The Product Protection & Productivity Benefits of

Advanced Vacuum Control

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For drying processes conducted under vacuum, precise control over process conditions is often critical. Accurately controlling the vacuum can help to significantly decrease total process time and improve process yields. Process control also helps to meet regulatory requirements. The specific case of a researcher working in a chemical synthesis lab is considered here as a real-world example of the various vacuum control options which are available, and the relative strengths and weaknesses of each.

Introduction

The process of discovering and reproducing biologics or chemical compounds at the R&D scale, and the subsequent scale-up to manufacturing processes, is often time intensive and therefor costly. Distillation and drying processes can be particularly time-intensive if process conditions are not effectively optimized. Furthermore, suboptimal process controls can diminish process yields because of sample loss. Environmental and economic benefits, such as enhanced solvent recovery and power savings, can also be forfeited by inadequately controlled process conditions. In addition to these technical drivers, GLP, GMP, ISO, and other regulations require that process data be collected and retained. Electronic vacuum process optimization can thus offer significant economic, process, and environmental benefits, while contributing to regulatory compliance. The benefits of process automation can easily exceed tens of thousands of dollars annually and yield a return on investment (ROI) well in excess of 1,000%. Advances in vacuum controls have made each of these objectives more attainable.

Bay-Area Biotech Needs to Improve Throughput

A prominent biotech firm based in the San Francisco Bay Area identified in a need to enhance the productivity of their research and development group. In particular, the R&D team wanted to identify a means to increase the number of compounds that could be synthesized every year. One step in the synthesis process identified for investigation was the evaporation process, where bench-top rotary evaporators were used to boil off solvents from synthesized compounds. Inadequate vacuum control of rotary evaporators led to longer process times, reducing the number of compounds which could be synthesized annually. Specifically, sub-optimal vacuum control resulted in the solvent mixture “bumping,” increasing the risk of loss of product during the evaporation process. In addition, the lack of effective automation generally prevented R&D staff from operating multiple rotary evaporators at a given time.

Approaches to Vacuum Control

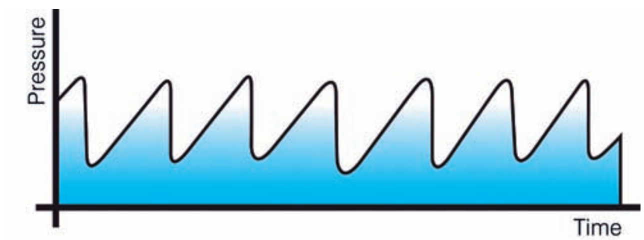
Vacuum control can be achieved in several ways. These approaches include

- “Two point” control
- Controllers and integrated pumping units which can detect a single solvent boiling point
- Integrated pumping systems which can sense multiple solvent boiling points and provide continuously-adaptive control.

Two Point Control

“Two point” control is the simplest form of vacuum control. It is often achieved by combining a pressure transducer, a solenoid valve, and a control module. The control module accepts a user input pressure level and compares that set point against the reading output by the transducer. The control module then sends an electronic signal to the valve, which causes it to open or close, as appropriate. As the measured pressure level rises above the set point, the valve will be opened, allowing the vacuum source (e.g., a pump) to reduce the pressure level. Once the pressure level goes below the set point, the valve will close again. This sequence of opening and closing is continuously repeated until the process is complete. The name “two point” control is derived from the fact that the controller actuates the valve based on the upper and lower bounds of the hysteresis band; this process is shown schematically in the figure below.

Figure 1: Two point vacuum control



The advantages of two point control are that it is a low cost approach to vacuum control and that it is well-suited to working with mixtures with known properties. Controllers based on this principle are readily available, and can easily be set-up to stream data to a computer for quality control or data analysis. The disadvantage of this approach is that it can be imprecise. This imprecision can lead to large pressure swings between the points at which the control valve opens and closes. Thus, this technique may not be a suitable approach when working with sensitive or high value materials.

Single Boiling Point Detection

In order to address this concern, manufacturers have developed products which have the ability to sense a solvent boiling point. Rather than requiring that a user enter a specific vacuum level, this control scheme allows the pressure level to be reduced by the vacuum source until an increase in pressure level is measured. This pressure increase is taken to indicate a marked increase in solvent evaporation rate. At this point in the process, the controller will then maintain this vacuum level so as to avoid bumping and sample loss. Vacuum can subsequently be adjusted by the user as necessary by entering a set point, much as with a two point controller. As such, the single boiling point detection approach marks a substantial step forward in vacuum control for drying applications.

