ProConnex® MixOne® RG-X Single-Use Mixers: Automated pH Adjustment

Technical Note

Overview

ProConnex® MixOne® RG-X Systems with KlariFi™ software feature automated pH adjustment to facilitate process control. This technical note provides an overview of the methodology, including variables affecting the pH adjustment response and results from functional testing.

The pH adjustment feature uses a dose-and-wait approach to gradually adjust the process pH to the user-defined setpoint. Rather than continuously running the pumps, the controller adds small, controlled doses of acid or base and then waits for the material to mix before evaluating the result. This method helps to minimize overshoot of the target pH and allows the system to adapt to a wide variety of process conditions.

Banded Control Response

The controller uses three response bands above and three bands below the setpoint, which determine the dose parameters based on the difference between the current pH value and the setpoint (*ΔpH*).

The dose parameters are the pump speed, dose duration, and dwell duration (wait time between doses). When *ΔpH* is large, the system uses higher pump speeds, longer dose times, and shorter dwell times. As the pH approaches the setpoint, the system reduces the pump speed and dose time while increasing the dwell time. A deadband around the setpoint represents an acceptable range where no acid or base is added. See Figure 1 for a visual representation of the control response bands.

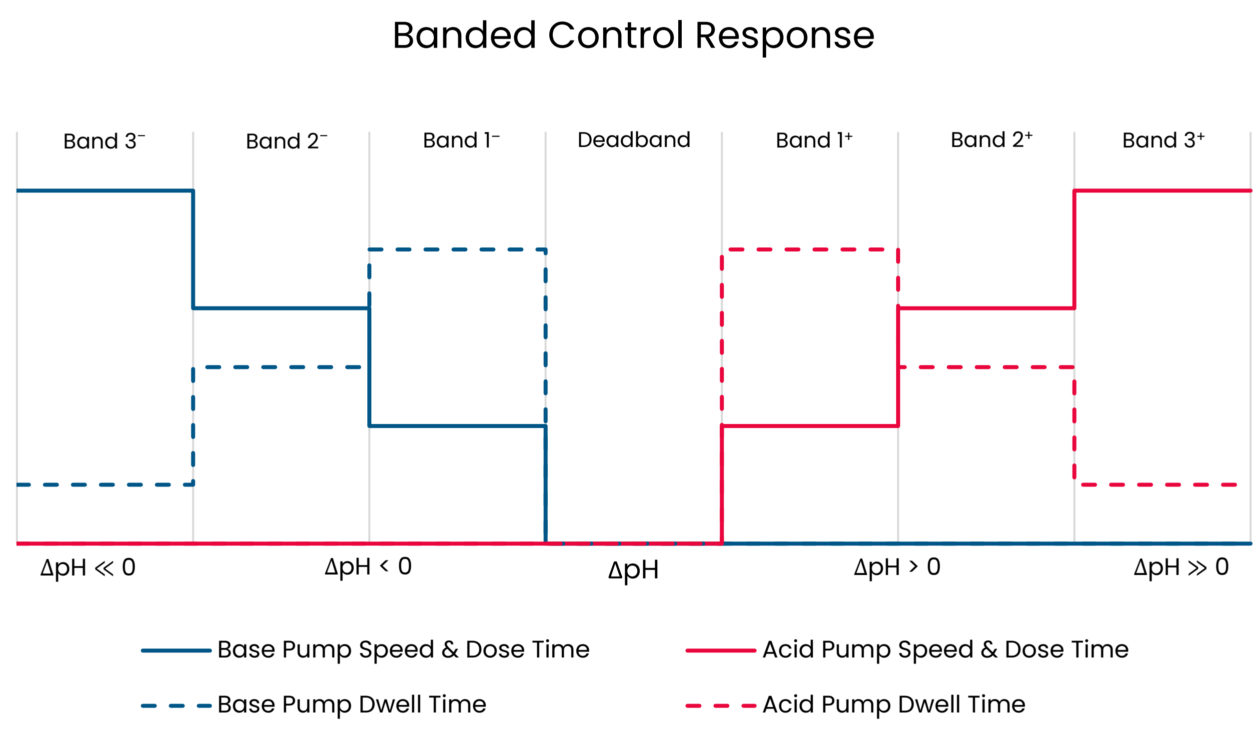

Figure 1. Visual representation of banded control response.

