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Modelling and simulation of occlusions in insulin pumps*

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***Abstract*— An open source simulation model of the mechanical properties of a fully functional insulin pump was made in Matlab Simscape. The model simulates realistic behavior of an insulin pump, parts of which are validated against real-world systems. Simulations include mechanical forces and internal pressures, and the following fluid dynamics. Failure modes, such as occlusions, can be simulated and the resulting simulations can give new insights on how these failures affect the pump and how to detect them.**

***Clinical relevance*— Realistic pump simulations can be used to analyze how pump failures affect the system and in turn how to most effectively detect them before posing a hazard to the user, increasing the safety and reliability of the system.**

I. INTRODUCTION

Continuous Subcutaneous Insulin Infusion (CSII) via insulin pumps has for many years been proven to be effective at treating diabetes. Many different insulin pumps are available to users, but the main principle remains the same; An insulin pump infuses insulin via an insulin infusion set (IIS) inserted into the tissue directly beneath the skin of the patient, with infusion rates (typically in terms of Units of insulin (U100), where 1U is defined as $\frac{1}{100}$ml of insulin) adjusted by the user based on their blood glucose level (BGL).

Insulin pumps have been found to be accurate in volume delivery, with a mean accuracy of $\pm 5\%$ when averaged over 72 hours [1], though the accuracy of each individual bolus can vary up to $\pm 15\%$. During the run-in phase, the first few hours after insertion of a new IIS, the inaccuracies can be even larger [1], likely due to varying friction forces within the pump mechanics and reservoir [2].

Pump failures can greatly affect the safety and reliability of the system. Failures like occlusion of the IIS, a blockage of the insulin delivery leading to a complete or partial stop of flow, is a relatively common occurrence for pump users, occurring anywhere from a few times a month to several times a week [3]. These types of failures can have high impacts on the users BGL unless detected and acted upon soon enough. Studies have shown that occlusion detection can take anywhere from 4 to 40 hours depending on infusion rates [4].

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Occlusions normally occur gradually after 2-3 days of use of the same IIS [5]. The main cause of occlusions is the chemical precipitation of insulin [6]. This leads to the formation of solid substances and fibrils of the insulin solution, which may clog up the transition between the wider tubing and the thinner cannula. This precipitations happens gradually over time, and can be accelerated by exposure to higher temperatures, changes in pH, agitation and physical stimulation [6].

Occlusions also has a chance of occurring shortly after insertion of a new IIS or due to kinking by other external factors, especially IIS with Teflon cannula has been found to have a 15% failure rate on insertion [7].

By simulating and examining the systems dynamics during pump failures it may be possible to find new methods of improving failure detection.

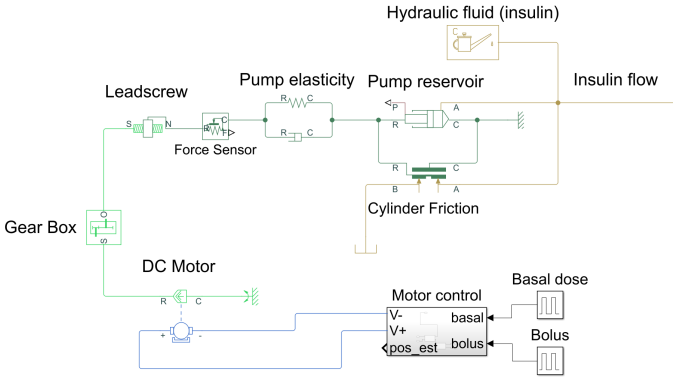
II. INSULIN PUMP SIMULATOR

In order to analyze the dynamics of the system, an insulin pump simulator was made and published open-source on GitHub [8]. The simulator aims to simulate a generic piston-driven insulin pump, and does not aim to recreate any one specific make or model. By simulating a physical pump, the aim is to be able to determine how pump failures such as occlusions of the infusion path affects the different parts of the pump system. Thus, the simulator may help determine what system parameters and states should be monitored in order to detect occlusions and other possible pump failures.

