

The Delay Is in the Syringe, Not the Line: Start-Up Lag and Flow Disturbance in Low-Rate Syringe Pump Infusion

Dr. A.K. Sharma

Professor, Computer Science & Engineering, School of Engineering & Technology, Career Point University, Kota, Rajasthan, India.

Email: drarvindkumarsharma@gmail.com, ak.sharma@cpur.edu.in

ABSTRACT

A syringe pump commands a plunger velocity, not a delivered flow. Before fluid reaches the patient the plunger seal must break free and the mechanical compliance of syringe and tubing must be pressurised. At the rates used for neonatal and critical-care vasoactive infusions these fixed volumes take a clinically significant time to displace. We built a lumped mechanical model with syringe and tubing compliance, catheter resistance and a plunger breakaway pressure, using representative values for four syringe sizes and four vascular access devices. We computed the time to reach 95 per cent of commanded flow across rates from 0.1 to 10 mL/h, the cumulative dose deficit over the first hour, and the volume displaced by a vertical movement of the pump. With a 50 mL syringe on a 28 G neonatal long line, start-up delay was 49.3 minutes at 0.1 mL/h, 11.6 minutes at 0.5 mL/h and 2.7 minutes at 10 mL/h. Plunger stiction contributed 95 per cent of the delay at the lowest rate against 17 per cent at the highest. Syringe size was the dominant controllable factor: at 0.5 mL/h a 5 mL syringe reached target in 2.0 minutes against 11.6 for a 50 mL. Catheter choice was not: a 30-fold range of resistance changed start-up by 2.1 minutes. Cumulative deficit at one hour was 79.5 per cent of the intended dose at 0.1 mL/h. Raising the pump 40 cm displaced 49 microlitres, equivalent to 29 minutes of infusion at 0.1 mL/h. Start-up lag at low rates is dominated by the syringe rather than the vascular access device. Selecting the smallest practicable syringe and fixing pump height address the two largest effects.

Keywords: biomedical engineering devices; syringe pump; infusion accuracy; medical device performance; neonatal intensive care; applied technology.

1. INTRODUCTION

Continuous infusion of vasoactive drugs, insulin and sedatives in neonatal and critical care is delivered by syringe pumps at rates that are frequently below 1 mL/h and sometimes below 0.2 mL/h [1,2,26,27]. At those rates the pump is operating near the bottom of its specified range, and the assumption that a commanded rate corresponds to a delivered rate becomes difficult to sustain.

The reason is mechanical rather than electronic. A syringe pump controls the linear velocity of a plunger with high precision. What reaches the patient is the fluid displaced past the syringe outlet, and between those two quantities sit the static friction of the plunger seal in the barrel and the elastic compliance of the barrel, the seal and the extension tubing [3-5].

Both effects absorb a fixed volume of fluid. The plunger does not move until the driving force exceeds its breakaway friction, and flow does not reach the commanded value until the compliant elements have been pressurised to the value required to drive that flow through the

catheter. At 10 mL/h those volumes are displaced within seconds. At 0.1 mL/h the same volumes take the better part of an hour.

The same compliance produces a second effect during steady operation. Any change in the pressure at the syringe outlet, including one caused by simply raising or lowering the pump relative to the patient, discharges or recharges the compliant volume and delivers an unintended bolus or an unintended interruption [6,7].

These phenomena are documented in the clinical engineering literature [18,19,25] and are reflected in standards for infusion device performance [8,9], but they are not usually expressed in a form that lets a clinician or a device selection committee compare the available choices. We quantify them and identify which choices matter.

1.1 Contributions

We give a lumped mechanical model with an explicit stiction term; start-up delay across flow rates, syringe sizes and access devices; the cumulative dose deficit over the first hour of an infusion; the volume displaced by vertical pump movement and the time to recover from it; and a practical selection guide identifying which factors are worth controlling.

2. MODEL

2.1 Mechanical Elements

The delivery path is modelled as a compliant volume in series with a resistive catheter [14,18]. Compliance C combines the syringe barrel and plunger seal with the extension set, and resistance R relates driving pressure to steady flow:

$$P_{steady} = Q \cdot R \quad (1)$$

Reaching that pressure requires displacing a volume into the compliant elements:

$$V_{charge} = C \cdot P_{steady} = C \cdot Q \cdot R \quad (2)$$

Delivered flow approaches the commanded value with first-order dynamics of time constant

$$\tau = R \cdot C \quad (3)$$

which is notable for being independent of flow rate: the charging volume grows in proportion to rate, so the time to displace it does not change. That term alone would make start-up delay rate-independent, which is not what is observed.