Pump Selection and Role Assignment
The user enters the pH of each reagent, and the system automatically determines which pump will raise or lower pH when activated.

Anti-drip Feature
A configurable anti-drip feature helps prevent overshoot caused by residual acid or base dripping from the inlet tubing after dosing stops. When enabled, the system briefly runs the previously active pump in reverse at low speed as soon as the pH value enters the deadband. Excess reagent is pulled back into the tubing rather than dripping into the process vessel.

Variables Affecting pH Adjustment Response

When tuning the banded dosing parameters for a specific application, several process variables should be considered.

1. **Vessel Volume**

   The volume of liquid in the vessel directly impacts the quantity of reagent needed to achieve a given pH shift. For example, a dose that causes a pH change of 0.5 in a 50 L batch may barely register in a 3000 L batch. Larger volumes generally require higher pump speeds, longer dose times, and longer dwell times to allow for proper mixing and settling. Operators should expect significant tuning differences between large- and small-scale units.

2. **Mixing Speed**

   Impeller speed affects the time for doses to disperse throughout the vessel and thus the response time of the pH sensor. Higher speeds promote faster homogenization, allowing shorter dwell times between doses. Lower mixing speeds require longer dwell times to ensure the pH sensor reading stabilizes before applying the next dose. Insufficient dwell time at low mixing speeds is a common cause of overshoot.

3. **Acid and Base Concentration**

   The molarity and type of acid or base used has a significant effect on control response. A highly concentrated reagent will cause a much larger pH change per unit volume than a dilute reagent. Strong acids and strong bases also produce sharper pH changes. Operators using concentrated reagents should start with slower pump speeds and shorter dose times to avoid overshoot.

4. **Setpoint Relative to Neutral**

   Because pH is measured on a logarithmic scale, control near neutral is more sensitive. Therefore, small doses while the pH is near neutral can cause relatively large pH swings, making pH prone to oscillation in this region. Setpoints close to neutral may benefit from more conservative Band 1 parameters, such as slower speeds, shorter dose times, and longer dwell times, to avoid overshoot. At extreme pH values (below 4 or above 10), there is more resistance to change in pH, allowing for more aggressive dosing with a smaller risk of overshoot and oscillation.

5. **Buffer Capacity of the Process Liquid**

   Some process liquids may contain buffers or other compounds that resist pH changes. A well-buffered solution requires substantially more reagent to shift pH compared to an unbuffered solution of the same volume. Operators working with buffered media should anticipate longer dose times or higher pump speeds than those typical for their vessel size.

6. **Tubing Size and Pump Delivery Rate**

   The pump tubing diameter impacts the volumetric flow rate at a given pump speed. MixOne RG-X vessel sizes up to 200 L are intended to be used with smaller tubing (3.2 mm ID) than vessel sizes 500 L and above (6.4 mm ID). Operators should verify actual delivery rates and adjust parameters accordingly.

Functional Testing

Initial tests were conducted using a 500 L vessel with two different fill volumes: 500 L and 250 L. Both tests used identical tuning parameters and identical acid and base reagents (Table 1).

Table 1. Test Conditions

Parameter	Value
Vessel size	500 L
Acid	1 M HCl
Base	1 M NaOH
Mixer speed	150 rpm
Fill volumes	500 L 250 L
Process fluid	Water

In each test, the system cycled through pH setpoints of 7.0, 3.0, 10.0, and back to 7.0 to evaluate control performance across a typical operating range.