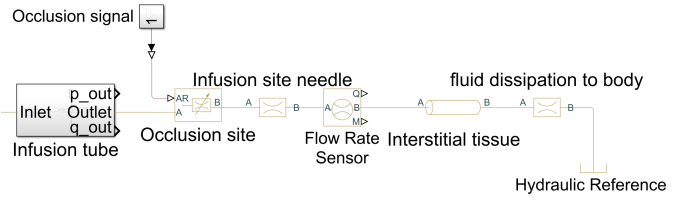
The simulator model was made in Matlab Simulink, version R2020b, using the Simscape toolbox. Simscape is a modelling tool made for rapid prototyping and simulations of physical systems, where the block diagram consists of physical model blocks. These blocks have their respective mathematical models built into each respective block and are connected to each other using their real-life physical signals such as voltage and current from an electrical power source and rotation and torque from a motor, resulting in an easily readable block diagram.

A. Simulator Structure and Design

A model of an insulin pump was made by decomposing the pump into its component parts. The model presented in this paper builds on the model presented in a webinar by Mathworks [9], which introduced the basic components of the infusion pump. The model presented here introduces additional elements, such as friction, modifications to the patient model, and a parametrization of the model.



(a) Pump mechanics.



(b) Infusion path.

Fig. 1: Simscape diagram of pump simulator

1) Pump Mechanics: The pump mechanics is shown in fig. 1a. A DC motor generates a mechanical force in the form of rotation and torque. The motor is powered by a voltage supply which is controlled by a simple motor control unit. The motor is controlled in open-loop, meaning there is no feedback from any system states back to the control block. The motor-control gives a voltage reference (between 0 and 3 volts) based on the desired input doses.

The output from the motor is geared down in a gear-box, reducing the rotation speed and increasing the output torque. This rotational force is then transformed into a translational motion through a mechanical lead-screw which in turn pushes into the pump reservoir (modelled as a hydraulic cylinder), causing fluid to flow out by converting the translational force into a hydraulic pressure.

Friction within the pump mechanics (gear box and lead-screw) and along the piston and pump reservoir is modeled as a combination of a spring-damper system, to simulate the elasticity of the system caused by deformation of the piston due to increasing stresses, as well as a cylinder friction block to simulate the friction forces along the reservoir cylinder proportional to the relative velocity of the piston as well as the pressure within the cylinder.

2) Infusion Path: The infusion tube is modelled as a hydraulic pipeline with flexible walls. The infusion tube is split into 3 tube elements of equal length, in order to examine the flow as it traverses throughout the tube.

At the end of the infusion tube is the infusion site needle, which is modeled as a fixed area orifice with a significantly smaller area compared to the rest of the infusion tube. An occlusion in the infusion tube modeled as a variable area orifice sits between the tube and infusion needle and can be used to simulate an occlusion in or near the infusion site. The opening of this orifice can be changed during simulation, thus being able to simulate both complete occlusions as well as partial and gradual occlusions.

To simulate the back-pressure posed by the interstitial tissue during infusions, a simplified model of the subcutaneous tissue was made. This is modeled as a flexible hydraulic tube, where fluid can accumulate and build up pressure while expanding the area, before slowly dissipating out to the surrounding tissue via a small ”leakage”.

B. Sensors and measurements

Various sensors and measurement tools are placed around the pump system to emulate physical points of measurement. On the DC motor, both the current passing through the motor as well as the voltage over it is measured with their respective sensors. A force sensor is placed between the lead-screw and the pump reservoir in order to measure the force applied from the pump motor onto the reservoir. In the pump reservoir, the position of the plunger piston is measured in order to monitor the actual position and comparing it to the estimated system state. A pressure sensor and a flow rate sensor is attached onto the input of each element of the infusion tube, measuring the pressure and flow at different points throughout the tube. An additional flow rate sensor is placed at the end of the infusion needle, measuring the exact flow leaving the system and entering the patient.

