Advancing bioprocess control:
Integrating software-hardware architectures to create new control options

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Introduction

What is standard hardware / software architecture for bioprocess control?

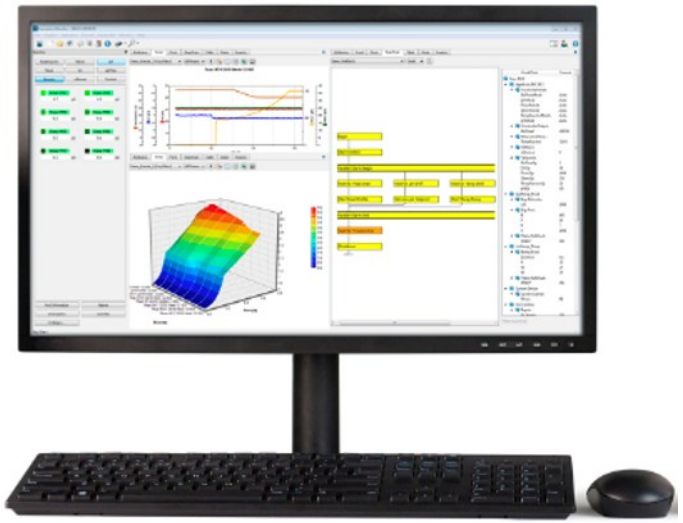
Basic setup: Bioreactor + Controller + Scada software











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Standard options controller

- Actuators:

  Stirrer / pumps / gas flow (valves or MFCs) / heating + cooling

  – Define Setpoint, switch ON / OFF

  – Calibration, Dose Monitor

- Sensors:

  pH / DO / Temperature / Level / etc

  – Calibration

  – Read out measurements

  – Control loops:

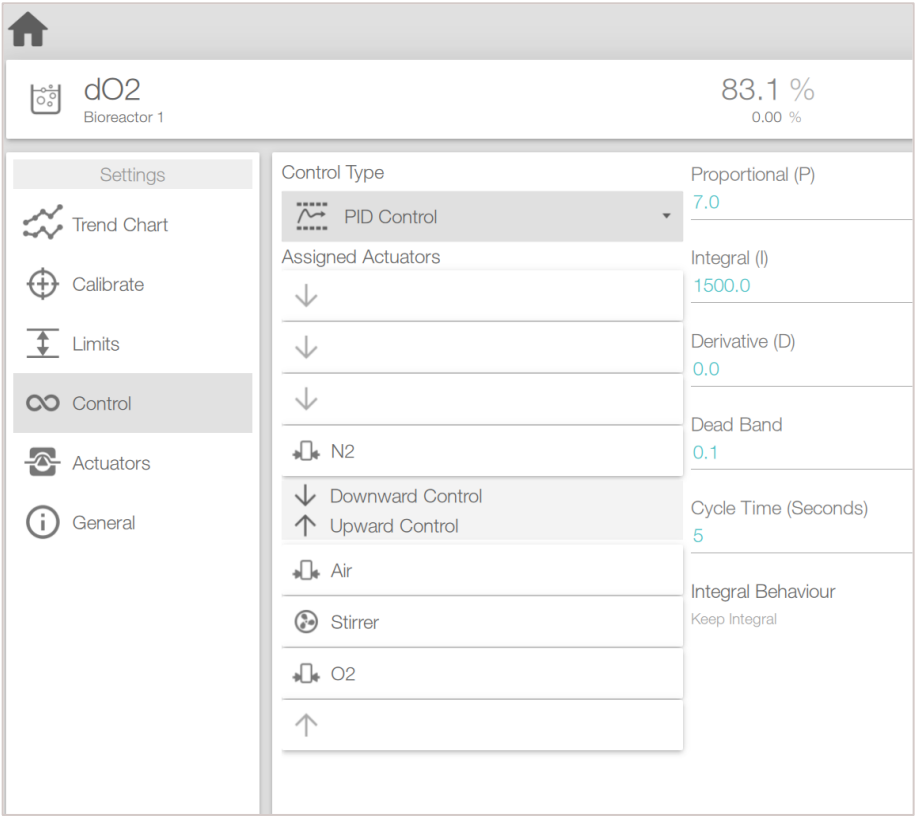
    - Assign actuator(s) for upward/downward control
    - Set setpoint, switch ON / OFF



