EUR. J. ENG. ED., 2000, VOL. 25, NO. 2, 165–175

Process and plant design in biochemical engineering education

YUSUF CHISTI†

Training in process and plant design is an essential feature of biochemical engineering education. Training is also an accreditation requirement. The requisite training is provided through a selection of design-relevant courses and a design project of substantial scope. This article outlines the rationale for meaningful training in engineering design and considers the structuring, the expectations and the resources needs of biochemical engineering design education. Biochemical engineering differs in important ways from its chemical engineering parent discipline and this needs to be taken into account in developing a relevant design training programme for biochemical or bioprocess engineers.

1. Why teach design?

Design is engineering practice at the highest level, but few engineers will experience anything other than routine design during their entire careers. Still fewer will do leading-edge design of significant scope and complexity. For many, the experience will be a once-in-a-lifetime kind. Nevertheless, design—that is, devising practicable engineered solutions that are ready for implementing—is the essence of engineering. Adequacy in design training is an accreditation requirement for engineering degrees in some jurisdictions. For chemical and biochemical engineering (Moo-Young and Chisti 1994) degrees in the UK, the accreditation body is the Institution of Chemical Engineers (IChemE).

Design derives from engineering principles, but it is influenced by many other factors, e.g. competition and market forces, legislation, public perception and company standards. There is also a component of art to engineered design; there is room for individual expression and innovation. Two design engineers given the same scope definition will often come up with different solutions, both equally satisfactory.

Design demands a high level of professional responsibility. Failures in design cost in lost performance and sometimes cause loss of life and property. Flaws in design are all too common. Many motor vehicle recalls, accidents at process plants, incidences of contamination in food and drugs, failures of medical devices and implants, and environmental disasters are direct consequences of flaws in engineering design. In summary, a capability for designing is what makes an engineer; hence, education in engineering design is essential. Let us now see what biochemical engineering design entails and how design might be taught.

2. What ought to be taught?

Instruction in design presupposes a good all-inclusive engineering background. That background, developed through coursework and possible short-term trainee

---

† Department of Chemical Engineering, University of Almería, E-04071 Almería, Spain. E-mail: ychisti@ualm.es.

European Journal of Engineering Education ISSN 0343-3797 print/ISSN 1469-5898 online

http://www.tandf.co.uk/journals

work in industry, culminates in a substantial design project, usually in the final year of the undergraduate degree. The requisite coursework and the project are discussed next.

2.1. *Background coursework*

Students encounter facets of design all through undergraduate training, e.g. aspects of heat exchanger or distillation column design, but that knowledge, being limited to specific items, is no substitute for design of entire processes and process equipment that function as a part of a complex plant. Interrelationships among plant operations cannot be properly considered in thinking of individual equipment. Moreover, courses on engineering fundamentals such as transport phenomena typically concentrate on principles and little time is allowed for treatment of issues relating to detailed design of equipment. Thus, in addition to the various other necessary courses, an undergraduate biochemical engineering curriculum should include a one-semester course on design and selection of process equipment. A satisfactory curriculum should also teach several other courses that are especially relevant to engineering design. There should be semester-long courses on each of the following: engineering drawing; process flowsheeting and simulation; and process economics and costing. This core of 'design' courses should teach most of the major topics noted in table 1.

Biochemical engineering is generally taught as a specialization within chemical engineering. The few programmes that award first degrees in biochemical engineering *per se* are also offshoots of chemical engineering departments. It is therefore essential to recognize the major differences between design education in chemical and biochemical engineering. Some distinguishing features of bioprocessing are: the biohazard and biosafety considerations (Collins and Beale 1992, Chisti 1998a); the specialist engineering associated with monoseptic processing, hygienic design and operation (Chisti 1992a, b, 1998a, Lydersen *et al.* 1994); and the issues of product contamination and cross-contamination (Willig and Stocker 1992, Chisti 1998a, 1999a). Also, the biocatalyst is often live and susceptible to many influences (Bailey and Ollis 1986, Chisti and Moo-Young 1991, Moo-Young and Chisti 1994, Chisti 1999b). Furthermore, the relative significance of some unit operations in chemical and biochemical processing is different. For example, distillation is relatively uncommon in bioprocessing, whereas chromatography is used frequently (Belter *et al.* 1988, Asenjo 1990, Wheelright 1991, Chisti 1998b). Membrane-based separations are especially frequent in bioprocessing. These differences need to be acknowledged in developing a satisfactory design training programme for biochemical engineers.