Dose band parameters were set symmetrically above and below setpoint using the values given in Table 2. Values were chosen for the purpose of illustrating the automated pH adjustment functionality and were not optimized to minimize overshoot or oscillations.

Table 2. Dosing band parameters

Band	|ΔpH|	Speed (rpm)	Dose Time (s)	Dwell Time (s)
Band 3	>2.00	200	15.0	5.0
Band 2	0.25–2.00	80	7.5	15.0
Band 1	0.05–0.25	20	3.5	20.0
Deadband	<0.05	N/A	N/A	N/A

Results & Discussion

Response Time

The time required to reach each setpoint was roughly proportional to the fill volume in each run.

Transitions toward neutral (pH 7) were consistently faster than transitions away from neutral, regardless of volume. The transition from pH 10 to 7 was completed in under 5 minutes for both fill volumes, while the transition from pH 7 to 3 took much longer. This behavior demonstrates the logarithmic nature of the pH scale discussed earlier.

Setpoint Stability

Each time the system reached the target pH, it then maintained the setpoint value within the deadband tolerance. However, the the pH value exhibited more oscillation at the pH 7 setpoint than at pH 3 or pH 10, especially in the larger fill volume. Overshoot as high as 0.5 pH was observed, confirming that setpoints near neutral require more conservative tuning.