Example advanced option controller: Cascade PID control

- Configurable Sensor-input-based Control loop
- Simple assignment of multiple actuators to up/downward control
- Sequential activation of actuators
- Control Type PID:
  Proportional / Integral / Derivative parameters
  used in calculation of Control Output value
- Optimal values for PID depend on
  - type of measurement
  - type of actuators assigned
  - type / size of bioreactor

  In Controller Manual an Overview table is given of
  optimized PID values applicable for many configurations



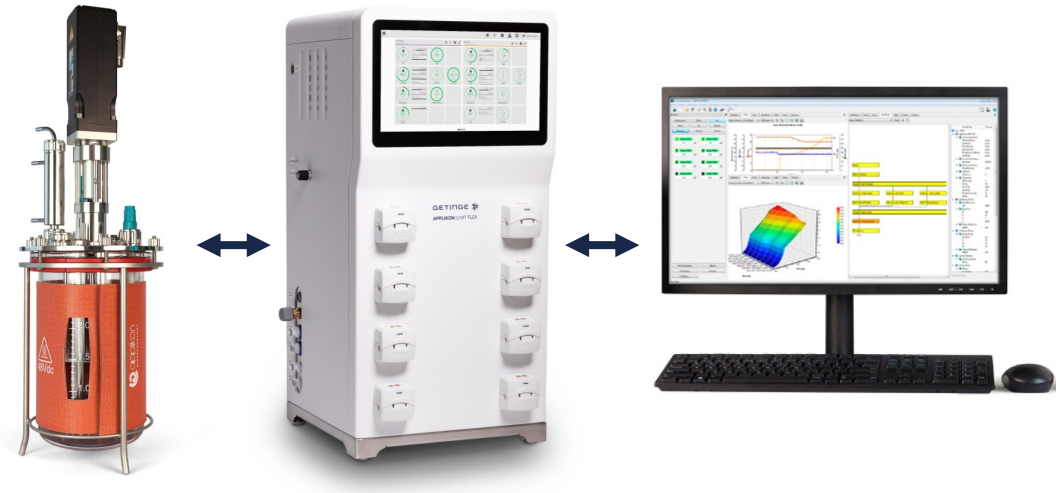
Additional layer of control: SCADA software

Lucullus® = Supervisory Control and Data Acquisition software

Bi-directional interface with Controller, receive and send data

Provides additional (time-based) control options:

- Create time-split between preparation and cultivation stages:
  Prepare Operation recipe with standard setpoints,
  apply setpoints only when Operation recipe reaches that step
- Ask operator for variable setpoint, apply value at later timepoint
- Time-based start / stop of actuators
- Apply time-based setpoint profiles to control loops (e.g. exponential Feed)
- Logic based actions: If … Then …
  Example: End of batch defined by depletion of glucose in broth
  No glucose consumption = less oxygen demand = stirrer ↓ and DissolvedOxygen ↑
  IF [DO > 50%] THEN [Start Feed pump at setpoint = x]