2.2. *Design project*

A design project attempts to simulate, as closely as is realistically possible in a university setting, the range of engineering design issues that are encountered and systematically addressed in a real commercial design effort. A design project also trains and tests students in integrating into a workable design the many engineering principles learnt in the various courses. A meaningful design project needs to have a sufficiently broad scope, preferably design of an entire process or significant parts of a large process. Table 2 lists a selection of processes for possible use in a biochemical engineering design exercise. A substantial design exercise provides opportunities for teamwork, developing skills in group communication and co-ordination of activities. This kind of design effort is the norm in industrial

Design course	Contents
Engineering drawing	Introduction to graphics communication. The engineering design process. Drawing tools. Sketching and lettering. Visualization for design. Engineering geometry fundamentals. Three-dimensional modelling. Multiview drawings. Plans, sections and perspectives. Standard graphics and flowsheeting practice. Dimensioning and tolerances. Working drawings. Mechanical drawings. Piping drawings. Welding drawings. Computer drawing. Extensive training on a suitable software package (e.g. DesignCAD)
Process flowsheeting and simulation	Flowsheet synthesis and decomposition. Modelling and analysis of flowsheets. Flowsheet simulation. Heat-exchanger networks and other examples of flowsheet analysis. Analysis of process alternatives. Use of computer-aided process design and simulation packages such as ASPEN, CHEMSHARE, CHEMCAD and SPEEDUP. Flowsheet optimization
Process economics and costing	Estimation of capital and operating costs. Time value of investments. Profitability analysis. Selection of alternatives. Optimization. Elements and types of contracts. Project management and scheduling. Critical path analysis
Equipment design and specification	Tanks and vessels. Agitators. Pumps. Valves. Compressors. Heat exchange equipment. Evaporators. Crystallizers. Dryers. Freeze and spray dryers. Distillation columns. Packed towers. Cooling towers. Gas–liquid contactors. Centrifuges. Sedimentation tanks. Depth filters. Membrane filters. Liquid–liquid extraction equipment. Cell disruption equipment. Chromatography equipment. Size reduction equipment. Materials of construction. Hygienic design of process machinery. Containment and biosafety. Preparation of bids. Plant layout

Table 1. Contents of design-relevant courses.

practice and it emphasizes the interactive component of the learning process. Completion of a substantial design project is an essential part of the training of a biochemical engineer and such a project is required of all IChemE-accredited chemical engineering degrees.

An engineer will typically encounter four levels of design: (i) product design; (ii) process design; (iii) plant design; and (iv) facility design. A biochemical engineer can expect to participate at all four levels, but other engineering disciplines are relied on substantially for details of plant and facility design. Undergraduate design projects typically focus on levels (ii)–(iv); product design is pre-established and provided to the students as product specifications. Specifications may be quite detailed, but the production plant capacity may be left to project teams to decide. Sometimes the ‘product’ is a service. In every case, the instructor should prepare a

Cell culture-derived production of tissue plasminogen activator (tPA) (Rouf et al. 1996)
Production of rabies vaccine
Production of recombinant Factor VIII in *Escherichia coli* (inclusion body)
Process for plasma-derived Factor VIII
Production of the antibiotic cyclosporin from the microfungus *Tolypocladium inflatum*
Production of poly(β-hydroxybutyric acid) bioplastic using the bacterium *Alcaligenes latus*
Production of microbial inoculants for enhanced nitrogen fixation
Process for reducing sulphur content of high-sulphur crude
Plant cell culture-based production of Taxol®
Production of eicosapentaenoic acid (an essential fatty acid) in microalgal photobioreactors
Process for spray-dried milk powder from raw milk
Enzymatic biotransformation of benzyl penicillin to 6-aminopenicillanic acid
Biological treatment of industrial wastewater contaminated with phenol and heavy metals
Bioremediation of hydrocarbon-contaminated soil
Biotreatment of odorous vapour contaminated with hydrogen sulphide and xylenes

Table 2. Bioprocess examples for use in a design project.

clear one-page scope of the design project. The relative emphasis given to the various aspects of design differs greatly, but process design is generally the main focus of a design project and this is followed closely by plant design. The following sections focus on the structuring, expectations and supervision of a biochemical engineering student design project.

