A theoretical model for catheter outflow concentrations

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1 Background

Patients on the Intensive Care Unit almost always require infusion therapy. The continuous and stable infusion of parenteral drugs (infused medication) is necessary to stabilize and treat the patient. Infusion pumps are used to deliver a continuous solutions of drugs. However, infusion technology was associated with one of the highest rates of medical errors of any medical technology [1]. Many of these errors were technical in origin [2].

There are a wide variety of different components to facilitate infusion therapy. These component include: syringes, infusion lines and catheters. Many of the components have different physical characteristics, which may result in different flow rate characteristics. For example, many components are compliant which causes a delay in flow rate onset. In that case, the administration of the drug to the patient is delayed as well. The slow onset of some drugs are known to have clinical consequences. Therefore, the variance in disposables poses a risk to the patient.

Another technical risk of infusion is multi-infusion. In clinical practice it is often required to combine multiple infusion pumps on one central line and catheter. This is necessary because the intravenous (IV) access site are limited. With each catheter insertion and puncture, there is an increased probability of infections. For this reason, clinicians limit the IV access sites to a minimum, especially in vulnerable patients in the ICU. However, there may be mutual influence between the parallel pumps that were combined on a single central line. Differences in pressure, combined with the physical characteristics of disposables may influence the expected catheter egress [3, 4].

To predict and describe infused drug administration concentration, the UMC will develop a simulation model. The drug concentration is proportional to the flow rate. Therefore, the objective of this report is to describe the basic theoretical mechanisms of a multi-infusion model that evaluates catheter outflow.

2 Methods

A multi-infusion system can be seen as a network of compliant and resistive tubes and flow sources. We considered the flows to be laminar, therefore, the Hagen-Poisseuille law can be used to describe it. The networks can be modelled using standard network theory and the Laplace-transformations. There are situations where this method is too limited, we will discuss these situations in the discussion section. Additionally, we will describe some of our prospective methods to go beyond these limitations. By doing so, we will outline our plan to reach our eventual goal to simulate an actual medication schedule for REG1 D3.4. This basic framework will, however, be used as the basic foundation of the multi-infusion simulation model.

2.1 Basics

Displacement driven system

We developed a basic concept to simulate a multi-infusion system. First a flow rate is generated by a force that is applied to the plunger. Figure 1 shows this mechanism.

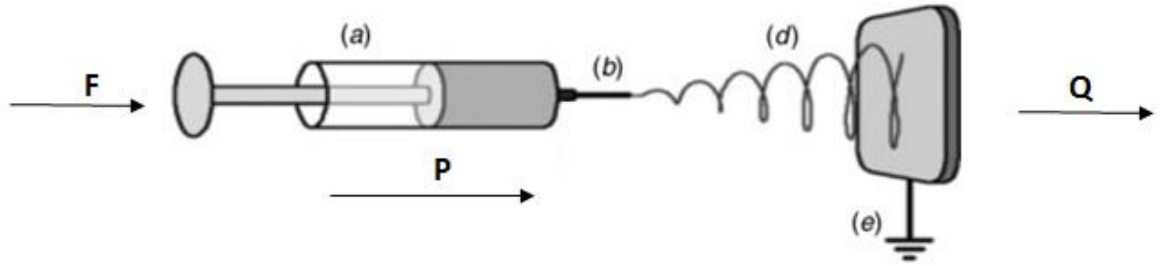

Figure 1. Syringe. A force (F) is applied to the plunger, this causes a pressure (P), which in turn causes a flow rate (Q).

Compliance

From experience we know that most components used in a multi-infusion system are significantly compliant. When pressure is applied to a tube, stress causes deformation. The following relations show this concept of Figure 1.

Pressure

$$P = F/A \qquad 1$$

Where F is force (N) and A is area (m^2)

Compliance is defined as:

$$C = \frac{\Delta V}{\Delta P} \qquad 2$$

Where ΔV is the volume difference and ΔP is the pressure difference.

It can be seen that applying a force causes a volume ΔV to be temporarily stored when a component is compliant. This in turn will cause a temporary difference in flow rate.

For most materials, the compliance can be simulated as a capacitance. The following formula shows the impedance of a capacitance in the s-domain:

$$Z(s) = \frac{1}{sC} \qquad 3$$

Where C is dependent on the material properties (e.g. Young's modulus).

