

Closed-Loop Systems in Anesthesia: Reality or Fantasy?

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Feedback is the process in which information about the past or the present influences the same phenomenon in the present or future. Feedback and control loops are ubiquitous in nature and the natural world and are essential to maintain homeostasis of organisms and entire ecosystems.¹

A closed-loop system is a control system with a feedback loop that automatically changes the output based on differences to the input signal. Most naturally occurring control systems are closed-loop systems. In engineering, an example of a simple closed-loop system would be the use of a thermostat to regulate room temperature. Other examples include the cruise-control function on cars and the computer mouse.

This edition of *Anesthesia & Analgesia* contains 3 articles relating to the use of closed-loop systems in anesthesia.²⁻⁴ So what advantage could these systems offer us in the operating room? The potential benefits are obvious: an automated system could allow us to control a target variable with greater accuracy. In addition, the system could not be distracted and would therefore reduce the potential for inattention and human error, as well as allowing the anesthesiologist to concentrate on other tasks.

The problem is that any system is dependent on an accurate and reliable input signal. Biological systems are complex, and any potential closed-loop system would have to be robust and reliable. Anesthesiologists would also need to understand the system that is operating. Dumont et al.² have provided an introduction into the field of control systems for the everyday anesthesiologist.

The simplest example of the use of a closed-loop system in anesthesia is to monitor and maintain neuromuscular blockade. With this system, there is a reliable noninvasive monitor that can feedback into a control loop. Several studies have shown that closed-loop control of neuromuscular blockade can achieve a steadier level of neuromuscular

block while infusing the minimum amount of the drug.⁵⁻⁷ However, this type of control while easy to achieve is also not widely adopted. Reliable neuromuscular blockade can be achieved simply; overdose carries little risk and can now be rapidly reversed.⁸

Of greater clinical interest is the use of a closed-loop system to maintain an adequate depth of anesthesia, constantly adjusting to avoid both under and overdosing of the patient. Interest in closed-loop control has been renewed since introduction of the Bispectral Index (BISTM, Covidien, Mansfield, MA) monitor as a target for depth of anesthesia monitoring. Several studies have shown that closed-loop isoflurane^{9,10} or IV anesthesia infusion systems¹¹⁻¹⁴ using the BIS can outperform anesthesiologists in terms of BIS variability, maintaining it within a narrower range.

This is perhaps not surprising; the systems are after all highly sophisticated and designed to constantly adjust to maintain the BIS within the target range. The broader question is whether this can be useful clinically. Any closed-loop system is only as reliable as its input signal. Although BIS is moderately accurate as a surrogate for depth of sedation, it has some limitations in its ability as an aid to anesthesia titration during anesthetic maintenance.^{15,16} There are some confounding factors, such as quality of the input signal, interference from the electromyographic signals,¹⁷ and the use of ketamine,¹⁸ that artificially raise the BIS number. Therefore, it is the role of the anesthesiologist to process this signal in its correct context along with hemodynamics and multiple other signals to maintain a correct depth of anesthesia. However, maybe a closed-loop system could act as a copilot providing accurate control of the target variable, in this case BIS, while under the supervision of the anesthesiologist.¹⁹ This system could offer the best of both worlds: the closed-loop system would provide constant and accurate control of target variable, and the anesthesiologist would be free to perform higher-level clinical tasks.

Another potential use of closed-loop systems is fluid administration via a goal-directed approach. There is a substantial body of evidence that goal-directed fluid therapy tailored toward optimization of stroke volume (SV) improves outcomes.²⁰ In patients receiving mechanical ventilation, dynamic predictors of fluid responsiveness such as pulse pressure variation (PPV) are the best predictor of fluid responsiveness²¹ and therefore a potential input signal for a closed-loop system.

Previous work has showed that the closed-loop optimization of SV is feasible¹⁹ and in a simulation (in silico) can provide a higher and steadier cardiac output than

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anesthesiologist management, when using a dynamic variable as an input²² or not.²³

The 2 articles from the same group in this issue of *Anesthesia & Analgesia* include testing the ability of closed-loop fluid administration systems in a simulation with different patient weights, starting blood volume and cardiac performance,³ and in vivo in a pig model of hemorrhage.⁴ Both studies used the same closed-loop fluid management system (LIR: learning intravenous resuscitator) to optimize SV. The LIR monitors SV, heart rate, mean arterial blood pressure, and PPV and uses these data along with actual observed responses from previous interventions to predict the percentage increase in SV should a standardized 500-mL fluid bolus be given to the patient. Based on this prediction, the controller will either give no fluid, a 100-mL mini-fluid challenge (test bolus), or a normal fluid challenge (250 mL). The different fluid boluses are given depending on the confidence of the controller of a positive response.

As is immediately obvious, this system is substantially more complicated than previously described anesthesia control systems with 1 input variable. Nevertheless, in a physiological model, the LIR was highly effective in resuscitating to within a clinically acceptable range of SV and blood volume regardless of weight, contractility, or starting blood volume. However, as stated in the article, physiologic systems are far more complicated than any model, and PPV has a number of limitations as a marker of fluid responsiveness in the clinical setting.

Hence, the first in vivo study of the LIR is of considerable interest. When transferred to an in vivo animal hemorrhage model, the LIR was able to maintain SV with reduced hemodynamic variability when compared with fluid management by an anesthesiologist.⁴ This is an important advance and paves the way for future studies in real surgical situations.

So where does this leave us? This concept is in its infancy and may be a long way from commercialization and clinical application. Closed-loop systems are not intended in any way to replace the anesthesia provider. However, we all know that the provision of anesthesia is frequently compared with piloting an aircraft. In the airline industry, closed-loop systems (autopilot—an essential part of the modern cockpit) have increased safety by reducing variability and enabling the pilot to concentrate on fewer tasks. This, perhaps, should be the goal of closed-loop systems in anesthesia. ■

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