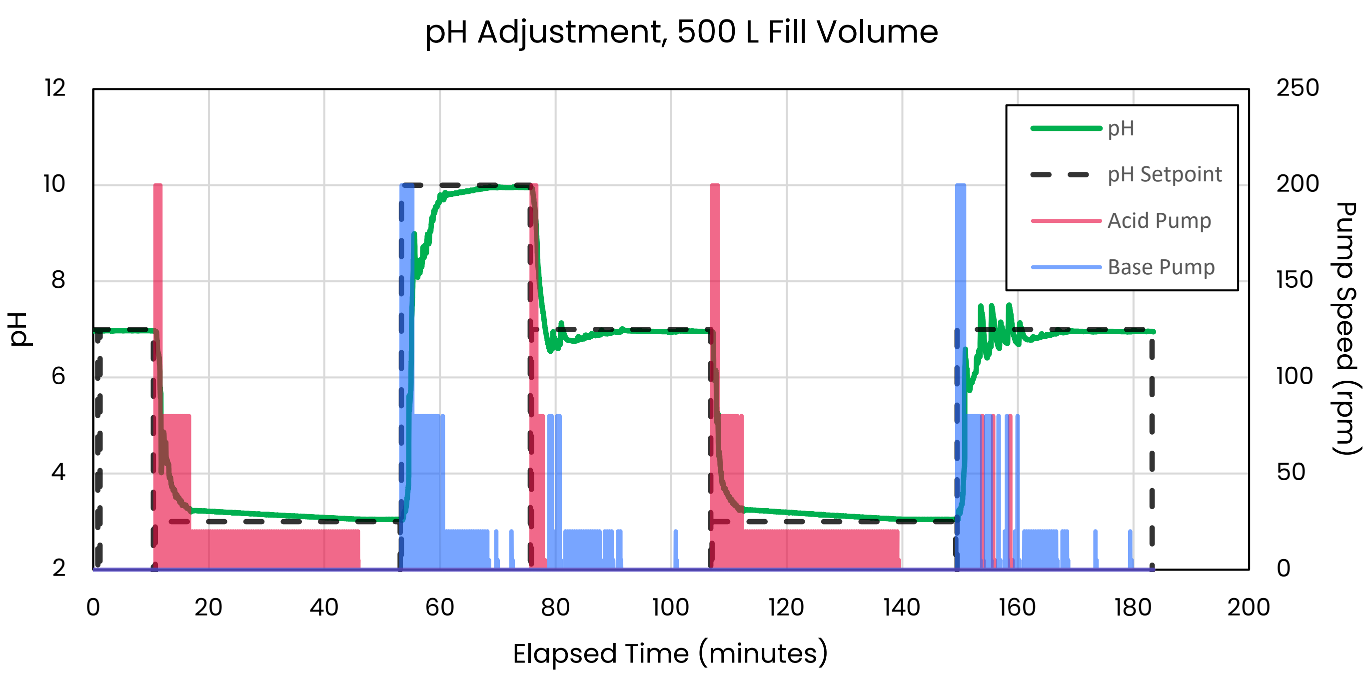

Figure 2. pH response data for 500 L test run

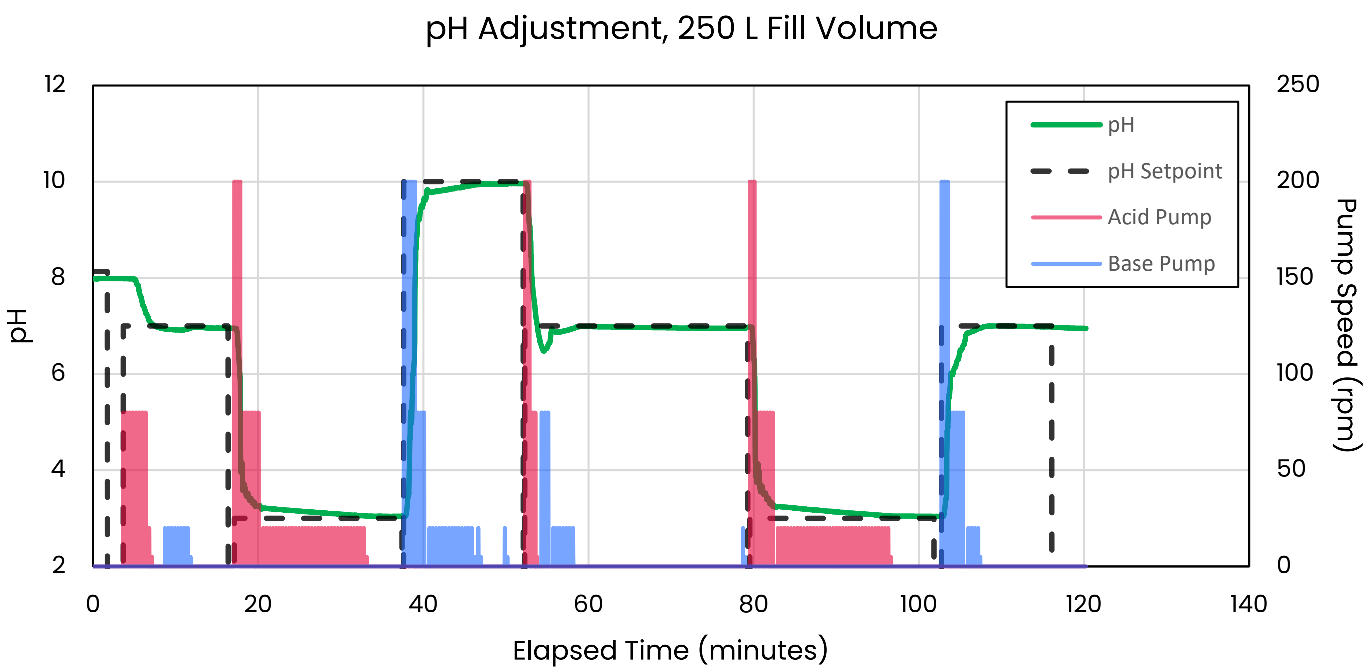

Figure 3. pH response data for 250 L test run

Conclusion

The test results demonstrate that the banded dosing response successfully adjusts pH across a typical operating range. The same tuning parameters maintained stable control at both 500 L and 250 L fill volumes.

When utilizing the MixOne RG-X pH adjustment feature, operators should tune control band parameters to suit the applications requirements, including volume, reagents, acceptable duration, and overshoot.

For more information on ProConnex MixOne RG-X Systems, visit repligen.com or contact your local Repligen bioprocessing sales specialist.

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