Flow sources and resistance

When a flow moves through a tube, it experiences resistance. This resistance is strongly dependent on the radius of the tube and can be described according to Poisseuille. The relation between the pressure difference ΔP (N/m^2) and volumetric flow rate Q (ml/s) is:

$$Q = -\int_0^{D/2} 2\pi v_z \, r \, dr = \frac{\pi D^4}{128\mu}\frac{\Delta P}{L} \qquad 4$$

$$\Delta P = \frac{128\mu L Q}{\pi D^4} \qquad 5$$

Where v is the flow velocity profile along the radius r (the cross-section of the tube). D is the diameter and L is the length of the tube. μ is the viscosity of the fluid.

From equation 5 it can be seen that the flow decreases with a decreasing diameter D and an increasing length L. We can generalize the resistance in the s-domain as R(s). The magnitude of this R(s) is thus proportional to L/D^4.

2.3 Validation

Validation was performed using basic laboratory observations.

An experiment was performed to validate our model outflow flow rate (Figure 5). Two pumps (pump 1 and pump 2) were combined using a multiple-in, single-out manifold were used. The flow rate was set to 5 ml/h. After steady state was acquired the flow rate of pump 1 was increased to 15 ml/h. Subsequently, after the steady state was again achieved, the flow rate of pump 1 was decreased to 6 5 ml/h. The output was measured using Coriolos M12 flow meters on the central line, was well as the parallel lines.

The standard deviation was calculate from the simulated and measured values.

An average absolute deviation was defined as follows:

$$Average\ Deviation = Average\left[100\%\frac{Measured - Simulated}{Simulated}\right] \qquad 6$$

Where measured and simulated are the measured and simulated flow rates in ml/h.

2.2 Laplace network system

We used circuit theory to acquire the expressions for any number of pumps. In our multi-infusion network, capacitances, resistances and flow sources are used to simulate the outflow of a multi-infusion setup. We found the expressions using Kirchhoff's law and superposition. Figure 2 shows the fundamental network.

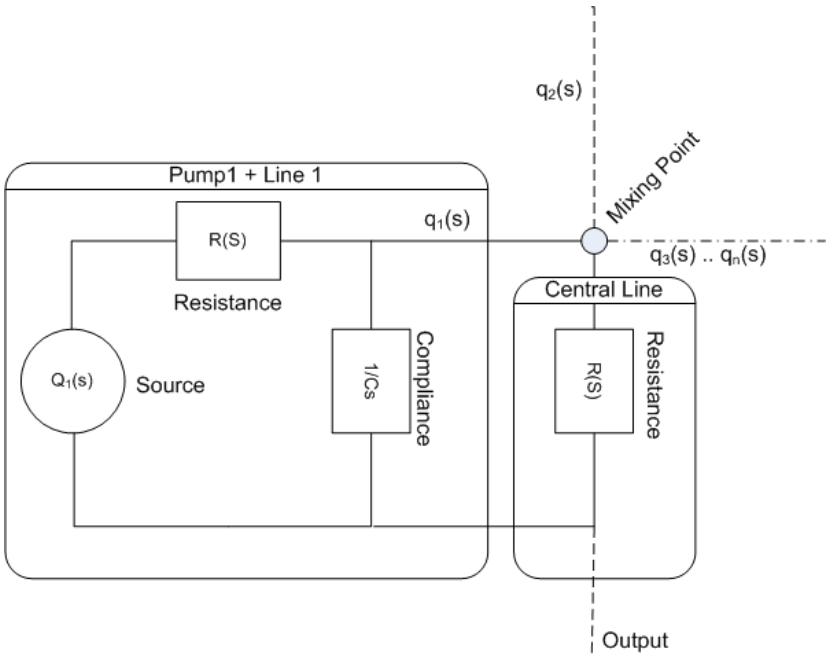

Figure 2. Laplace network. Q_1, Q_2 .. Q_n are sources (pumps). q_n is the flow rate output of $pump_n$ (before the mixing point). q_0 is the cumulative output flow rate.

2 Results (REG1 D3.2, D3.3)

Using the methods described, a system of 3 pumps was simulated (Figure 3). The initial flow rates were 2 and 1 for pumps 2 and 3, respectively. At time t=0, pump 1 was started, showing a typical start-up curve. At t=0.6, pump 1 is set to 1. It can be seen that the flow rates of the parallel pumps 2 and 3 react to the pressure difference caused by the flow rate changes of pump 1.