The rate dependence comes from the second element. The plunger does not begin to move until the pressure behind it exceeds a breakaway value P_{stick} , and reaching that pressure requires displacing

$$V_{stick} = C \cdot P_{stick} \quad (4)$$

which is a fixed volume independent of rate. The time to displace it is V_{stick} / Q , and that is inversely proportional to rate. Total start-up delay to a fraction of commanded flow is therefore

$$t_{95} = \frac{V_{stick}}{Q} - \tau \cdot \ln(0.05) \quad (5)$$

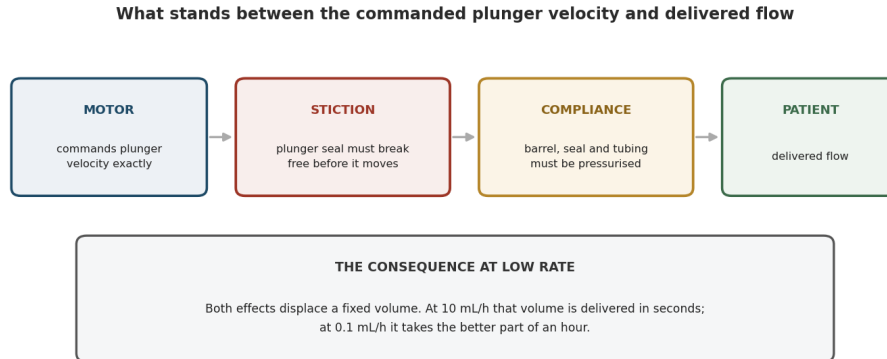


Fig.1: The mechanical elements between commanded plunger velocity and delivered flow.

2.2 Parameter Values

Compliance and breakaway pressure were assigned by syringe size, both rising with barrel diameter: a larger barrel has more elastic wall and a larger seal circumference, and requires a higher pressure to overcome seal friction. Extension tubing contributes a further 0.32 mL per bar-equivalent. Catheter resistances span a 30-fold range from a wide-bore peripheral cannula to a fine neonatal long line.

Values are given in Tables 1 and 2. They are representative of commonly used disposables and are chosen to reproduce the magnitude of delays reported in the device literature; they are not measurements of a specific product, and a service evaluating its own consumables should substitute measured values into the accompanying script, implemented in Python using NumPy, SciPy and Matplotlib [28-30].

Table 1: Model parameters.

Syringe	Total compliance (mL/mmHg)	Breakaway pressure (mmHg)	Charge volume at 0.5 mL/h on a 28 G neonatal long line (mL)
5 mL	5.80e-4	18	0.0021
10 mL	7.30e-4	24	0.0027
20 mL	1.00e-3	33	0.0037
50 mL	1.67e-3	47	0.0062

Table 2: Vascular access device resistance.

Device	Resistance (mmHg per mL/h)	Steady pressure at 0.5 mL/h (mmHg)
24 G peripheral cannula	0.90	0.45
28 G neonatal long line	7.40	3.70
2 Fr umbilical catheter	3.10	1.55
20 G peripheral cannula	0.25	0.13

3. RESULTS

3.1 Start-Up Delay across Flow Rates

Table 3 and Figure 2 give the time to reach 95 per cent of commanded flow with a 50 mL syringe on a 28 G neonatal long line. It was 49.3 minutes at 0.1 mL/h, 11.6 minutes at 0.5 mL/h, 6.9 minutes at 1 mL/h and 2.7 minutes at 10 mL/h.

The decomposition explains the shape. The compliance-charging term was 2.22 minutes at every rate, as Equation 3 requires. The stiction term fell from 47.1 minutes at 0.1 mL/h to 0.5 minutes at 10 mL/h, and accounted for 95 per cent of the total at the lowest rate against 17 per cent at the highest.

This matters for how the problem is approached. If the delay were dominated by compliance charging it would be reduced by lowering the resistance of the line. Because it is dominated by stiction at the rates of clinical concern, it is reduced by choosing a syringe with a lower breakaway force and a smaller compliance, and not by changing the line at all.

