Displacement Micropump with Check Valves for Diabetes Care—The Challenge of Pumping Insulin at Negative Pressure

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Contributor: Eric Chappel

The displacement micropump with passive check valves is an attractive solution for precise insulin infusion in patients with type 1 diabetes. Unlike most insulin pumps that push insulin from a cartridge using a piston, a displacement micropump will first pull insulin from the reservoir before infusion into the patient. This dual sequence introduces new challenges in terms of insulin stability, notably if the reservoir is not pressurized. After an introduction to displacement micropumps and a brief review of the insulin degradation mechanism, micropump design rules are discussed in light of microfluidic theory.

Keywords: MEMS micropump; displacement pump; check valves; pump failure mode; insulin delivery; diabetes care

Diabetes is a chronic metabolic disorder characterized by high blood sugar levels that cause serious damage over time. Type 1 diabetes, also called insulin-dependent diabetes, is a condition in which little or no insulin is produced by the beta-cells of the pancreas. Daily administration of insulin is essential to the survival of people with type 1 diabetes.

Traditionally, insulin is administered by subcutaneous injection using an insulin syringe or pen. Advanced insulin delivery systems include patch pumps which administer fast-acting insulin 24 h a day to meet the body's needs, via a fine cannula placed subcutaneously. Continuous subcutaneous insulin infusion (CSII) has proven to be effective in diabetes care. These programmable pumps can deliver both basal and bolus doses of insulin. Basal insulin delivery rates are programmed by the physician to meet individual patient needs. Insulin pumps can also deliver bolus insulin to minimize blood glucose deviations after meals. The recent improvement in blood glucose meter accuracy enabled closing the loop thanks to specific algorithms and wireless communication between a continuous glucose meter and the delivery system for one (insulin) or two hormones (insulin and glucagon). Most commercially available insulin pumps feature a piston mechanism connected either to an insulin infusion device or to a cannula patch and occlusion detection system. The accuracy of bolus and basal rate delivery, in nominal conditions, showed globally good results in agreement with the manufacturers' specifications. Larger deviations are observed at short observation windows (typically less than 1 h in basal rate), due to the inherent noise induced by the pumping engine itself and the so-called stick–slip effect of the piston against the internal wall of the insulin container. Other insulin pump designs have been studied to improve short-term variability of insulin delivery and shorten occlusion detection time. Indeed, insulin delivery systems are designed to detect occlusion, which consists of a partial or complete blockage of insulin delivery, by monitoring the in-line pressure. Occlusion detection is crucial to maintain the blood glucose level in an acceptable range. However, despite improvements in the catheter design to reduce the occurrence of silent occlusion, this failure mode remains difficult to detect, especially at low flow rates, as in-line built-in pressure increases slowly over time. Median occlusion detection times (ODT) at 0.1 U/h ranging from 4 h to more than 40 h in commercial insulin pumps were reported. Occlusion may occur shortly after insertion of the infusion set, but generally increases after 2 or 3 days of use. The effect can be related to a kinking of the catheter or the soft cannula, a cannula leakage, the chemical precipitation of insulin, or the fibrin formation at the needle tip.

Depending on whether the externally applied energy is converted into fluid kinetic energy, micropumps can be categorized as nonmechanical or mechanical micropumps. These later devices are usually further divided into displacement or dynamic micropumps depending on whether mechanical energy is periodically or continuously transferred to the working fluid. Micropumps with passive check valves have indeed demonstrated interesting features in terms of occlusion detection and delivery accuracy. Numerous actuation mechanisms were associated with this micropump structure,
Such a displacement pump engine is connected to the insulin reservoir and either an infusion set or a cannula that is directly inserted into the skin (patch pump). Sensors can monitor the pressure to detect any events that may induce over- or underdelivery. For basic safety reasons, the pressure relative to the atmosphere in the insulin reservoir is generally zero or slightly negative. During the filling phase of the pumping cycle, a negative pressure is generated in the pumping chamber to open the inlet valve and draw insulin from the reservoir. The fact that the insulin experiences a negative pressure is a significant difference from other insulin delivery systems, except the implantable pump MIP developed by Minimed to infuse U400 insulin via the intraperitoneal route. The pressure of the MIP reservoir is –275 ± 70 mbar to prevent the risk of overdose induced by leakage and the risk of pocket fill.

Most infusion systems are piston pumps that simply push the insulin present into the reservoir to the patient. To illustrate the difference between the two systems, the presence of air in the insulin reservoir is considered. Except in the case of prefilled cartridges, it is difficult to avoid the presence of air, especially if insulin, before being injected into the reservoir, is first extracted from a vial by the patient using a syringe. Air bubbles in a piston pump reservoir can generate an overdose in the event of depressurization (e.g., in an airplane). In the reservoir of a displacement pump with check valves, air can block the valves due to capillary effects and degrade delivery accuracy if air remains in the pumping chamber. The risks for the patient are therefore radically different: over- or underdelivery.

To tackle the challenges of infusing insulin with a displacement pump having check valves, a brief description of the pumping mechanism is first presented, together with an analysis of the link between design, pumping performances, and rapid occlusion detection. The compatibility of this pumping mechanism with the fragile insulin molecule is then reviewed in detail, with a comprehensive analysis of the failure modes. Finally, some insights about the design rules that can be implemented to improve the displacement micropump reliability and thus mitigate the risks associated with this pumping mechanism are presented.

References