Following the Laplace network system (Figure 2) the flow from pump 1 (q1) can be described as:

$$q1 = \frac{1}{r1}\left(\frac{Q3}{\frac{1}{r0}+\frac{c1s}{1+c1r1}+\frac{c2s}{1+c2r2s}+c3s\left(1+\frac{r3}{r0}+\frac{c1r3s}{1+c1r1s}+\frac{c2r3s}{1+c2r2s}\right)}-\frac{Q3}{(1+c1r1s)\left(\frac{1}{r0}+\frac{c1s}{1+c1r1}+\frac{c2s}{1+c2r2s}+c3s\left(1+\frac{r3}{r0}+\frac{c1r3s}{1+c1r1s}+\frac{c2r3s}{1+c2r2s}\right)\right)}\right)-\frac{1}{r2}\left(\frac{Q1}{\frac{1}{r0}+\frac{c2s}{1+c2r2s}+\frac{c3s}{1+c3r3s}+c1s\left(1+\frac{r1}{r0}+\frac{c2r1s}{1+c2r2s}+\frac{c3r1s}{1+c3r3s}\right)}-\frac{ip1}{(1+c2r2s)\left(\frac{1}{r0}+\frac{c2s}{1+c2r2s}+\frac{c3s}{1+c3r3s}+c1s\left(1+\frac{r1}{r0}+\frac{c2r1s}{1+c2r2s}+\frac{c3r1s}{1+c3r3s}\right)\right)}\right)+\frac{-\frac{ip1}{\frac{1}{r0}+\frac{c2s}{1+c2r2s}+\frac{c3s}{1+c3r3s}+c1s\left(1+\frac{r1}{r0}+\frac{c2r1s}{1+c2r2s}+\frac{c3r1s}{1+c3r3s}\right)}+\frac{ip1\left(1+\frac{r1}{r0}+\frac{c2r1s}{1+c2r2s}+\frac{c3r1s}{1+c3r3s}\right)}{\frac{1}{r0}+\frac{c2s}{1+c2r2s}+\frac{c3s}{1+c3r3s}+c1s\left(1+\frac{r1}{r0}+\frac{c2r1s}{1+c2r2s}+\frac{c3r1s}{1+c3r3s}\right)}}{r1} \quad (7)$$

The formulas of q_2, q_3 can be acquired in a similar fashion. q_0 is the total (i.e. cumulative) outflow.

Figure 4 shows the effect of an increased compliance (C_2) in the outflow of pump 2. From equation 2 it is expected that a larger volume can be collected by the compliance. The units used are arbitrary. However, with laboratory experiments we expect to acquire realistic physical parameters in order to describe the R's en C's with realistic values.

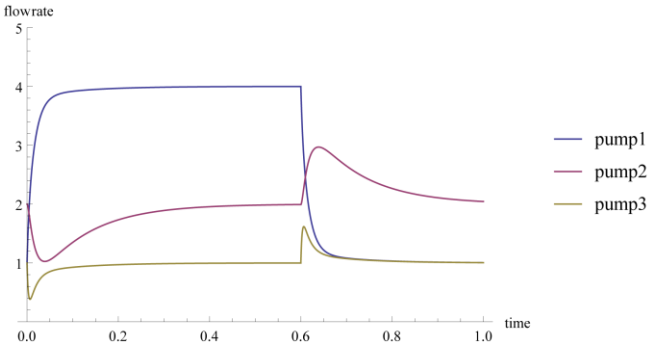

Figure 3. Flow rate plot of pumps 1 – 3.

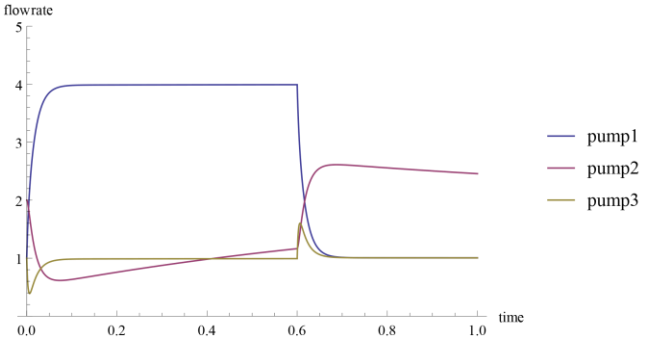

Figure 4. Flow rate plot of pumps 1-3 with large C_2

2.1 Validation

Figure 5 shows the validated and measured results.