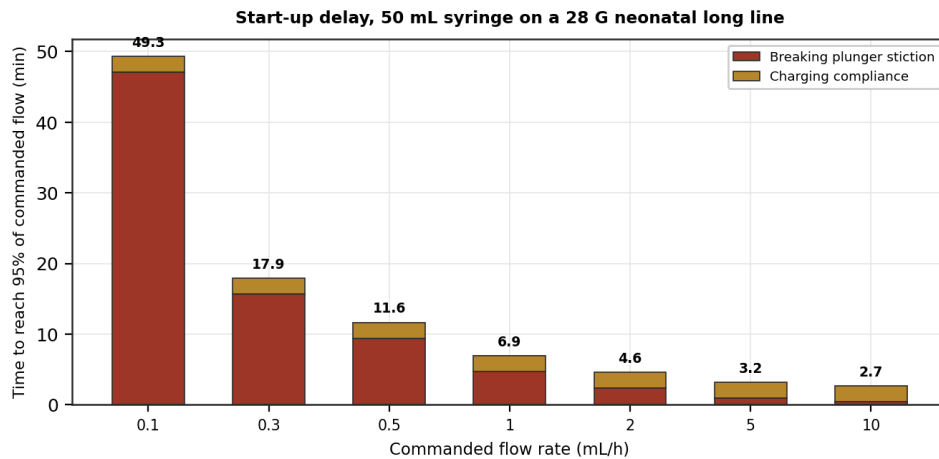


Fig.2: Start-up delay by flow rate, decomposed into stiction and compliance charging.

Table 3: Start-up delay by commanded flow rate.

Rate (mL/h)	Charge volume (mL)	Steady pressure (mmHg)	Stiction delay (min)	Compliance delay (min)	Total (min)
0.1	0.0012	0.7	47.1	2.22	49.3
0.3	0.0037	2.2	15.7	2.22	17.9
0.5	0.0062	3.7	9.4	2.22	11.6
1.0	0.0124	7.4	4.7	2.22	6.9
2.0	0.0247	14.8	2.4	2.22	4.6
5.0	0.0618	37.0	0.9	2.22	3.2
10.0	0.1236	74.0	0.5	2.22	2.7

50 mL syringe on a 28 G neonatal long line.

3.2 Syringe Size Is the Controllable Factor

Table 4 and Figure 3 vary syringe size at 0.5 mL/h. Start-up delay was 2.0 minutes with a 5 mL syringe, 3.1 with a 10 mL, 5.3 with a 20 mL and 11.6 with a 50 mL — a 5.8-fold range.

Both mechanisms scale with barrel size and reinforce each other. Compliance rises with the elastic area of the barrel wall and the seal, and breakaway force rises with seal circumference, so the charge volume and the stiction volume both grow with the syringe.

The clinical tension is that a larger syringe needs changing less often, and syringe changeover is itself a well-recognised source of infusion interruption and haemodynamic disturbance. Our results do not resolve that trade, but they price one side of it: choosing a 50 mL syringe over a 5 mL to avoid changeovers costs 9.6 additional minutes of delayed onset at every start and every rate change.

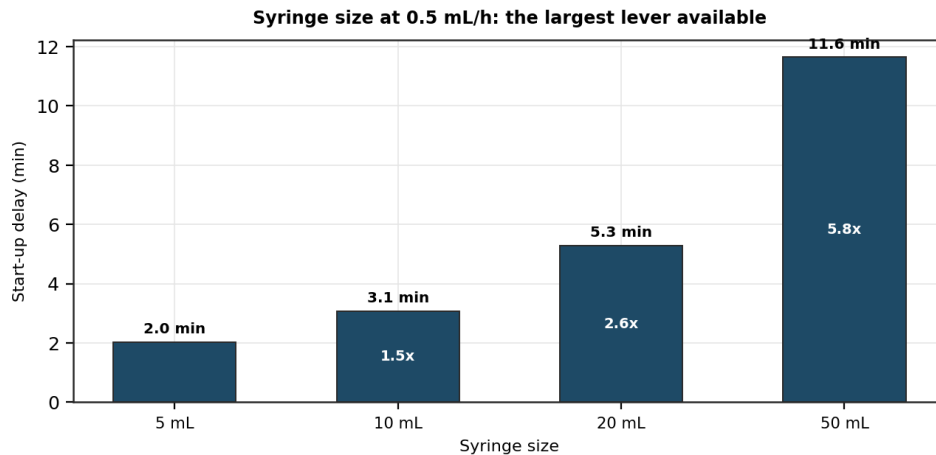


Fig.3: Start-up delay by syringe size at 0.5 mL/h.

Table 4: Effect of syringe size at 0.5 mL/h.