All sensors are considered ideal, returning the exact value of the respective state and do not affect the system states in any way. The sensors does not take measurement method, technology or noise into consideration, and as such does not emulate any one specific way of measurement.

C. Simulator parameters

All the component blocks used in the model require a multitude of parameters in order to complete the mathematical model. All parameter values used in the simulation are based on real-world values and dimensions wherever possible. Some values are however difficult to generalize due to vastly different designs between different pumps or lack of detailed documentation of internal mechanisms, like the gear-ratio of the gear box or precision of the lead-screw. These types of parameters were therefore estimated via experiments, based on the other known parameters and system performance.

The pump reservoir was chosen to have a volume of $3\,\mathrm{ml}$, holding a total volume of 300U of insulin, a common size among different insulin pumps. The reservoir is assumed to be a cylinder, $2.5\,\mathrm{cm}$ in height. The lead size of the lead screw was chosen to be $0.1\,\mathrm{cm}$ per revolution, which is among the smallest and most precise lead sizes commonly available in lead screws. With this, one revolution of the screw ($0.1\,\mathrm{cm}$ translation) equates to 12U of insulin.

For the DC motor parameters, the specifications of a Faulhaber Series 0816 003 SR motor was used as an example, though any other DC or stepper motor within similar specifications will work. All physical parameters are as specified in the respective data-sheet.

The hydraulic fluid, or insulin, has some specific fluid dynamics properties. Insulin has a slightly higher mass density than water, at $1090\,\mathrm{kg\,m^{-3}}$ [10] at room temperature ($20\,^{\circ}\mathrm{C}$). The intrinsic viscosity of insulin depends on several different factors, such as pH and temperature [11]. Assuming the pump operates at $20\,^{\circ}\mathrm{C}$ and the insulin has a pH of 7.5, the intrinsic viscosity is $9\,\mathrm{cm^3\,g^{-1}}$ [11]. The kinematic viscosity is defined as $v = \frac{\mu}{\rho}$, where μ is the intrinsic viscosity and ρ the mass density of insulin. The insulin will then have a kinematic viscosity of $8.9250 \times 10^{-6}\,\mathrm{m^2\,s^{-1}}$. The kinematic viscosity increases with temperature, the insulin becoming thicker and more viscous as temperature increases.

The infusion set is assumed to made of a flexible material that will expand when the internal pressure increases and has a static pressure-diameter coefficient of $2 \times 10^{-10}\,\mathrm{m\,Pa^{-1}}$. The length and diameter of the tube is set to a length of $60\,\mathrm{cm}$ ($20\,\mathrm{cm}$ per tube element) and internal diameter of $1\,\mathrm{mm}$.

The size of the infusion site needle uses a standard size of $0.286\,\mathrm{mm}$ diameter. The occlusion site can be set to have an opening size equal to that of the infusion tube (no occlusion), a complete occlusion with no opening, or anything between.

The base pressure of the subcutaneous tissue is assumed to be equal to atmospheric pressure, though some studies have estimated the pressure to be slightly below atmosphere at $-1.3\,\mathrm{mbar}$ [12]. The tissue does however put up a back pressure to resist infusions, proportional to infusion rate. The back-pressure from the infusion site and patient simulator was parameterized such that the expanding volume is a few millimeters across while not pressurized. The volume and stiffness of the area was tuned such that a $0.3\,\mathrm{ml}$ fluid delivered at rates between $0.01\,\mathrm{ml\,min^{-1}}$ and $0.1\,\mathrm{ml\,min^{-1}}$ generated a responses within the median range found in studies on subcutaneous tissue pressure response [13], [14].