3. The teaching: structure and outcomes

A substantial design project typically requires a semester-long effort by a team of four to six students. At commencement the students should be provided with a brief scope of the design project, a schedule for attaining critical milestones, submitting the progress reports, and the final project report. The students should be advised on how the design project exercise will be graded.

The project teams need to be paced through the instructor-established schedule. A schedule may specify deadlines for some of the milestones noted in table 3. The deadlines for items in table 3 determine the write up and reporting dates only; the deadlines do not mean that an item has been ignored up to that point. For example, issues of cost and biosafety would need to be considered all through conceptual and detailed engineering. Student teams require continual monitoring and mentoring. Both the team and the individuals need to be evaluated at critical stages of the design project. Individual assessments ensure that non-performing team members cannot hide behind group effort.

After production capacity has been decided and a process option has been selected from among several possible alternatives, the next step is to prepare a process block diagram or a conceptual flowsheet (Walas 1991). A block diagram identifies all the major process operations, materials and energy streams, and any recycle loops; the quantities of the principal inputs and outputs are shown. Later, the block diagram becomes the basis for the detailed process flowsheet. The process flowsheet shows, and identifies with unique codes, all process streams and process equipment. Major instrumentation are shown. The composition of streams is given, quantities of flows are shown, and stream temperature and pressure are noted. Additional equipment-specific details are provided, e.g. the volume of a bioreactor, the motor horsepower and the operating temperature.

Initial literature and data collection
Capacity definition
Development of conceptual process flow diagram
Completion of material and energy balances
Synthesis of detailed flowsheet
Process simulation and optimization report
Equipment specification sheets
Detailed bioreactor design
Mechanical design of bioreactor
Bioreactor drawings
Cost calculations and economic analysis
Feasibility report
Process flow description
Biosafety report
Environmental impact statement
Project report

Table 3. Possible milestones in a design project.

The information obtained during detailed process design is used to develop specifications for all major process items. The specifications are summarized in separate equipment specification sheets for each item of equipment (Walas 1991). The specifications note every essential detail including capacity, type, materials of construction, surface finishes, and so forth (Chisti 1992a, b, Lydersen *et al.* 1994). Each member of a design team should be made responsible for detailed mechanical design of one non-standard process item (e.g. the bioreactor, sedimentation tank, extraction columns, spray drier). Mechanical drawings thus obtained become part of the relevant specification sheet.

Whereas the focus of the design effort should be on the bioprocess aspects, some peripheral operations provide good opportunities for an enhanced design project. Thus, some members of a design team may address the detailed engineering of the clean-in-place system (Chisti and Moo-Young 1994, Chisti 1999a), the facilities for production and distribution of water-for-injection (Goldberg 1997), the waste collection and decontamination system, and so forth. A design project also provides opportunities of evaluation of process alternatives by parallel design teams.

3.1. *Design report*

Typically, a design report should be about 30 printed pages, double spaced, excluding appendices. The report includes a table of contents, a summary, a statement of objectives, introductory matter, a block diagram of the process, material and energy balances, a detailed process flowsheet and flow description. In addition, there are sections on safety, environmental impact, plant layout, capital demands (effect of scale) and profitability, and a concluding statement regarding techno-economic feasibility. The appended matter contains the detailed design calculations with a clear presentation of the methods used, a listing of the principal equipment and the equipment specification sheets (Walas 1991), mechanical drawings, cost calculations (Bailey and Ollis 1986, Humphreys 1991, Peters and Timmerhaus 1991, Perry and Green 1997) and references.

The final project report should have two to three pages on biosafety aspects (Chisti 1998a). Noted, specifically, should be the biohazard level classification of the process, and a tabular listing of the specific design and operation features that will be needed for the equipment and the facility (Chisti 1998a). This is necessary even for a 'generally recognized as safe' (GRAS) process. When the biohazard containment requirements are unknown, e.g. for a completely new process for which developmental information may not yet be complete, the design team should specify exactly what information will be needed for establishing the containment categories. A reasonable tentative containment category should be assigned with some justification and the design should proceed. Risks associated with a non-viable bioproduct (Chisti 1998a), e.g. due to its bioactivity or allergenic character, should be noted and their impact on equipment and facility design and operational practices should be identified. Other significant non-biological hazards should be noted, e.g. flammable solvents, high pressure, static electricity, toxic chemicals, and so on (Perry and Green 1997). Appropriate engineering and operational practices should be specified to mitigate the hazard. Hazards associated with peripheral operations such as cleaning should not be ignored (Chisti 1999a). Consideration should be given to decontamination of the biowaste prior to treatment or discharge.

