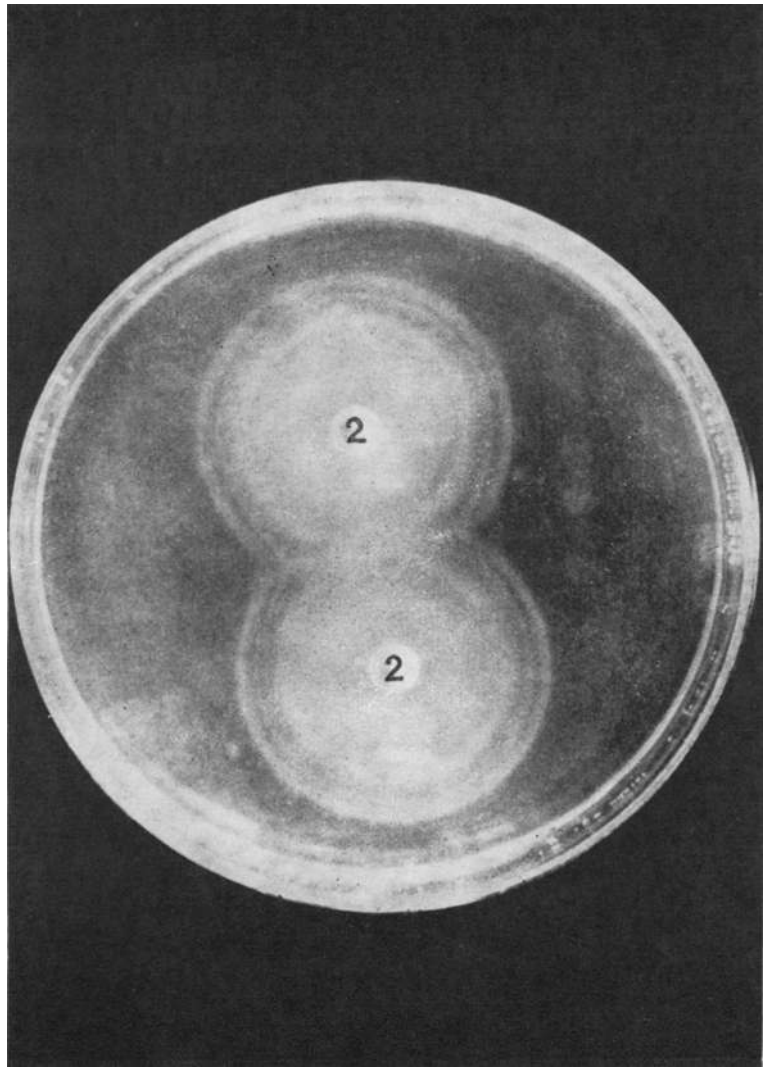

PLATE 2. Movement of LT2 cells in a tryptone medium with 0.3% agar. 2, LT2 SU 452 Hfr.

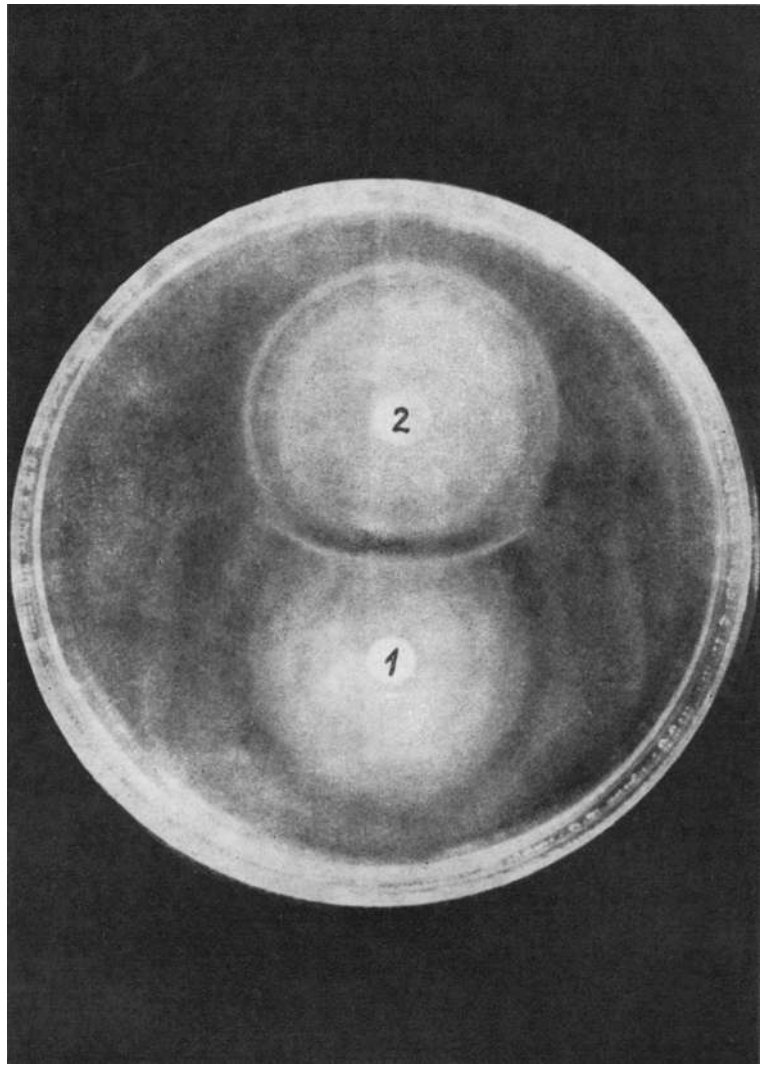

PLATE 3. Movement of LT2 cells in a tryptone medium with 0.3% agar. 1, LT2 SU 86 F^-; 2, LT2 SU 452 Hfr.