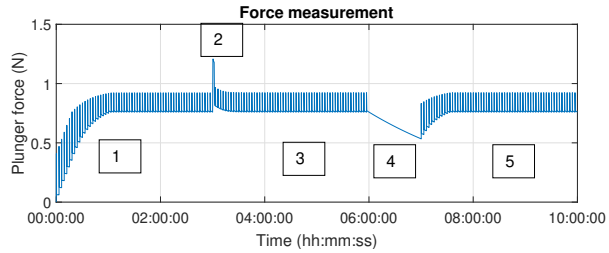
The friction coefficient was chosen to be within the ranges of the data presented in [2]. The Coulomb friction ranges from $0.5\,\mathrm{N}$ to $1.5\,\mathrm{N}$, with an additional breakaway friction force coefficient ranging from 1.0 to 1.5. The parameters of the spring-damper system was chosen in order to achieve force dynamics similar to that presented by Thornton et al. [2], with values from $5 \times 10^{-4}\,\mathrm{N\,m^{-1}}$ to $5 \times 10^{-5}\,\mathrm{N\,m^{-1}}$ for the spring, and $5 \times 10^{-4}\,\mathrm{N/(m/s)}$ to $5 \times 10^{-5}\,\mathrm{N/(m/s)}$ for the damper.

III. SIMULATION RESULTS

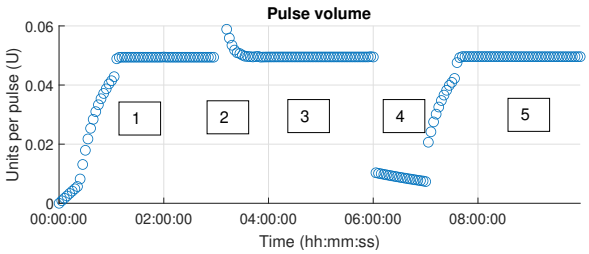
A. Normal Operation

To validate the performance of the simulator, a typical pumping sequence was simulated using the same sequence as used in other studies on physical systems [2]. The pumping sequence aims to replicate a real patients usage of an insulin pump, split up into 5 distinct parts. First, a 1U/h basal rate (0.05U per pulse, every three minutes) is given for three hours. Then a 10U mealtime bolus is given, before returning to basal delivery of 1U/h for three hours. Following this, the pump is shut off for 1 hour, before returning to a basal delivery again. The result of this simulation is shown in fig. 2.

During the first period after infusion start there is an initial run-in phase where the pumps delivery accuracy is significantly reduced. As shown in fig. 2a, the plunger force gradually increases over time for the first hour of the simulation as it slowly overcomes the friction forces of the pump reservoir. The force later stabilizes around the breakaway friction force of the cylinder friction. During this phase, the piston plunger is held back by friction and becomes slightly deformed due to the increasing forces. This leads to a reduced flow out of the pump reservoir, as shown in fig. 2b. When the plunger force is stabilized around the breakaway friction, the volume delivery is stable around the target value of 0.05U per pulse.



(a) Plunger force



(b) Pulse volume. The bolus has been omitted.

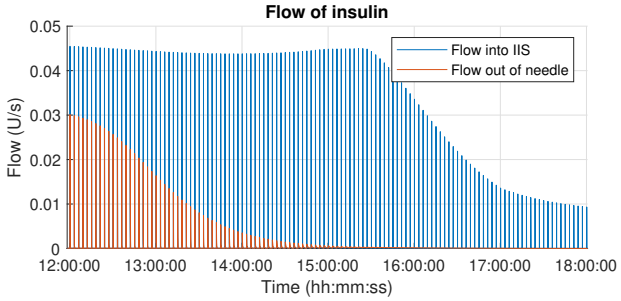
Fig. 2: Plunger force and pulse volume of simulator during a realistic pump profile. Region $\{1, 3, 5\}$ depicts basal delivery of 1U/h, region $\{2\}$ shows a 10U bolus, region $\{4\}$ shows a 1hour pump shut-off.

When the mealtime bolus is given, the force applied to the plunger increases, leading to increased pressure within the system and over-delivery of insulin for the first few basal pulses following the bolus. When the pump is shut down (region 4 in fig. 2), fluid delivery is not completely stopped. The built up tension in the pump mechanics from the deformation of the plunger due to friction pushes some insulin out of the reservoir even though the motor is not active. During the 1 hour shut-off, the pump delivers a total of 0.18U. After the shut-off, the pump returns to basal delivery after a new (but shorter) run-in phase.