The report should have a page or two on the layout of the processing plant and how the plant integrates with the building. This is important in many bioprocesses where the product generally moves from 'dirty' to progressively clean areas during processing. Movement of personnel, equipment and conditioned air in a facility is dictated by the containment needs and the need to protect the product against contamination (Lydersen *et al.* 1994, Chisti 1998a). All this is taken into account in engineering a layout. In addition, a bioprocess plant would usually need to comply with the current 'Good Manufacturing Practices' regulations (Willig and Stocker 1992), which need attention right from the design stage.

The report should have a section on economic assessment (Bailey and Ollis 1986, Humphreys 1991, Peters and Timmerhaus 1991, Perry and Green 1997) of the process, including the investment capital needs, the annual operational expenses, the cost of production per unit of product and return-on-investment calculations. There should be a commentary on the principal contributors to costs, possible methods of enhancing economic return, and a possible sensitivity and optimality analysis. Detailed cost calculations, any assumptions and the methods used should be noted in an appendix.

A concluding section should consider issues of process feasibility: Is it technically possible? What are the critical stumbling blocks? In what areas is the technology insufficiently developed? What specific knowledge is lacking and how might it be obtained?

3.2. *Seminar presentations*

In addition to a written project report, an oral presentation of the design in a group effort by team members is recommended. Such presentations provide the team with an opportunity for public communication of their ideas. Choices can be questioned by the instructor and a knowledgeable audience made up of members of the other design teams. The presenting team can rationally defend its preferred process and the design methods.

3.3. *Role of the computer*

Computer-aided process and plant design is well-established in the petrochemical industry and it is also becoming increasingly common in bioprocessing (Goldberg 1997). Computer software packages exist for design and selection of individual process items such as pumps, compressors and heat exchangers, and also for developing and simulating integrated flowsheets. Any meaningful design training effort needs to recognize this reality. Computer-aided flowsheeting programmes enable rapid evaluation of the many 'what if?' scenarios. Posing suitable questions and critical evaluation of the answers should be an important part of the design exercise.

Well-known computer-aided flowsheet design and simulation packages such as ASPEN, CHEMSHARE, PROCEDE, CHEMCAD, HYSIM, HEXTRAN and SPEEDUP are not always suited to bioprocess applications. Bioprocess operations such as cell disruption, two-phase aqueous extractions, protein precipitations, and so forth may not have equivalents in chemical processing. Models for some of these bioprocess operations are poorly developed. In addition, there are generally few physical property data for biological systems and this leads to much uncertainty. When data are available, the inherent variability of biological systems causes problems. Many bioprocesses function as batch operations. Design software that may be particularly relevant to bioprocessing includes packages such as BatchPro Designer® (batch processes), EnviroPro Designer® (waste treatment processes) and the relatively new BioPro Designer® (bioprocesses). As always, any user of bioprocess design software must understand the design methodology used by the software and the results of simulations should be assessed critically.

4. Design teaching resources

How well a student design project succeeds in its intended training function depends on the quality and availability of the necessary resources, such as a suitable instructor, design data, and facilities for data processing and for project teamwork. These aspects are discussed next.

4.1. The teacher

Can anyone teach design? Supervision, guidance and evaluation of a design project require experienced engineering judgement. In view of the professional responsibility that goes with design, a design project instructor ought to be a qualified engineer with a licence to practise, for example an engineering graduate with a Professional Engineer (PEng) designation in North America, a graduate Chartered Engineer (CEng) in the UK, or a EurIng designation holder in Europe. The excitement and flavour of design come out only when the teacher has participated him/herself as a design or project engineer in a commercial project of significant scope. Unfortunately, many professors in engineering schools have no industrial engineering experience, let alone a demonstrated expertise in design engineering. Lapses in engineering education, particularly in design engineering, explain at least some of the alarmingly frequent engineering failures.