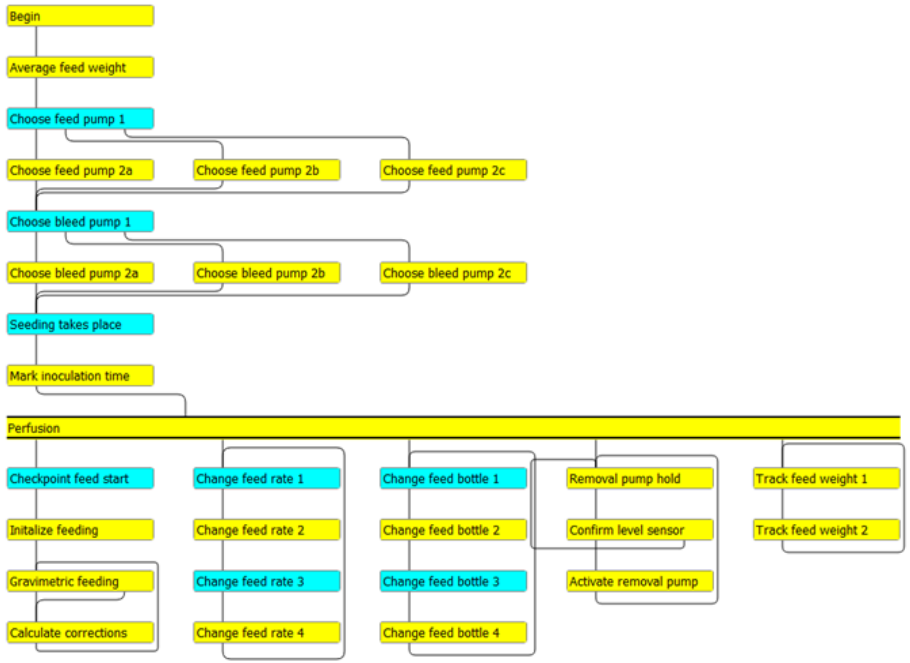


More advanced options in SCADA software

SCADA software not only provides time-based control options,
in addition calculations can be used to extend available control options:

- Example of Online calculation:
  OUR (Oxygen Uptake Rate) in mmol O2 / h / liter broth
  Inputs for calculation:
  – Difference %O2 between ingoing and outgoing gas flow
  – Gas flow in normalized L gas / minute
  – Calculated current reactor broth volume
- Store calculated data in database, “Virtual sensor”
- Based on Virtual sensor do actions:
  e.g. IF OUR is rising too much,
  culture might run into oxygen limitation
  THEN Limit Feed going in
  to reduce oxygen demand in bioreactor

- Example of mixing Manual input with Automatic steps:
  Gravimetric feeding



Smart combinations to create new control options

To keep new options simple, use strengths of existing controllers

Controller

Advantages:

- Simple interface
- Direct link to hardware

Disadvantages:

- Manual input only, no automatic time-based events
- No calculations possible
- No IF … THEN … logic available

SCADA software

Advantages:

- Option for automatic time-based events
- Calculations possible
- Free logic-based programming (e.g. IF … THEN …)

Disadvantages:

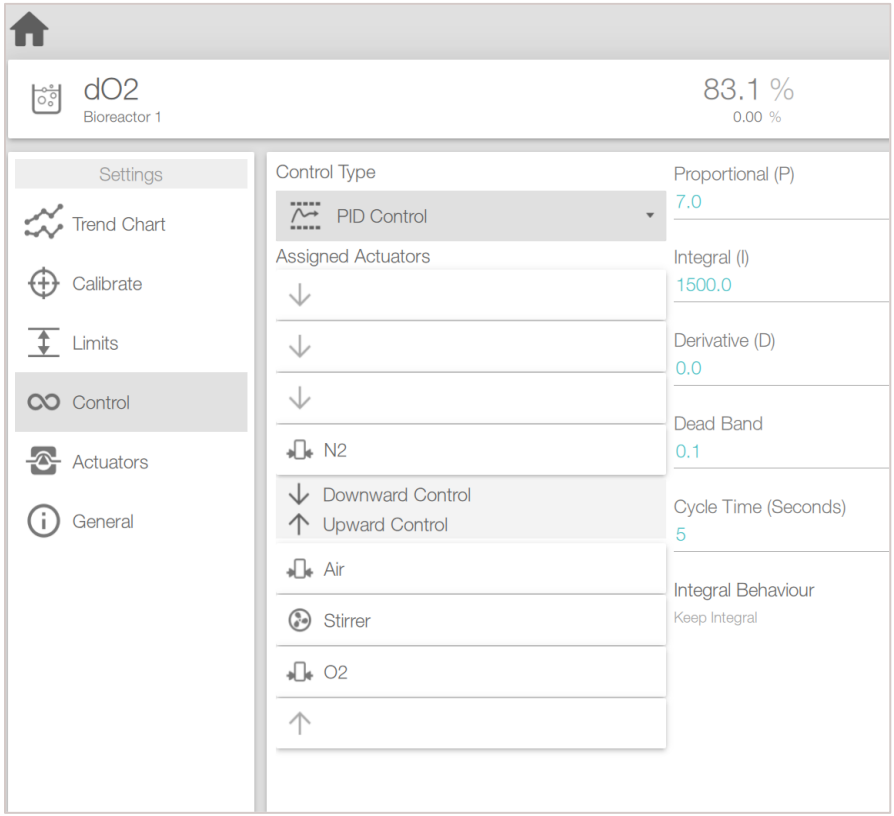
- Sometimes big recipes with complex programming
- No general check on logic available,
  testing needed to make sure Operation Recipe correct

