Life Sciences

INDUSTRY

- **Control and sequencing**
- **Recipes**
- **Batch control and reporting**
- **Setpoint programming**
- **Bespoke displays**
- **Alarm management**
- **21 CFR Part 11**

The Fermentation Process

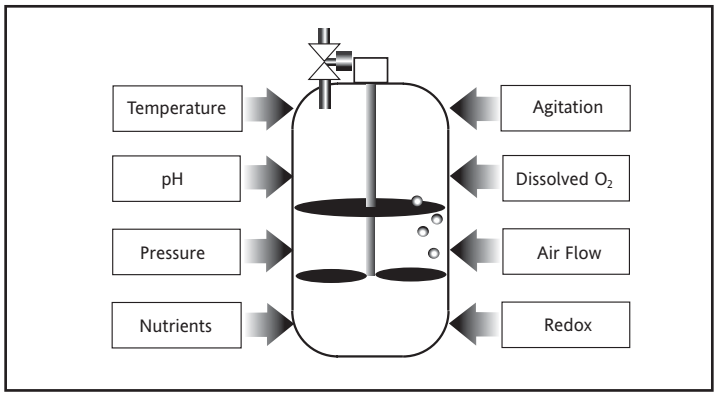
Application Note

Fermentation is widely used within the Pharmaceutical and Food industries. It requires the cultivation in submerged culture of an identified micro-organism (mainly bacterial) as a monoculture under defined environmental conditions. The incubation regime imposed is designed to maximise the productivity of the organism of interest by providing optimal conditions for population growth (biomass). The product of interest might be a bioactive metabolite or recombinant protein.

During an incubation cycle a nutrient energy source (e.g. glucose) is added and the biomass and end product will increase as this is depleted.

Fermenter design and control

Incubation control necessitates the precise control of a number of parameters. Of primary importance are:



Temperature, pH, DO_2 or Redox, agitation, pressure, foam control, auxiliary feed or a combination of these controllers.

The control of these and any other parameters is most usually carried out in fermenter vessels specifically designed for the purpose and accommodating various working volumes depending on the yield and production requirements. Laboratory scale vessels could have a capacity of just 10 litres or less whereas production vessels may be as large as several thousand litres.

The smallest units may incorporate an electrical heater and feed stocks (e.g. Nutrient and pH control agents) may be fed from flasks via peristaltic pumps. Larger vessels have an integral jacket for controlling temperature via hot or cold water and allowing indirect sterilisation using injected steam. Where larger quantities of feed stock are required they may be held in separate pressurised tanks and fed via a 'thrust pump' arrangement of valves.

The actual fermentation process is known as the Incubation Phase and is just part of the batch cycle. A complete fermentation cycle can typically include the following steps (depending on vessel design):

- Empty (blank) sterilisation of vessel and pipework using direct steam injection
- Charging with base medium
- Indirect sterilisation via steam injected into the vessel jacket
- Cooling and jacket drain
- Pre-inoculation – vessel environment under control

- Inoculation – Injection of a small sample of the monoculture
- Incubation – The Fermentation process itself
- Harvesting – Product removed ready for extraction processes

The R&D and Clinical Trials environments in which many small scale fermenters operate are such that it is not possible to predict the nature of any particular fermentation process either in terms of culture or incubation conditions. Production facilities must also cater for a variety of products each having precisely defined incubation profiles.

A control system must therefore provide flexibility in the way in which accurate and repeatable control of the fermentation environment is achieved and will include the following features:

- Precise loop control with setpoint profile programming
- Recipe Management System for easy parameterisation
- Sequential control for vessel sterilisation and more complex control strategies
- Secure collection of on-line data from the fermenter system for analysis and evidence
- Local operator display with clear graphics and controlled access to parameters

Eurotherm® Eycon™ Visual Supervisor

The Eurotherm® visual supervisor is ideal for fermentation applications because it combines all these key features into a single compact unit:

- **Powerful loop and sequence control**
- **Flexible graphics**
- **Setpoint programmer**
- **Batch control and reporting**
- **Audit trail**
- **XGA touchscreen display to IP65**
- **Secure data logging and trending**
- **Recipe management**
- **Alarm management**
- **Access control and electronic signatures**

21 CFR Part 11 - 'Ready to use!'

Fermentation plants are in industries likely to require validation to the requirements of the FDA, EMEA or other applicable regulatory body. The visual supervisor has been widely used in validated processes including freeze dryers, autoclaves, reactors, fermenters, purified water systems, tablet coating machines, etc.

21 CFR Part 11
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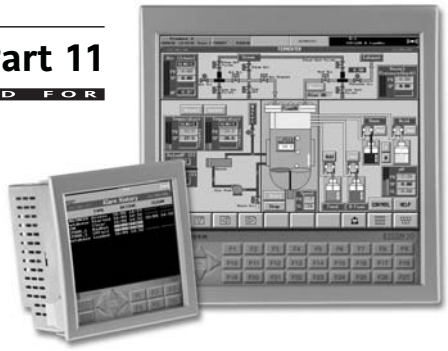

The Auditor feature on the visual supervisor has been specifically designed to meet the requirement of the FDA's 21 CFR Part 11 including:

- Controlled user access
- Secure data logging in tamper resistant format
- Audit trail recording user actions and changes to process parameter
- Electronic signature

With the Auditor feature, Electronic signature is configurable for all actions which may be performed from the visual supervisor display including the customised display and standard features such as batch, recipe changes, access control changes, etc.

Scalable architecture

A complete system can be created in combination with T2550 DIN rail I/O bases. Connection is via ELIN and I/O is scalable by adding 4. 8 or 16 slot bases as required. A range of I/O modules caters for the various interfaces required:

Analogue inputs	Temperature, pressure, RPM, VVM and probes for pH, DO2 etc. Additional measurements: Weight, CO2 etc.
Analogue outputs	Water/Steam control valves, Air Flow/Pressure regulators
Digital inputs	Foam detection, high level limit, bursting disc
Digital outputs	Valve control solenoids, pump control etc.

System building blocks:

- Single fermenter (single Eycon™ visual supervisor)
- Fermenter group (most Eycon™ visual supervisor functions support up to 4 independent fermenter units)
- Multiple units with supervisory workstation(s)

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