Syringe	Compliance (mL/mmHg)	Charge volume (mL)	Stiction delay (min)	Total delay (min)
5 mL	5.80e-4	0.0021	1.3	2.0
10 mL	7.30e-4	0.0027	2.1	3.1
20 mL	1.00e-3	0.0037	4.0	5.3
50 mL	1.67e-3	0.0062	9.4	11.6

3.3 The Access Device Is Not the Problem

Table 5 and Figure 4 vary the vascular access device across a 30-fold range of resistance, from 0.25 to 7.40 mmHg per mL/h.

Start-up delay moved only from 9.5 to 11.6 minutes, a spread of 2.1 minutes, because resistance enters only through the compliance-charging term which contributes a small and rate-independent part of the total.

We report this as a negative result because the opposite belief is common. A slow-starting infusion on a fine neonatal long line invites the inference that the line is restricting flow, and changing to a wider device is a natural response. On this model it would achieve almost nothing, while the syringe sitting in the pump accounts for most of the delay and is easier to change.

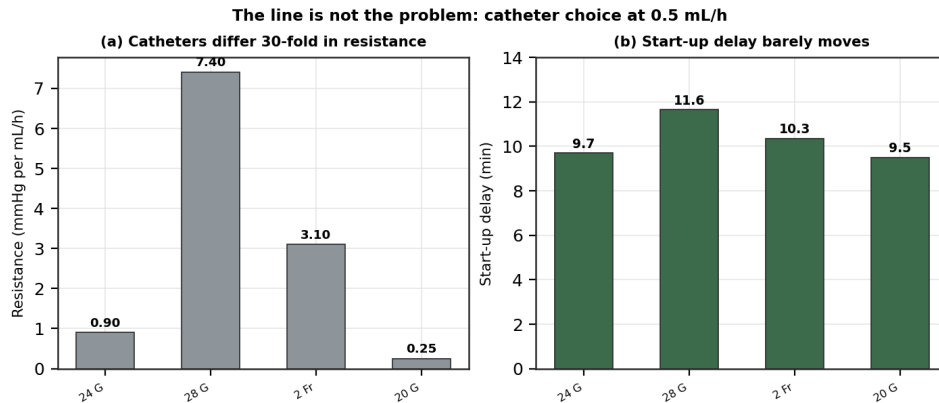


Fig.4: Catheter resistance against its effect on start-up delay.

Access device resistance does matter for other things — occlusion alarm thresholds, the pressure reached during a flush, and the volume of the post-occlusion bolus — but not for start-up lag at these rates.

Table 5: Effect of vascular access device at 0.5 mL/h.

Device	Resistance (mmHg per mL/h)	Charge volume (mL)	Start-up delay (min)
24 G peripheral cannula	0.90	0.0008	9.7
28 G neonatal long line	7.40	0.0062	11.6
2 Fr umbilical catheter	3.10	0.0026	10.3
20 G peripheral cannula	0.25	0.0002	9.5

3.4 The First Hour of an Infusion

Figure 5 gives delivered flow and cumulative deficit over the first 90 minutes. At 0.1 mL/h the cumulative deficit at one hour was 0.0795 mL, or 79.5 per cent of the intended dose, equivalent to 48 minutes of infusion never delivered.

At 0.5 mL/h the deficit was 16.7 per cent and at 2.0 mL/h it was 4.9 per cent.

Table 6 places the delay against the elimination half-lives of drugs given by this route. At 0.5 mL/h the 12-minute delay with a 50 mL syringe corresponds to 5.8 half-lives of a short-acting catecholamine and 1.9 half-lives of intravenous insulin, but only 0.1 of a half-life of morphine.

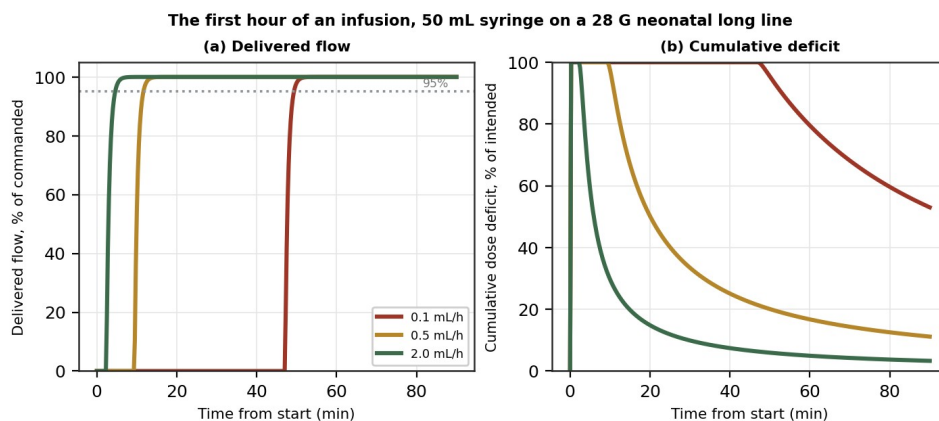


Fig.5: Delivered flow and cumulative dose deficit over the first 90 minutes.