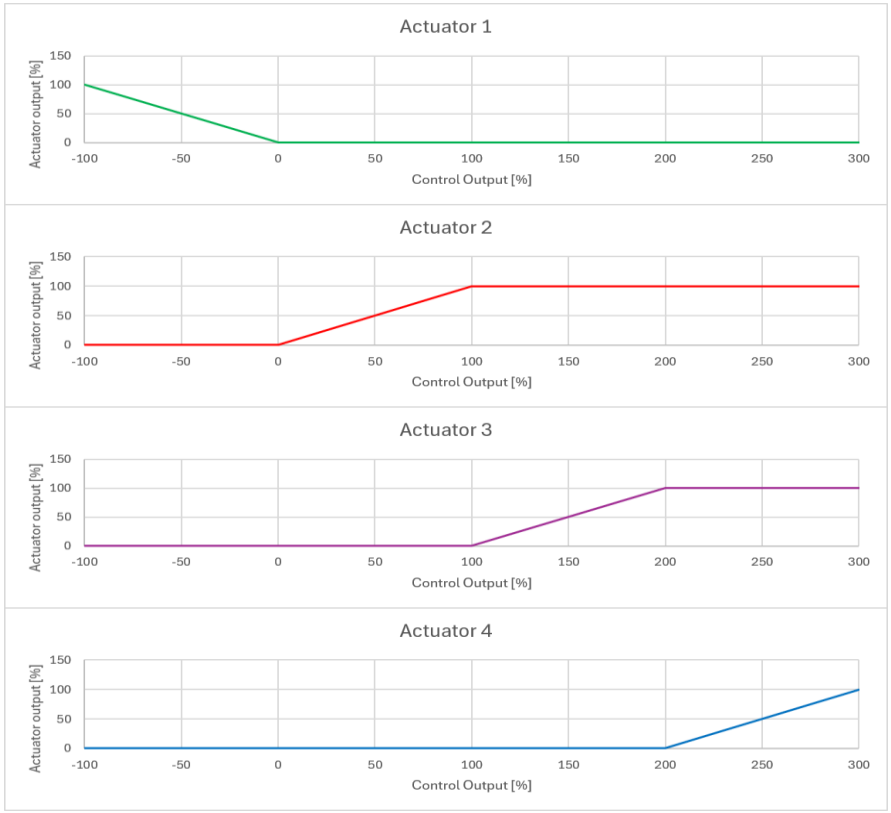
How can we use the Advantages of both systems and avoid their Disadvantages?

Example 1: PID control with simultaneous actuator output (intro)

Controller has simple method for setting up PID control loop with 4 actuators

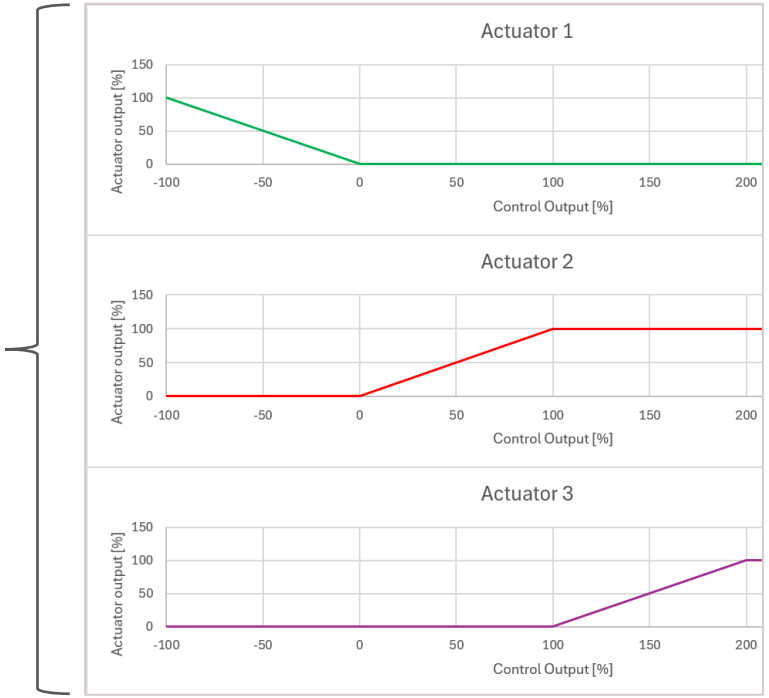
Actuators are activated sequentially, no option for simultaneous activation