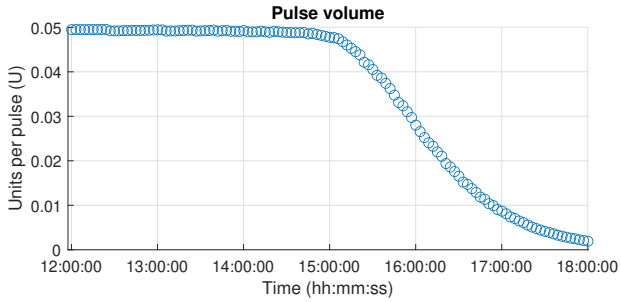
Overall, the total volume delivered over the 10 hour simulation is 18.24U, 4% less than the requested 19U. The pump dynamics, including delivery accuracy as well as run-in phases and delivery during pump shut-off, matches those observed in studies performed on physical pumps [1], [2].

B. Occlusions

A partial occlusion, where the occlusion site gets gradually smaller as time progresses from $t = 0$, was simulated using a basal delivery rate of 1.0U/h. The flow of insulin is plotted

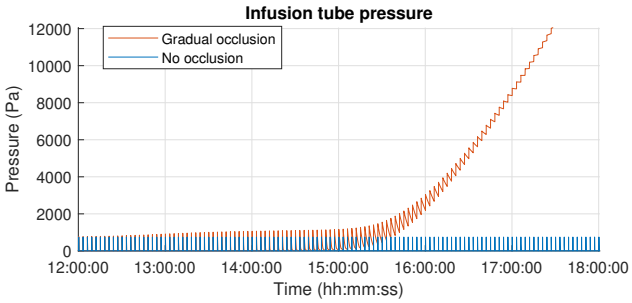


(a) Flow entering the IIS compared to flow exiting IIS during gradual occlusion.

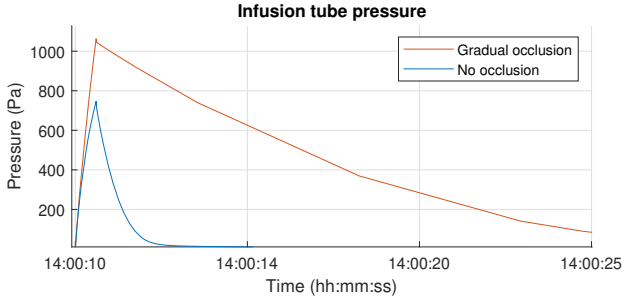


(b) Volume per pulse exiting the needle during gradual occlusion.

Fig. 3: Simulation of gradual occlusion, occlusion site becoming increasingly smaller from $t = 0$. First 12 hours have been omitted.



(a) Pressure measured at the inlet of the IIS during gradual occlusion compared to no-occlusion.



(b) Closer view on pressure response of one pulse during partial occlusion.

Fig. 4: Pressure dynamics during gradual occlusion.

in fig. 3a, where the first 12 hours of the simulation has been omitted. The plot shows significantly different flow dynamics between the insulin flowing into the IIS compared to the insulin flowing out of the needle. During normal operation (no occlusion), the restrictive area of the infusion needle reduces the flow rate of the fluid flowing into the patient. During occlusions, the occlusion site provides an additional such restriction, reducing the flow further as the occlusion becomes increasingly more narrow. The volume flowing out of the needle, as plotted in fig. 3b, is however not affected by this initial resistance. As the amplitude of the flow-pulses becomes lower, the width of the pulse increases and the area under the graph remains the same such that the volume infused remains unchanged. As the width of the pulse approaches the pulse frequency however (180s), a decrease in delivered volume is observed, happening around 15 hours into the simulation. It is at this point that the flow out of the pump (entering the IIS), which has remained stable around reference value up until this point, starts showing signs of occlusion as the flow gradually gets reduced.