This approach was introduced to the market as part of integrated pumping units (combining a vacuum controller and pump into a single piece of equipment). More recently, VACUUBRAND has introduced a stand-alone unit called the “CVC 3000 detect” which provides the same single boiling-point detection capability when paired with an existing vacuum source, such as a vacuum network, individual vacuum pump, or central vacuum system. Collectively, this class of products is a good solution when working with simple mixtures and when full automation is not necessary.

Continuously Adaptive Control

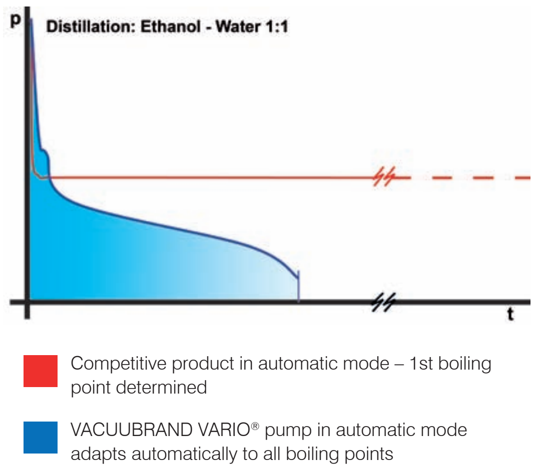
When working with more complex mixtures, or when full automation is necessary, it is often worthwhile to consider the class of integrated pumping units which provide continuously adaptive control. These pumping units work by continuously adjusting pump motor speed based on the apparent rate of solvent evaporation, as measured by the integrated pressure sensor. Reducing pump motor speed will allow the pressure level to rise and in turn cause evaporation to cease. Increasing pump motor speed will cause the pressure level to decrease and increase solvent evaporation. Because diaphragm pumps can be controlled in this way through a wide range of motor speeds, this allows for extraordinarily precise vacuum control as compared to that obtained from two point control.

In order to achieve this level of integration, units that offer continuously adaptive control incorporate both a vacuum pump and a controller. So, naturally, these units do cost more than stand-alone controllers. However, they are comparable in cost to the price of pumping units which feature single boiling point detection capability, while providing productivity, operating, and service cost benefits. These benefits serve to more than offset any upfront incremental cost.

Continuously adaptive control is particularly amenable to working with multi-component solvent mixtures, highly sensitive or costly materials, or when a fully-automated approach is desirable. Because solvent boiling is continuously optimized, units that offer continuously adaptive control can significantly reduce process times. This is especially helpful in cases with solvent mixtures in which vapor pressure and optimum vacuum conditions change continuously over the duration of the process. Further, by instantaneously optimizing vacuum levels along a changing pressure curve, the continuously variable motor speed substantially reduces bumping. There is also the benefit of process automation.

In Figure 2 (top right), the red line shows the pressure curve when relying on single boiling-point detection for the evaporation of a 1:1 mixture of water and ethanol. In contrast, the blue curve shows the pressure-time profile when using VACUUBRAND's continuously adaptive VARIO® control. One can see that both the continuously adaptive control unit and single boiling-point detection unit pick up the first boiling point. However, only the pumping unit with continuously adaptive control can adjust automatically to an unlimited number of boiling points, thereby fully automating the process. This yields substantial productivity benefits in both the research lab and the production environment since the scientist or engineer can use this benefit of VARIO® pumping units, along with the automated documentation capability, to develop optimal processes in very short time frames by reducing or eliminating the need to follow an iterative procedure. Beyond process development, full automation also ensures protection of starting materials and reliable, reproducible, documented process conditions.

Figure 2: Process time advantage of VARIO® control.



PC3001 VARIO PRO

Result & Conclusion

After assessing the control needs of the Bay Area biotech customer, VACUUBRAND advised the customer to adopt pumping units featuring continuously adaptive control. The customer agreed, and elected to purchase the VACUUBRAND's PC 3001 VARIO^{PRO} vacuum system to eliminate bumping and to gain full advantage of the time-saving potential of process automation. The customer reports notable time savings, and exceedingly rare instances of bumping. Due to these benefits, the customer has made repeated purchases of PC 3001 VARIO^{PRO} pumping units for use in several laboratories.