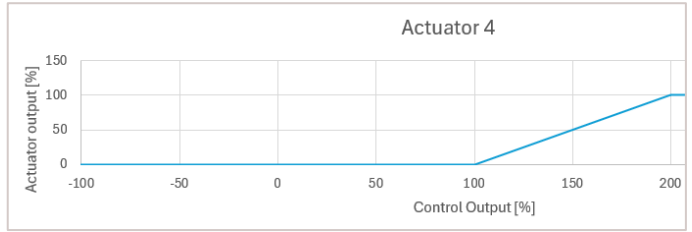




Example 1: PID control with simultaneous actuator output (solution)

- On controller program only 3 actuators in PID loop = Control Output (CO) will range between -100 and +200
- On SCADA software use as inputs:
  - Control Output
  - Low limit Actuator 4 (setpoint at Actuator output = 0%)
  - High limit Actuator 4 (setpoint at Actuator output = 100%)
- Create Formula:
  When Control Output is between value 100 - 200,
  send setpoint to Actuator 4 rising from Low to High limit

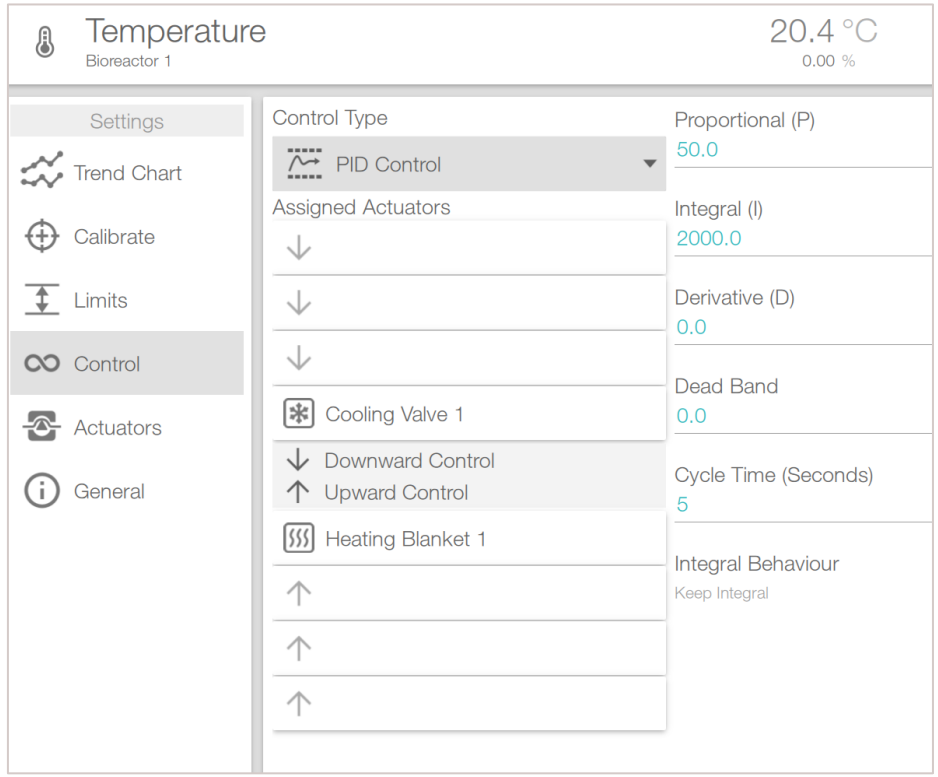




- **Result: Simplicity of setting up PID loop in Controller, combined by SCADA input for simultaneous actuator control**