4.2. Information sources

A good design is based on good information. Access to a good library is essential. Finding and using relevant information and establishing the need for further work in areas where there is insufficient data are aspects of design training. Initially, the design teams need to become familiar with any available know-how of a given process, any patents and the state of research. A well-planned database search will quickly reveal what is available. Either CD-ROM or, preferably, online access to data sources is necessary. Some important guides to published information are the *Chemical Abstracts* and CAS ONLINE, *Biological Abstracts* and Biosciences Information Service (BIOSIS), AGRICOLA (AGRICultural OnLine Access) and the *Current Biotechnology Abstracts*. The references provided by these abstracting services help in locating the specific patents and publications that may have some of the information needed.

Some useful journals that publish information relevant to bioprocess engineering are listed in table 4. The tables of contents and sometimes the abstracts of articles in the listed journals may be viewed at the publishers' Internet sites. Much technical information is available also in major reference works and some of these are identified in table 5 for various aspects of bioprocessing. Many chemical technology

Advances in Biochemical Engineering and Biotechnology
Applied and Environmental Microbiology
Biochemical Engineering Journal
Bioprocess Engineering
Bioseparation
Biotechnology Advances
Biotechnology and Bioengineering
Biotechnology Letters
Biotechnology Progress
Biotechnology Techniques
Chemical Engineering
Chemical Engineering Science
CRC Critical Reviews in Biotechnology
Cytotechnology
Enzyme and Microbial Technology
Industrial and Engineering Chemistry Research
Journal of Applied Microbiology and Biotechnology
Journal of Biotechnology
Journal of Chemical Technology and Biotechnology
Journal of Fermentation and Bioengineering
Journal of Industrial Microbiology and Biotechnology
Nature Biotechnology
Process Biochemistry
Transactions of the Institution of Chemical Engineers, Part C

Table 4. Journals related to biochemical engineering.

Bioprocess aspect	References
Animal cell culture	Lubiniecke 1990, Chisti 1999b, c, Spier 2000
Bioreactor design	Bailey and Ollis 1986, Atkinson and Mavituna 1991, Van't Riet and Tramper 1991, Chisti 1992a, b, 1989, 1998c, 1999b–d
Biosafety	Collins and Beale 1992, Chisti 1998a
Cleaning operations	Chisti and Moo-Young 1994, Chisti 1999a, Robinson *et al.* 1999
Downstream bioseparations	Belter *et al.* 1988, Asenjo 1990, Atkinson and Mavituna 1991, Wheelright 1991, Lydersen *et al.* 1994, Verrall 1996, Goldberg 1997, Chisti 1998b
Enzymes	Bailey and Ollis 1986, Wheelright 1991, Atkinson and Mavituna 1991, Godfrey and West 1996
Facility layout	Lydersen *et a*l. 1994, Chisti 1998a
General aspects	Moo-Young 1984, Bailey and Ollis 1986, Atkinson and Mavituna 1991, Rehm *et al.* 1993, Lydersen *et al.* 1994, Wiseman 1995, Flickinger and Drew 1999, Chisti 1999e
Good manufacturing practice	Willig and Stocker 1992
Process microbiology	Bailey and Ollis 1986, Crueger and Crueger 1990, Robinson *et al.* 1999

Table 5. Some reference books on various aspects of bioprocessing.

reference books provide guidance relevant to bioprocessing (*Kirk-Othmer Encyclopedia of Chemical Technology* 1991, Arpe 1995, Turton *et al.* 1997, Perry and Green 1997). The Internet is a useful source of information (Lee *et al.* 1998). Vendors' catalogues and Internet web sites often provide data to help with sizing and selection of process equipment. Some of these web sites have facilities for online estimation of equipment sizes or provide downloadable software for rough sizing. In general, information on process machinery is relatively easily obtained compared with information on processes.

4.3. Data processing and teamwork facilities

Modern design is highly computer reliant; hence, the design teams require access to dedicated computer workstations located in close proximity to facilities for group meetings and discussions. The computers should be preloaded with the necessary software; minimally, software is needed for word processing, spreadsheet calculations, drafting, flowsheet synthesis and simulation, Internet connectivity, off-line or online literature search capabilities, e-mail and for possible assistance with project management.