The relevance of the delay therefore depends entirely on the agent [12,17]. For a drug whose effect is established over hours, an eleven-minute lag is immaterial. For a catecholamine titrated against blood pressure minute by minute, it means the first several titration steps are made against a delivery system that has not yet reached the previous setting, which is a recipe for over-titration followed by an overshoot when the line finally charges [24].

Table 6: Start-up delay in relation to drug half-life.

Agent	Elimination half-life (min)	Delay in half-lives at 0.5 mL/h	Clinical relevance of the lag
Adrenaline	2.0	5.8	High
Dopamine	2.0	5.8	High
Morphine	120.0	0.1	Low
Insulin	6.0	1.9	Moderate
Vecuronium	60.0	0.2	Low

3.5 Moving the Pump

Table 7 and Figure 6 quantify the effect of vertical movement. Raising a 50 mL syringe pump 40 cm relative to the patient adds 29.4 mmHg of hydrostatic pressure at the syringe outlet, displacing 49 microlitres into the patient as an unintended bolus.

At 0.1 mL/h that volume represents 29 minutes of infusion delivered at once. Lowering the pump by the same distance withdraws the same volume into the compliant elements, so the patient receives nothing for 29 minutes while it recharges.

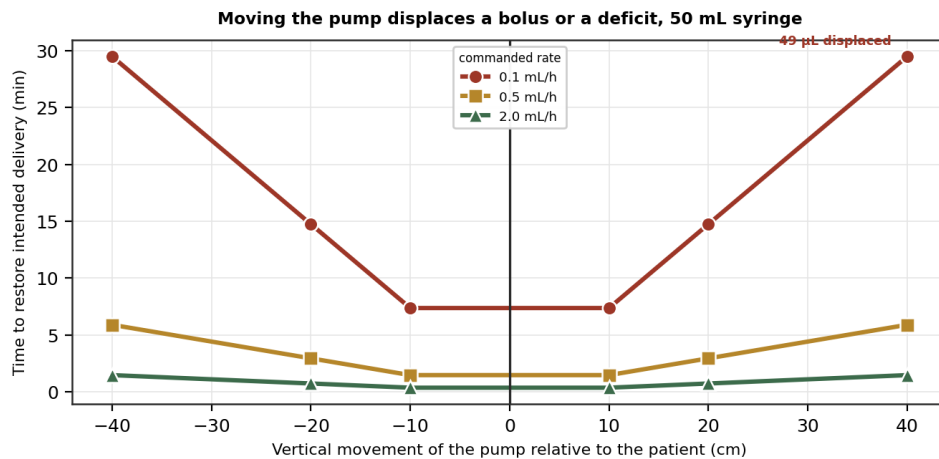


Fig.6: Time to restore intended delivery after a vertical movement of the pump.

At 2.0 mL/h the same movement corresponds to 1.5 minutes, which is unlikely to be noticed. The disturbance is a fixed volume, so its clinical significance scales inversely with rate exactly as the start-up delay does.

This is a routine event. Pumps are raised and lowered when a cot is adjusted, when a patient is transferred between trolley and bed, and when a pole is repositioned, and the movement is not usually regarded as an intervention on the infusion. On these figures, at the lowest rates it is one.

Table 7: Volume displaced by vertical movement of a 50 mL syringe pump.

Height change (cm)	Pressure change (mmHg)	Volume displaced (μL)	Minutes at 0.1 mL/h	Minutes at 0.5 mL/h	Minutes at 2 mL/h
-40	-29.4	-49.2	29.5	5.9	1.5
-20	-14.7	-24.6	14.7	2.9	0.7
-10	-7.4	-12.3	7.4	1.5	0.4
10	7.4	12.3	7.4	1.5	0.4
20	14.7	24.6	14.7	2.9	0.7
40	29.4	49.2	29.5	5.9	1.5

4. DISCUSSION

4.1 Principal Findings

Four findings follow. Start-up delay at 0.1 mL/h was 49 minutes with a 50 mL syringe, of which 95 per cent was plunger stiction rather than compliance charging. Syringe size changed that delay 5.8-fold at 0.5 mL/h while a 30-fold change in catheter resistance changed it by 2.1 minutes. Cumulative dose deficit at one hour reached 80 per cent of intended at the lowest rate. And a 40 cm vertical movement displaced 49 microlitres, 29 minutes of infusion at that rate.