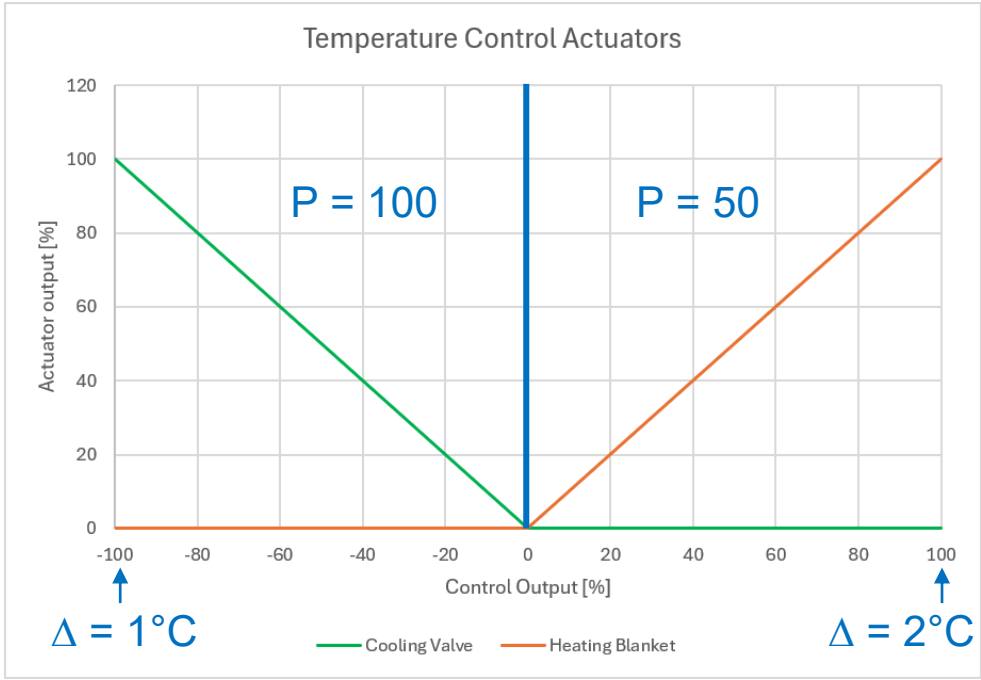
Example 2: PID control with different P/I/D values per actuator (intro)

- Controller has simple method for setting up PID control loop for Temperature with Heating Blanket and Cooling Valve as Actuators
- Example configuration: Heating goes much faster than cooling e.g. due to difference in surface area and temperature differential
  - *heating blanket can reach 80°C*
  - *tap water for cooling 20°C*
- For smooth Temperature control P-value for heating should be lower than P-value for cooling
- In Controller no option to change P-value based on logic, only manual changes allowed



Example 2: PID control with different P/I/D values per actuator (solution)

- On controller program standard 2 actuators in PID loop = Control Output (CO) will range between -100 and +100
- On SCADA software use as inputs:
  - Control Output
- Create Formula:
  - when Control Output is > 0 set P to 50,
  - when Control Output is < 0 set P to 100
  - if needed, reset I-value as well at CO=0

