An artificial pancreas system could mean less hassle and fewer health complications for people with diabetes.

FREEDOM

An Artificial Pancreas System now undergoing clinical trials in Santa Barbara could relieve people with diabetes of the burden of constantly monitoring their blood sugar and dosing themselves with insulin.

Sharon Sorensen’s blood glucose level is higher than it should be. After decades of living with diabetes, she’s keenly aware of the potential fluctuations in her blood sugar and adept at limiting them with carefully timed doses of insulin. Today, though,
Sorensen is taking part in a clinical trial, and she’s turning over control of her blood sugar levels to an “Artificial Pancreas System” developed by researchers at UC Santa Barbara in collaboration with Sansum Diabetes Research Institute (SDRI).

Sorensen is wearing a continuous blood glucose monitor that takes readings every five minutes from a sensor on her stomach. A pump taped to her arm is poised to deliver doses of insulin, when necessary. These devices have freed many people with diabetes from the unpleasantness of insulin injections and given them a better way of keeping tabs on their blood sugar. Sorensen has used glucose monitors and insulin pumps for years, but she’s had to be the go-between: using the readings from the monitor to figure out the necessary appropriate dose of insulin and then activating the pump to deliver it.

Researchers at UCSB and at SDRI, also in Santa Barbara, want to make Sorensen’s life—and the lives of the millions of other people with type 1 diabetes—easier and healthier by automating the process.

“We have these two parts and what’s missing is the brain to get the sensor and pump talking to each other,” says Howard Zisser, director of Clinical Research and Diabetes Technology at SDRI. “That’s where the engineers come in?”specifically, a UCSB team led by Chemical Engineering Professor Frank Doyle, who holds the Mellichamp Chair in Process Control and brings a biological control perspective to the problem.

A decade ago, Doyle had the idea of taking a model-based control approach that’s been used for decades in the refining industry, and more recently, by automakers in anti-lock braking systems, and adapting it for medical applications.

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level is nudging the upper limit of her healthy range. This high start is intentional?a challenge to the system.

He?s since worked with colleagues at UCSB and SDRI to develop a control system that could be the brains of an automated insulin delivery system. The Artificial Pancreas System (APS) developed in Santa Barbara provides a framework to link a continuous glucose monitor with a sophisticated algorithm to determine the amount of insulin necessary to keep that level within a healthy range, and then sends that information to an insulin delivery device (pump). The components ?talk? to each other using Bluetooth or another wireless communications protocol.

The goal of the work, which is sponsored by the Juvenile Diabetes Research Foundation (JDRF) as part of its Artificial Pancreas Project, is to relieve people with type 1 diabetes of the burden of monitoring their blood sugar levels and determining and administering an appropriate dose of insulin?a responsibility that can be particularly problematic for children and teenagers with diabetes?and so help them live longer, healthier lives.

?If we have a way to automatically deliver the appropriate dose of insulin,? says Eyal Dassau, a senior investigator at UCSB and lead scientist for the APS project, ?that will minimize the risk for long-term complications.?

Researchers around the world are working on artificial pancreas systems, but Doyle says the artificial pancreas algorithm developed in Santa Barbara is unique in two respects: it?is completely automatic, and it?is very flexible. It?is the first fully automatic closed loop system?it doesn?t require any user input, unlike other setups that need human help to transfer data, and it?is built upon a software system (the APS) that?is compatible with three kinds of insulin pumps and two glucose monitoring systems, and can be expanded to accommodate other devices. It can also be used with any algorithm, offering researchers around the world a powerful tool for developing artificial pancreas technology.

?The collaboration between UCSB and SDRI is an excellent example of how our strengths in engineering and science have impact on an important and growing medical
problem of our times,? says SDRI Board Member and UCSB?s Dean of Mathematical, Life and Physical Sciences Pierre Wiltzius.

The UCSB/SDRI system is now being tested in clinical trials at SDRI and at 12 other locations around the world. Sorensen, who lives in Solvang, is one of 15 patients participating in the trials in Santa Barbara. ?It would be wonderful if this work helps people,? she says, ?and if it helps me, that?s even better.?

?This is a very, very exciting period for us,? Doyle says. ?These algorithms that we have been prototyping and developing for the last 10 years are finally moving into the clinical phase.?

For Sorensen, that means a full day spent at SDRI, with the APS controller tucked into a pouch next to her. Today, it?s in charge?and on trial.