The organising point is that all four effects are fixed volumes divided by flow rate. Nothing about the pump degrades at low rates; the same millilitre-scale volumes simply take proportionally longer to move, and below about 1 mL/h that duration becomes comparable to the timescale on which the drugs are titrated.

4.2 Relation to Existing Work

Start-up delay and flow irregularity in syringe pumps at low rates are documented in the biomedical engineering and anaesthesia literature, with bench studies reporting delays of tens of minutes at rates below 1 mL/h and quantifying the bolus produced by height changes and by syringe exchange [3-7,10,11]. Related in vitro and modelling studies have examined the effects of carrier flow, dead volume and manifold design in multi-infusion systems [13-16,20-22], and flow-controlled pump designs have been proposed to address low-rate performance directly [23]. Standards for infusion pump performance specify test conditions and trumpet-curve reporting that capture short-term flow variability [8,9].

Our contribution is the decomposition. By separating the stiction term from the compliance term we can identify which component dominates at which rate and therefore which design or selection decision acts on it. The finding that access device choice has almost no effect follows directly from that decomposition and is, we think, worth stating explicitly because the intuition runs the other way.

4.3 Practical Guidance

Figure 7 summarises the guidance. Two points deserve comment.

Select the smallest syringe the infusion duration permits. This acts on both mechanisms simultaneously and is the only choice in the list that produces a several-fold change. Where a larger syringe is chosen to reduce changeover frequency, the decision should be made knowing that it costs additional minutes of delayed onset at every start and every rate change, not only at the first connection.

Fix the height of the pump relative to the patient and treat any change as an intervention. A vertical movement is a bolus or an interruption whose size the staff member making it cannot

see. Where pumps must be moved, doing so at the moment of a planned reassessment rather than during a period of haemodynamic instability costs nothing and removes an unexplained disturbance from the record.

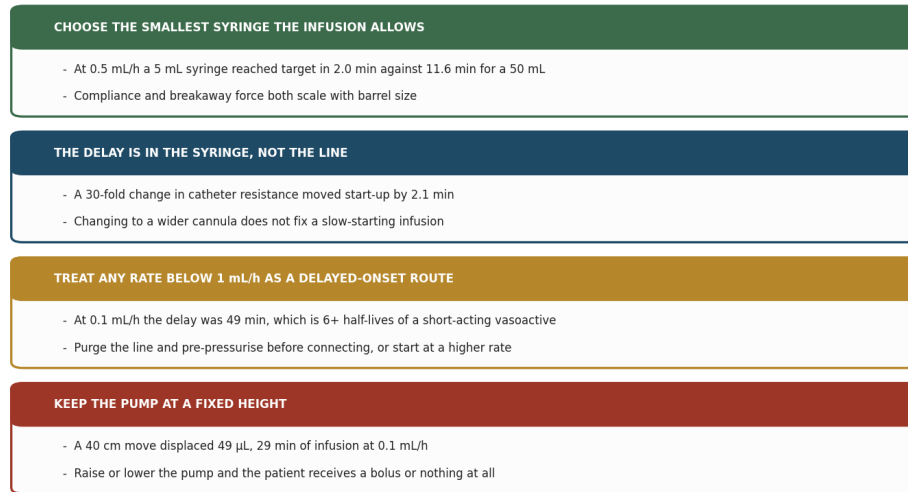


Fig.7: Practical guidance for low-rate syringe pump infusion.

5. LIMITATIONS

This is an analytical lumped model with parameter values chosen to be representative rather than measured. Compliance and breakaway pressure vary between manufacturers, between production lots and with the age of the disposable, and both are affected by storage temperature and by how long the syringe has been loaded. The magnitudes reported should be read as indicative and the orderings as robust.

Stiction is modelled as a single breakaway pressure followed by free movement. Real plunger seals exhibit stick-slip behaviour, in which the plunger advances in small jumps, producing oscillatory flow rather than the smooth first-order approach we model. That behaviour would add short-term variability around the trajectory shown without changing the time to reach target.