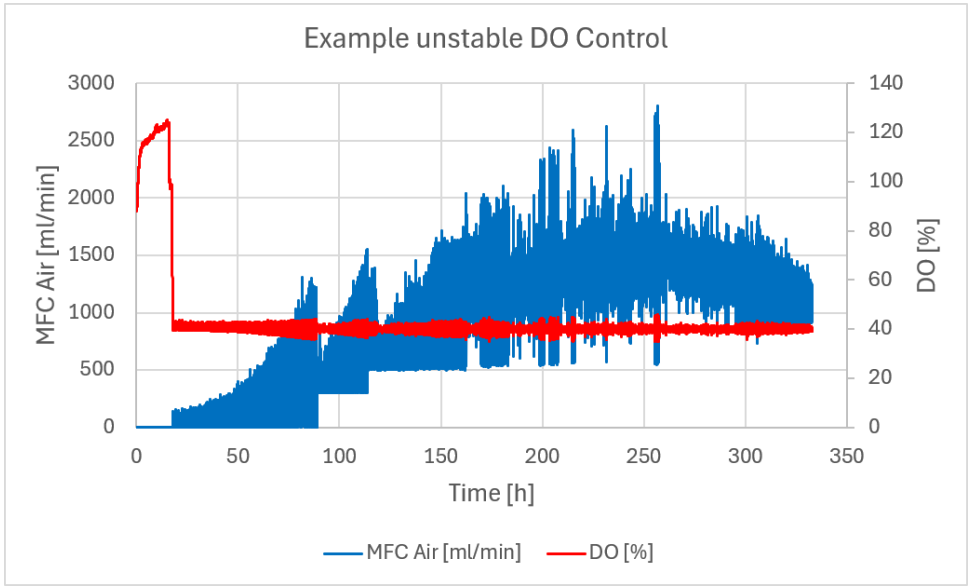


- **Result: Simplicity of setting up PID loop in Controller, combined by SCADA input for changing P-value**

- Take Note: Control Output is directly linked to P-value in formula (CO = P * error + ….), therefore a more elaborate formula is needed for P-value switch-point at CO ≠ 0

Example 3: Instability DO control (intro)

- Depending on culture conditions the DO Control loop can cause strong fluctuations in actuator control
  - Root cause varying, e.g. high culture viscosity
  - DO sensor readings fluctuate due to air bubbles getting trapped momentarily under tip of DO sensor and/or insufficient mixing
  - Biological constraints might prevent solving fluctuations via adjusting cultivation settings, e.g. increase stirrer speed
- In this example DO regulated at reasonably stable level, but Air flow varying wildly: Offgas measurements impossible
- Variation Air flow somewhat tempered by manually adjusting lower limit air flow

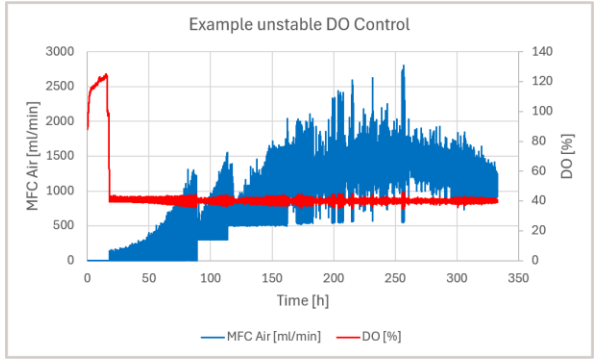


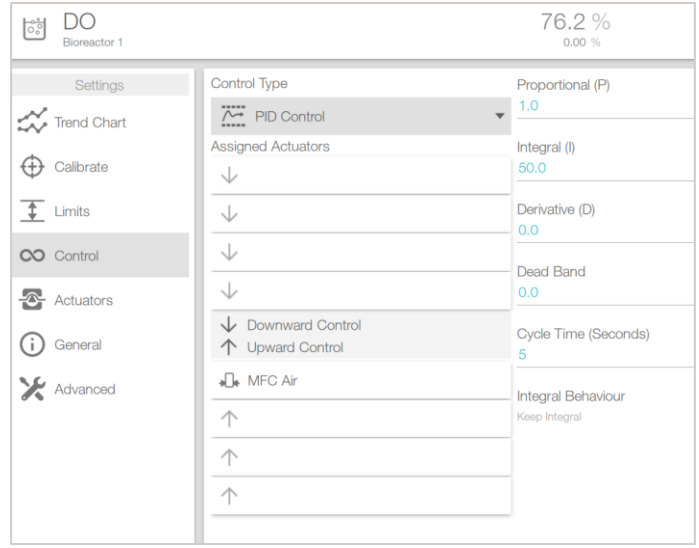
➔ Might this type of manual adjustment of limit be translated into automatic control program?

Example 3: Instability DO control (solution)

- Limiting variability Air flow might be achieved by allowing only upward control, i.e. only allow MFC setpoint to be adjusted upward, not downward
- Implementation on Controller as usual, with PID control Loop linked to DO sensor
- Implementation on SCADA software:
  - Input = SetPoint value MFC Air
  - Create new variable ‘Memory MFC’
  - Create formula: If current SP MFC-Air > Memory value,
    Then store current SP value as new Memory value
  - Continuously send ‘Memory MFC’ value to Controller as input for Low Limit of MFC-Air Actuator.