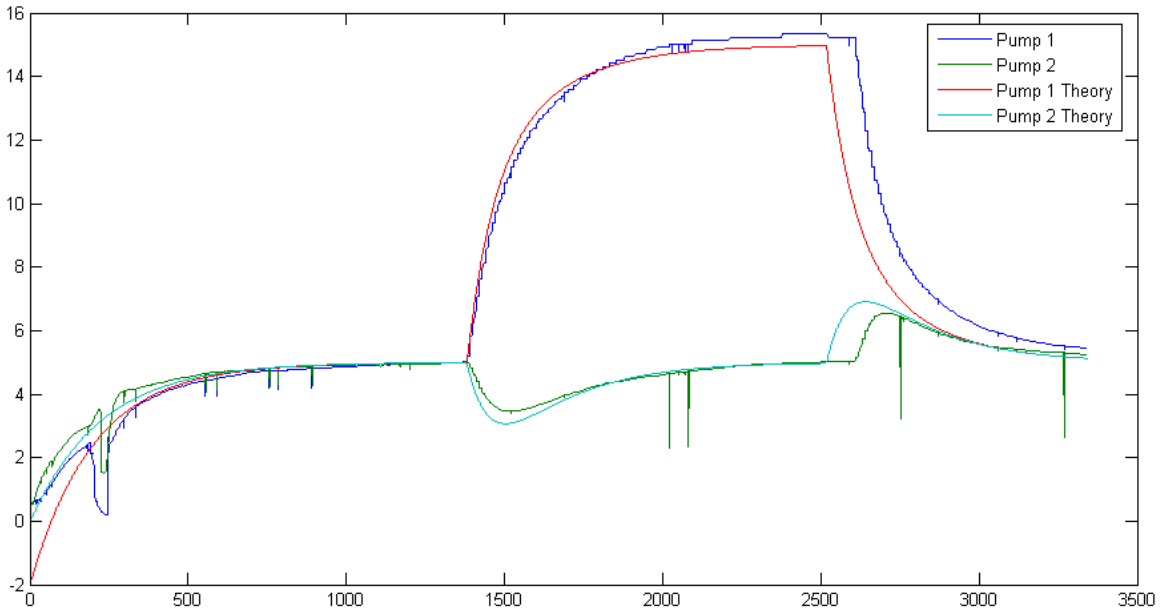

Figure 5. Theoretical (pump1 and 2 theory) and measured (pump 1 and 2) output.

The standard deviation of pump 1 is:	0.94 ml/h
The average deviation of pump 1 is:	3.96%
The standard deviation of pump 2 is:	0.36 ml/h
The average deviation of pump 2 is:	4.28%

3 Discussion

The results agree with our basic laboratory observations. However, using only the Laplace-transform and circuit theory has some limitations.

The most important limitation is that the flow of individual solutions originating from different pumps cannot be traced. For example, a solution of 0.1 mg/ml Dobutamine originating from pump 1 is administered through a line. When another pump is increased, the exact effect on the Dobutamine concentrations cannot be simulated. Only the effect on the flow rate of the Dobutamine and other solutions as a whole can be predicted, yet the increase of one pump has a temporary effect on the Dobutamine mass flow rate. This is because the mixture still present in the tube is administered with a new cumulative flow rate. Additionally, the model is unable to simulate different mixing point. This means that the model assumes that all lines are connected at the same location to the central line, while in reality this may not always be the case.

Outlook

The limitation of the model can be solved by applying another transformation on top of the Laplace model. This transform is called the z-transform. Z-transform enables us to convert a multi-infusion network into arrays. These arrays contain information about the fluid concentrations for every point in space and time. Using this method we are able to exactly simulate the concentration outflow of the different solutions originating from the pumps. In addition, the method allows us to simulate cases where the parallel pumps are not connected to the same mixing point junction. Affords to further validate the model will continue.

Reference List

1. Husch M, Sullivan C, Rooney D et al. Insights from the sharp end of intravenous medication errors: implications for infusion pump technology. Qual Saf Health Care 2005;14(2):80-86.
2. Kohn L, Corrigan J, Donaldson M. To Err Is Human: Building a Safer Health System. The National Academies Press; 2000.
3. Snijder RA, Egberts ACG, Lucas P, Lemmers PMA, Timmerman AMDE. Dosing errors and potential clinical impact in preterm infants due to flow rate variability in multi-infusion syringe pump setups: an in vitro inline absorption spectrophotometry study. UMC (unpublished) 2014.
4. Timmerman AM, Riphagen B, Klaessens JH, Verdaasdonk RM. Confirmation of uncontrolled flow dynamics in clinical simulated multi-infusion setups using absorption spectral photometry. 2010;75560U.