Similar dynamics can be observed in the pressure within the infusion tube. The pressure within the IIS during the gradual occlusion is plotted in fig. 4a, where the pressure can be observed to increase exponentially as the volume delivery is decreased (after 15 hours). Before this point, the amplitude of the pressure peaks are only slightly elevated compared to the pre-occlusion values. However, the width of the pulses are gradually increasing, similar to that of the flow out of the IIS. Fig. 4b shows a close-up view on one pressure pulse during the occlusion simulation, 1 hour before the volume delivery is reduced. It can be observed that the pressure pulses follows a exponential decaying function as the pressure decreases, on the form of

$$p(t) = p_{peak} e^{-\frac{t}{\tau}} \tag{1}$$

where p_{peak} is the maximum pressure observed and τ is some time-constant determining the rate of decay of the function, where $p(\tau) \approx 0.37 p_{peak}$. While the time-constant measured during a pre-occlusion pulse is 0.7 seconds, the τ measured at the pulse in fig. 4b is 7 seconds, a 10 times decrease in rate of decay more than one hour before the volume delivery is affected.

Signs of occlusions may also be observed in other system states, such as the piston force (not plotted). The force increases exponentially as the occlusion becomes greater, but does not show much sign until after volume delivery is reduced. Similar trends are observed in the step-length of the plunger (not plotted), where the length of each motor step becomes smaller and smaller as the force increases.

IV. DISCUSSION

A. Simulator dynamics

The simulator is able to achieve realistic results with dynamics similar to real life insulin pumps based on the data available. The simulator shows a realistic run-in phase with significantly reduced delivery accuracy, as found in several studies [1], [2], as well as realistic back-pressure induced

by boluses as found in real-world studies [13], [14]. The simulator also models the over-delivery of insulin which can happen even when the pump is shut off [2].

These dynamics can prove useful when combined with more complex simulators used in the modelling of the glucose-insulin metabolism, typically done in artificial pancreas research, as short-term inaccuracies in insulin delivery may have significant impacts on glucose levels.

B. Occlusion detection

The simulations show promising results when it comes to occlusion detection. Measuring the flow out of the pump may however not give a representative view of the flow actually leaving the needle and entering the patient, due to the different dynamics along the tube. Due to the elastic properties of the IIS, which can expand and deform slightly under pressure, as well as the compressibility of the flow media, there may be differences in observed flow along the tube especially during occlusions. Furthermore, the flow measured at the inlet of the IIS did not show any significant changes until after volume delivery was reduced. To get the most accurate flow measurements, the sensor must be placed in or after the infusion needle, which is unfeasible in practice.

Features in the pressure within the IIS may give a better indication on occlusions. By not only looking at the maximum amplitude of the pressure, but also looking at the rate of change in pressure after a bolus, it may be possible to predict occlusions before it actually affects the volume delivery. The pressure can for instance be relatively easily measured via a pressure transducer placed within the pump reservoir or someplace along the tube close to the pump.

C. Limitations of the simulator model

The greatest limitation to the accuracy of the simulator is the lack of available data from measurements on physical insulin pumps. While the overall accuracy over time as well as dynamics of larger boluses are well documented in several studies, no data could be found on the subcutaneous tissue response to small boluses the size of one typical basal delivery pulse. Thus, there may be some uncertainties to the simulators accuracy for small volumes as it has been tuned based on data from larger volume experiments.

All measurements from the simulations are from idealized sensors and there are no other disturbances that may affect the values other than the actual system states. In reality, the sensors would likely be susceptible to both measurement noise as well as other environmental disturbances, leading to less accurate measurements. Therefore, the measurements achieved in these simulations may be unrealistically clean, i.e. occlusion detection may be significantly more challenging using measurements from sensors on a physical system.

V. CONCLUSIONS

A model of an insulin infusion pump was made, available as open-source [8], able to simulate both normal infusion as well as fault conditions. The simulator can be used to improve currently available insulin-glucose simulation models, and can also be used to improve the safety and reliability of insulin pumps by providing a tool for the development of novel methods for infusion failure detection.

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