We model a single syringe on a dedicated line. Multi-infusion setups sharing a common access device interact strongly: a rate change or flush in one line alters the pressure seen by the others and displaces their compliance, which is a larger source of unintended bolus than anything modelled here and is a natural extension [15,20,21].

Catheter resistance is treated as constant. In practice it varies with viscosity, temperature, partial occlusion by fibrin and the position of the limb, and a partially occluded line raises resistance enough to make the compliance term matter more than our results suggest.

Finally, we quantify delivery and not effect. Translating a dose deficit into a haemodynamic consequence requires pharmacokinetic and pharmacodynamic modelling of the specific agent and patient, and the half-life comparison in Section 3.4 is an ordering device rather than such a model.

6. CONCLUSION

At the flow rates used for neonatal and critical-care infusion, a syringe pump reaches its commanded delivery slowly. With a 50 mL syringe on a 28 G neonatal long line, the time to 95

per cent of commanded flow was 49 minutes at 0.1 mL/h and 11.6 minutes at 0.5 mL/h, and the cumulative deficit over the first hour reached 80 per cent of the intended dose at the lowest rate.

Plunger stiction rather than compliance charging accounted for 95 per cent of that delay, which locates the problem in the syringe. Changing from a 50 mL to a 5 mL syringe reduced the delay 5.8-fold, while a 30-fold change in vascular access device resistance changed it by 2.1 minutes.

The same compliance makes the infusion sensitive to pressure changes during steady operation: a 40 cm vertical movement of the pump displaced 49 microlitres, 29 minutes of infusion at 0.1 mL/h. Selecting the smallest practicable syringe and keeping the pump at a fixed height address the two largest effects, and neither requires a different pump.

DECLARATIONS

Ethics approval and consent to participate. Not applicable. This is an analytical modelling study. No patients, human participants, clinical data or bench measurements from a specific device were involved.

Consent for publication. Not applicable.

Data availability statement. This is an analytical modelling study; no patient, clinical or experimental datasets were used. All results were generated by an analysis script developed by the author in Python using NumPy, SciPy and Matplotlib [28-30]. Every model parameter is reported in full in Tables 1 and 2, and all figures and all values in Tables 3 to 7 can be reproduced from these parameters using Equations 1 to 5. The analysis script is available from the corresponding author upon reasonable request.

Conflict of interest. The author declares no competing interests, financial or non-financial, in relation to the subject matter of this manuscript. The author has no financial or advisory relationship with any manufacturer of infusion pumps, syringes, extension sets or vascular access devices.

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REFERENCES

1. Sherwin CMT, Medlicott NJ, Reith DM, Broadbent RS. Intravenous drug delivery in neonates: lessons learnt. *Arch Dis Child*. 2014;99(6):590-94.
2. Murdoch IA, Cameron FJ. Smart infusion devices and low-flow drug delivery in paediatric intensive care. *Intensive Care Med*. 1998;24(9):989-90.
3. Neff T, Fischer J, Fehr S, Baenziger O, Weiss M. Start-up delays of infusion syringe pumps. *Paediatr Anaesth*. 2001;11(5):561-65.
4. Weiss M, Fischer J, Neff T, Baenziger O. The effects of syringe plunger design on drug delivery during vertical displacement of syringe pumps. *Anaesthesia*. 2000;55(11):1094-98.
5. Neff SB, Neff TA, Gerber S, Weiss MM. Flow rate, syringe size and architecture are critical to start-up performance of syringe pumps. *Eur J Anaesthesiol*. 2007;24(7):602-08.