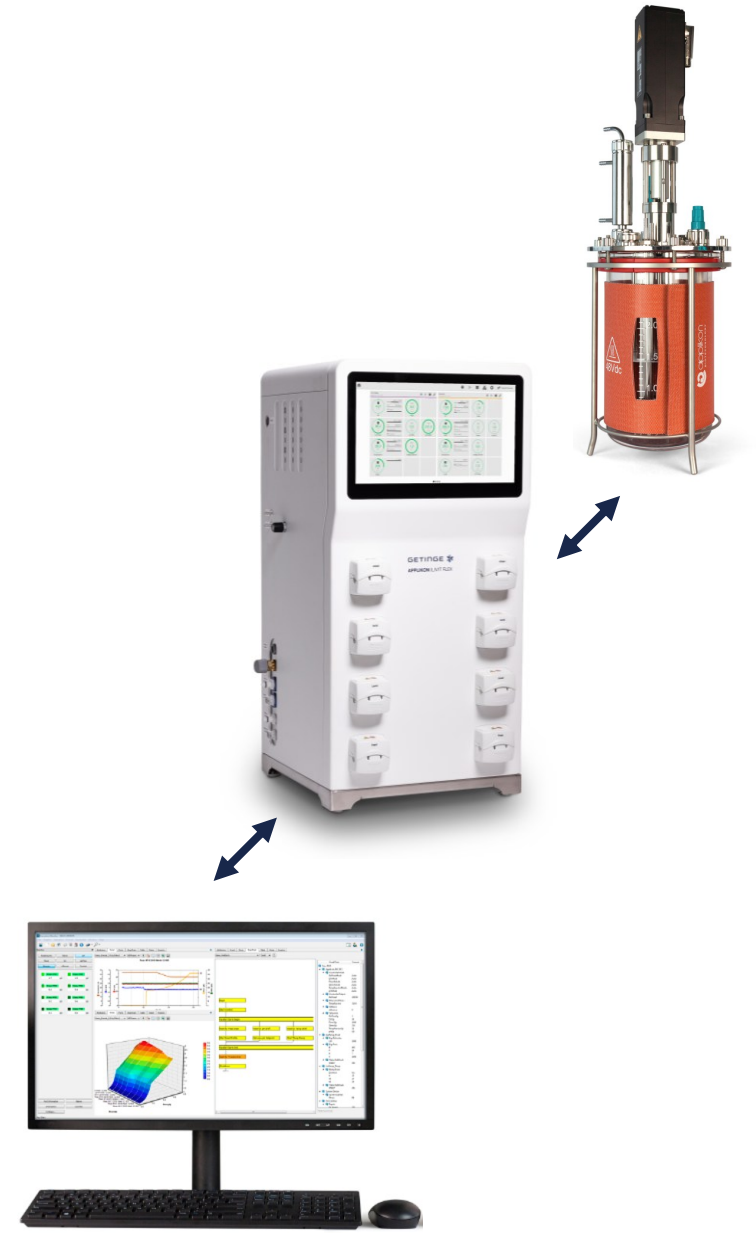
- **Result: Simplicity of setting up PID loop in Controller, combined by SCADA input for preventing actuator setpoint going down**





Overview basic design idea for new control options

- In the standard setup of bioreactor + controller + SCADA software each part has its own strengths and weaknesses
- If a specific Control option in one of the setup components is not versatile enough, check the exact operation and limits of this Control option
- Next check whether another component of the setup can provide
  - the additional versatility needed for the intended new Control option
  - what interface options there are between the components
  - what the simplest method is to add the additional feature to the Control option
- After creating the new Control option, thoroughly test the functionality in different scenarios, as interactions between e.g. Controller and SCADA software can sometimes create unforeseen effects on Control output



Conclusions

- In the standard architecture, in which Bioreactor + Controller + SCADA software are all linked together, each of the components have their own strengths regarding Control options

- By a smart combination of the best features of each component in the architecture, new Control options can be created, which are:
  - simple in setup
  - provide options not available in single architecture components

- After the new Control option is created, tested and saved, it is available for anyone to apply it in their cultivations



Questions ?

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