Sorensen is one of about 24 million Americans who have diabetes?roughly 8 percent of the U.S. population, according to the Centers for Disease Control and Prevention (CDC). Type 2 is by far the most common form of diabetes, but Sorensen has type 1, an autoimmune disease in which the body attacks the cells in the pancreas that produce insulin, a hormone that regulates blood sugar levels. People with type 1 diabetes must receive insulin delivered by injection or a pump in order to survive. Santa Barbara was one of the first places in the world where it was available, thanks to the work of William Sansum, who was the first physician to purify and administer insulin in the United States back in 1923.

Poorly controlled blood sugar levels can lead to serious complications, including heart attack, stroke, blindness, kidney disease and nervous system problems that sometimes necessitate amputation. According to the CDC, people with diabetes have twice the risk of death as others of a similar age.

By late morning Sorensen?s blood sugar level has flatlined, which means she can finally eat. This ?unannounced meal? is the second challenge for the system.
Howard Zisser (left) of Sansum Diabetes Research Institute and UCSB Engineering Professor Frank Doyle monitor the performance of the artificial pancreas system during a clinical trial in Santa Barbara.

As Sorensen knows from decades of experience—she was diagnosed in 1966, not long after the birth of her first child—living with diabetes requires constant vigilance and commitment.

It takes a while for people with diabetes to understand how their blood sugar levels are affected by food, exercise and stress, and to learn how to anticipate those effects and how to counter them by delivering a carefully timed and measured dose of insulin—which is toxic at high concentrations, and can’t be counteracted.

“It’s a job,” Sorensen says. “It’s frustrating and it’s tiresome and there are times when you just want to be done with it, although she does see an upside: “It’s been a blessing in a way because my family and I eat better and we exercise.”

On the morning of the trial, Sorensen skipped breakfast, as instructed by the research team, and by 9 a.m., when the trial begins, her blood glucose level is nudging the upper limit of her healthy range. This high start is intentional, Doyle says, as a “challenge” to the controller—a test of how quickly it can get Sorensen’s blood sugar under control.

As the morning progresses and the automated system does its job, Sorensen’s glucose level eases downward.

Readings taken every five minutes by the glucose monitor—which are confirmed by blood draws every half hour during the 8-hour trial—are sent wirelessly to a laptop computer, which is connected to a projector screen on a wall. As the readings accumulate, a line on a graph creeps forward. Out ahead of it, another line indicates the blood sugar levels predicted by the controller; “It amazes me how accurate it is,” Sorensen remarks.
One of the strengths of the UCSB/SDRI system is its predictive control, which Doyle compares to the strategy of a chess master: moves are planned in advance, with the player constantly incorporating the new information from each opposing move. To fine-tune the control algorithm, Sorensen wore the glucose sensor before the trial, so the researchers could ?learn? how her body functions.

The system performs admirably during the morning of Sorensen?s trial, and by late morning, her blood sugar level has flat-lined. ?That?s not usually a good thing in medicine,? Zisser quips, but in this case it is, particularly for Sorensen, who?s ravenous. It means she can finally eat. This ?unannounced meal? is the second challenge for the system.

As Sorensen works her way through a half-sandwich and salad, her blood sugar level begins to climb, but it?s soon brought under control by the APS, which determines that a burst of insulin is needed and prompts the pump to deliver a dose.

A system like this won?t be on the market for at least a few years?a commercially available version would include various safety protections?but as the Santa Barbara researchers put this setup to the test, they?re figuring out ways of improving on it.

?If we could get faster and more reliable ways of measuring blood sugar, and faster, more efficacious ways of delivering insulin,? Doyle says, ?we could push the system much farther.? To that end, the research team will soon begin two JDRF-funded trials, one using quick-acting inhaled insulin, and another using a delivery device that squirts insulin directly into the abdominal cavity. ?That gets the insulin where it needs to be, much like the pancreas does,? Doyle says.

?This isn?t a cure,? he adds, ?but we want to ease the burden for people with diabetes.?

Zisser sees the collaboration between UCSB and SDRI as key to the team?s success and refers to the APS work as ?medically inspired engineering?or engineering-inspired medicine. It?s one of the great advantages we have here.? Dassau agrees, saying, ?We don?t believe engineers can work in a vacuum. We need a ?sanity check.? It?s better, when you design something, to have the voice of the M.D.s.?