5. Concluding remarks

Capabilities for process and plant design are essential for biochemical engineering practice. Well-structured engineering degree programmes provide design training through coursework that culminates in a substantial design project. A design project requires careful planning and close monitoring by the instructor. The student design teams need to be paced through a pre-established schedule that is firmly adhered to. Grading of teams and individuals at critical stages of the project and the necessary feedback help in early identification and resolution of problems. A successful design effort requires, in addition to the instructor, access to databases, a good library, data processing facilities and facilities for regular group meetings.

Design involves choices—an accommodation among many, often conflicting, demands. There are concerns of safety, costs, reliability, controllability, environmental impact, serviceability, time to production, scalability, turndown capability, and many others. An 'optimal' design is often not the best in terms of individual criteria of optimality.

References

Arpe, H.-J. (ed.), 1995, *Ullmann's Encyclopedia of Industrial Chemistry* (New York: Wiley-VCH).

Asenjo, J. A. (ed.), 1990, *Separation Processes in Biotechnology* (New York: Dekker).

Atkinson, B. and Mavituna, F., 1991, *Biochemical Engineering and Biotechnology Handbook*, 2nd edn (New York: Macmillan).

Bailey, J. E. and Ollis, D. F., 1986, *Biochemical Engineering Fundamentals*, 2nd edn (New York: McGraw-Hill).

Belter, P. A., Cussler, E. L. and Hu, W.-S., 1988, *Bioseparations: Downstream Processing for Biotechnology* (New York: Wiley).

Chisti, Y., 1989, *Airlift Bioreactors* (London: Elsevier).

Chisti, Y., 1992a, Build better industrial bioreactors. *Chemical Engineering Progress*, 88(1), 55–58.

Chisti, Y., 1992b, Assure bioreactor sterility. *Chemical Engineering Progress*, 88(9), 80–85.

Chisti, Y., 1998a, Biosafety. In G. Subramanian (ed.), *Bioseparation and Bioprocessing: A Handbook*, Vol. 2 (New York: Wiley-VCH), pp. 379–415.

Chisti, Y., 1998b, Strategies in downstream processing. In G. Subramanian (ed.), *Bioseparation and Bioprocessing: A Handbook*, Vol. 2 (New York: Wiley-VCH), pp. 3–30.

Chisti, Y., 1998c, Pneumatically agitated bioreactors in industrial and environmental bioprocessing: hydrodynamics, hydraulics and transport phenomena. *Applied Mechanics Reviews*, 51, 33–112.

Chisti, Y., 1999a, Modern systems of plant cleaning. In R. Robinson, C. Batt and P. Patel (eds), *Encyclopedia of Food Microbiology* (London: Academic Press), pp. 1806–1815.

Chisti, Y., 1999b, Shear sensitivity. In M. C. Flickinger and S. W. Drew (eds), *Encyclopedia of Bioprocess Technology: Fermentation, Biocatalysis, and Bioseparation*, Vol. 5 (New York: Wiley), pp. 2379–2406.

Chisti, Y., 1999c, Mass transfer. In M. C. Flickinger and S. W. Drew (eds), *Encyclopedia of Bioprocess Technology: Fermentation, Biocatalysis, and Bioseparation*, Vol. 3 (New York: Wiley), pp. 1607–1640.

Chisti, Y., 1999d, Solid substrate fermentations, enzyme production, food enrichment. In M. C. Flickinger and S. W. Drew (eds), *Encyclopedia of Bioprocess Technology: Fermentation, Biocatalysis, and Bioseparation*, Vol. 5 (New York: Wiley), pp. 2446–2462.

Chisti, Y., 1999e, Fermentation (industrial): basic considerations. In R. Robinson, C. Batt and P. Patel (eds), *Encyclopedia of Food Microbiology* (London: Academic Press), pp. 663–674.

Chisti, Y. and Moo-Young, M., 1999, Fermentation technology, bioprocessing, scale-up and manufacture. In V. Moses, R. E. Cape and D. G. Springham (eds), *Biotechnology: The Science and the Business*, 2nd edn (New York: Harwood Academic), pp. 177–222.

Chisti, Y. and Moo-Young, M., 1994, Clean-in-place systems for industrial bioreactors: design, validation and operation. *Journal of Industrial Microbiology*, 13, 201–207.

Collins, C. H. and Beale, A. J. (eds), 1992, *Safety in Industrial Microbiology and Biotechnology* (Oxford: Butterworth-Heinemann).

Crueger, W. and Crueger, A., 1990, *Biotechnology: A Textbook of Industrial Microbiology*, 2nd edn (Madison: Science Tech Publishers).