6. Weiss M, Banziger O, Neff T, Fanconi S. Influence of infusion line compliance on drug delivery rate during acute line loop formation. *Intensive Care Med.* 2000;26(6):776-79.
7. Lonnqvist PA, Lofqvist B. Design flaw can convert commercially available continuous syringe pumps to intermittent bolus injectors. *Intensive Care Med.* 1997;23(9):998-1001.
8. International Electrotechnical Commission. IEC 60601-2-24: Medical electrical equipment - Part 2-24: Particular requirements for the basic safety and essential performance of infusion pumps and controllers. Geneva: IEC; 2012.
9. Association for the Advancement of Medical Instrumentation. Infusion devices standards collection. Arlington: AAMI; 2020.
10. Kern H, Kuring A, Redlich U, Dopfmer UR, Sims NM, Spies CD, et al. Downward movement of syringe pumps reduces syringe output. *Br J Anaesth.* 2001;86(6):828-31.
11. Schmidt N, Saez C, Seri I, Maturana A. Impact of syringe size on the performance of infusion pumps at low flow rates. *Pediatr Crit Care Med.* 2010;11(2):282-86.
12. Bartels K, Moss DR, Peterfreund RA. An analysis of drug delivery dynamics via a pediatric central venous infusion system: quantification of delays in achieving intended doses. *Anesth Analg.* 2009;109(4):1156-61.
13. Lovich MA, Doles J, Peterfreund RA. The impact of carrier flow rate and infusion set dead-volume on the dynamics of intravenous drug delivery. *Anesth Analg.* 2005;100(4):1048-55.
14. Lovich MA, Kinnealley ME, Sims NM, Peterfreund RA. The delivery of drugs to patients by continuous intravenous infusion: modeling predicts potential dose fluctuations depending on flow rates and infusion system dead volume. *Anesth Analg.* 2006;102(4):1147-53.
15. Tsao AC, Lovich MA, Parker MJ, Zheng H, Peterfreund RA. Delivery interaction between co-infused medications: an in vitro modeling study of microinfusion. *Paediatr Anaesth.* 2013;23(1):33-39.
16. Moss DR, Bartels K, Peterfreund GL, Lovich MA, Sims NM, Peterfreund RA. An in vitro analysis of central venous drug delivery by continuous infusion: the effect of manifold design and port selection. *Anesth Analg.* 2009;109(5):1524-29.
17. Parker MJ, Lovich MA, Tsao AC, Deng H, Houle T, Peterfreund RA. Computer control of drug delivery by continuous intravenous infusion: bridging the gap between intended and actual drug delivery. *Anesthesiology.* 2017;127(2):266-78.
18. Timmerman AM, Snijder RA, Lucas P, Lagerweij MC, Radermacher JH, Konings MK. How physical infusion system parameters cause clinically relevant dose deviations after setpoint changes. *Biomed Tech.* 2015;60(4):365-76.
19. Snijder RA, Konings MK, Lucas P, Egberts TC, Timmerman AD. Flow variability and its physical causes in infusion technology: a systematic review of in vitro measurement and modeling studies. *Biomed Tech.* 2015;60(4):277-300.
20. Decaudin B, Dewulf S, Lannoy D, Simon N, Secq A, Barthelemy C, et al. Impact of multiaccess infusion devices on in vitro drug delivery during multi-infusion therapy. *Anesth Analg.* 2009;109(4):1147-55.
21. Foinard A, Decaudin B, Barthelemy C, Debaene B, Odou P. The impact of multilumen infusion devices on the occurrence of known physical drug incompatibility: a controlled in vitro study. *Anesth Analg.* 2013;116(1):101-06.
22. Bartels K, Moss DR, Peterfreund RA. Tubing dead volume and infusion dynamics. *Anesth Analg.* 2010;110(2):644-45.
23. Batliner M, Weiss M, Dual SA, Grass B, Meboldt M, Schmid Daners M. Evaluation of a novel flow-controlled syringe infusion pump for precise and continuous drug delivery at low flow rates: a laboratory study. *Anaesthesia.* 2019;74(11):1425-31.

24. Klem SA, Farrington JM, Leff RD. Influence of infusion pump operation and flow rate on hemodynamic stability during epinephrine infusion. *Crit Care Med*. 1993;21(8):1213-17.
25. Chiswick ML, Bendall M. Syringe pump delivery: the hidden hazard of low flow rates. *Arch Dis Child*. 1994;70(3):F216.
26. Sherwin CMT, Medlicott NJ, Reith DM, Broadbent RS. Neonatal drug delivery: reappraising the standard of care. *Curr Pharm Des*. 2015;21(39):5666-76.
27. van der Eijk AC, van Rens RM, Dankelman J, Smit BJ. A literature review on flow-rate variability in neonatal IV therapy. *Paediatr Anaesth*. 2013;23(1):9-21.
28. Harris CR, Millman KJ, van der Walt SJ, Gommers R, Virtanen P, Cournapeau D, et al. Array programming with NumPy. *Nature*. 2020;585(7825):357-62.
29. Virtanen P, Gommers R, Oliphant TE, Haberland M, Reddy T, Cournapeau D, et al. SciPy 1.0: fundamental algorithms for scientific computing in Python. *Nat Methods*. 2020;17(3):261-72.
30. Hunter JD. Matplotlib: a 2D graphics environment. *Comput Sci Eng*. 2007;9(3):90-95.