Flickinger, M. C. and Drew, S. W. (eds), 1999, *Encyclopedia of Bioprocess Technology: Fermentation, Biocatalysis, and Bioseparation*, Vols 1–5 (New York: Wiley).

Godfrey, T. and West, S. (eds), 1996, *Industrial Enzymology*, 2nd edn (London: Macmillan).

Goldberg, E. (ed.), 1997, *Handbook of Downstream Processing* (London: Chapman and Hall).

Humphreys, K., 1991, *Jelen's Cost and Optimization Engineering*, 3rd edn (New York: McGraw-Hill).

Kirk-Othmer Encyclopedia of Chemical Technology, 1991, 4th edn (New York: Wiley).

Lee, L. E. J., Chin, P. and Moser, D. D., 1998, Biotechnology and the Internet. *Biotechnology Advances*, 16, 949–960.

Lubiniecke, A. S. (ed.), 1990, *Large-scale Mammalian Cell Culture Technology* (New York: Dekker).

Lydersen, B. K., D'Elia, N. A. and Nelson, K. L. (eds), 1994, *Bioprocess Engineering: Systems, Equipment and Facilities* (New York: Wiley).

Moo-Young, M. (ed.), 1984, *Comprehensive Biotechnology*, Vols 1–4 (Oxford: Pergamon Press).

Moo-Young, M. and Chisti, Y., 1994, Biochemical engineering in biotechnology. *Pure & Applied Chemistry*, 66, 117–136.

Perry, R. H. and Green, D. W. (eds), 1997, *Perry's Chemical Engineers' Handbook*, 7th edn (New York: McGraw-Hill).

Peters, M. S. and Timmerhaus, K. D., 1991, *Plant Design and Economics for Chemical Engineers*, 4th edn (New York: McGraw-Hill).

Rehm, H.-J., Reed, G., Pühler, A. and Stadler, P. (eds), 1993, *Biotechnology*, Vols 1–13, 2nd edn (Weinheim: VCH).

Robinson, R., Batt, C. and Patel, P. (eds), 1999, *Encyclopedia of Food Microbiology*, Vols 1–3 (London: Academic Press).

Rouf, S. A., Moo-Young, M. and Chisti, Y., 1996, Tissue-type plasminogen activator: characteristics, applications and production technology. *Biotechnology Advances*, 14, 239–266.

Spier, R. E. (ed.), 2000, *Encyclopedia of Cell Technology*, vols 1–2 (New York: Wiley).

Turton, R., Bailie, R. C., Whiting, W. B. and Shaeiwitz, J. A., 1997, *Analysis, Synthesis and Design of Chemical Processes* (Englewood Cliffs: Prentice Hall).

VAN'T RIET, K. and TRAMPER, J., 1991, *Basic Bioreactor Design* (New York: Dekker).

VERRALL, M. S. (ed.), 1996, *Downstream Processing of Natural Products: A Practical Handbook*, (Chichester: Wiley).

WALAS, S. M., 1991, *Chemical Process Equipment: Selection and Design* (Newton, MA: Butterworth-Heinemann).

WHEELRIGHT, S. M., 1991, *Protein Purification: Design and Scale up of Downstream Processing* (New York: Hanser).

WILLIG, S. H. and STOCKER, J. R., 1992, *Good Manufacturing Practices for Pharmaceuticals: A Plan for Total Quality Control* (New York: Dekker).

WISEMAN, A. (ed.), 1995, *Handbook of Enzyme Biotechnology*, 3rd edn (London: Ellis Horwood).

About the author

Yusuf Chisti is a Professor in Chemical Engineering with the University of Almería, Spain. He obtained MSc and PhD degrees in biochemical and chemical engineering from the University of London, UK, and the University of Waterloo, Canada, respectively. He is a Chartered Engineer, CEng, in the UK. His previous appointments were with Chembiomed Ltd, Edmonton, Canada, and the University of Waterloo, Canada. He has authored about 130 publications, including a much-cited book. His work addresses bioreactor engineering, downstream bioseparations and environmental biotechnology. He is Editor of *Biotechnology Advances* and advises on editorial boards of the *Encyclopedia of Bioprocess Technology, Fermentation, Biocatalysis, and Bioseparation* and the *Journal of Biotechnology*.