Quantitative Problems in Anesthesia

David R. Moss, MD
Tufts Medical Center
Boston, MA

1 Don't cry over spilt sevoflurane

While setting up the OR you accidentally drop a 250 mL bottle of sevoflurane. It shatters when it hits the ground.

1. Assuming the OR is a sealed container of dimensions $25 \cdot 20 \cdot 10$ ft, what is the steady-state concentration, c_{ss} of sevoflurane in the room (in ppm)?

Room temperature is 25℃, the density of sevoflurane is 1.52 g/mL and its molecular weight is 200.

At steady-state the sevoflurane liquid has completely vaporized. How much sevoflurane gas is produced? At STP (0℃ and 1 atm), 1 mole of gas occupies 22.4 L. At 25℃, this constant increases (Charles's Law, temperature in Kelvin):

$$22.4(\frac{298\text{K}}{273\text{K}}) = 24.5 \text{ L/mol}$$

How many moles are in 250 mL of liquid? Molecular weight is the number of grams per mole. And since density is grams per mL, we find

$$(250 \text{ mL})(\frac{1.52 \text{ g}}{\text{mL}})(\frac{\text{mol}}{200 \text{ g}}) = 1.9 \text{ mol}$$

i.e.

$$(1.9 \text{ mol})(\frac{24.5 \text{ L}}{\text{mol}}) = 46.6 \text{ L sevo gas}$$

The volume of the OR is lwh,

$$(25)(20)(10) = (5000 \text{ ft}^3)(\frac{28.3 \text{ L}}{\text{ft}^3}) = 141,500 \text{ L}$$

Hence the steady state concentration is

$$\frac{46.6}{141,500} = 329 \times 10^{-6} = 0.03\% = 329 \text{ ppm.}$$

2. If the ventilation system is on and operating at the industry-standard flow rate of 15 room volume exchanges per hour, how long will it take before the concentration in the room falls below 2 ppm, the OSHA ceiling on occupational exposure to volatile anesthetics?

Let's find a general expression for $c(t)$, the concentration of sevo at time t.

With 15 room volume exchanges per hour, it takes 4 minutes to exchange V. We define this to be the time constant, τ. Therefore if c is the concentration of sevo at any particular time, $\frac{cV}{\tau}$, is the volume of sevo cleared per minute. This must be equal to the rate of change, $V\frac{dc}{dt}$. Thus,

$$V\frac{dc}{dt} = -\frac{cV}{\tau}$$

$$\frac{dc}{c} = -\frac{1}{\tau}dt$$

Integrating both sides,

$$\int \frac{dc}{c} = \int -\frac{1}{\tau}dt$$

$$ln(c) = -\frac{t}{\tau} + K$$

i.e,

$$c(t) = Ke^{-\frac{t}{\tau}}$$

But at time $t = 0$ we know that $c(t) = c_{ss}$, so $K = c_{ss}$ and

$$c(t) = c_{ss}e^{-\frac{t}{\tau}} \qquad \text{(Figure 1)}$$

Solving for t,

$$2 = 329e^{-\frac{t}{4}}$$

$$t = 20.4 \text{ min}$$

3. What is the initial rate of change in concentration (in ppm/min)?

Differentiating, we have

$$c'(t) = -\frac{c_{ss}}{\tau}e^{-\frac{t}{\tau}}$$

Thus,

$$c'(0) = -\frac{329}{4} = -82.3 \text{ ppm/min}$$

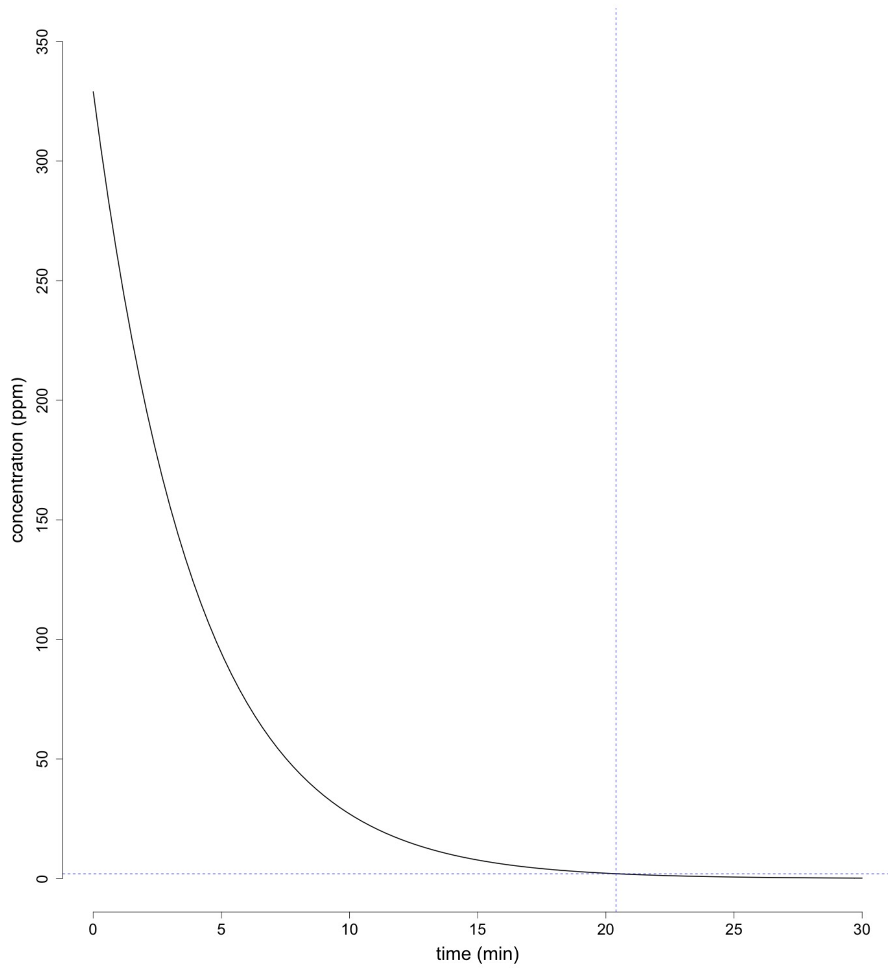

Figure 1: Sevo concentration vs time

2 Fun with E-cylinders

If a full O_2 E cylinder (1900 psi) contains 660 L of O_2 at STP, what is the radius of the cylinder in terms of its height, $r(h)$?

The volume, V, of a cylinder of height h and radius r is given by:

$$V = \pi r^2 h$$

Hence,

$$r = \sqrt{\frac{V}{\pi h}}.$$

To get at V, recall

$$P_1 V_1 = P_2 V_2 \qquad \text{(Boyle's Law)}$$

Given that a full E-cylinder holds 660 L of O_2 at STP and P_{atm}= 14.7 psi,

$$V = (\frac{14.7}{1900})660 \text{ L} = 5.1 \text{ L}$$

Therefore,

$$r(h) = \sqrt{\frac{(5.1)(61\frac{in^3}{L})}{\pi h}} = \frac{9.95}{\sqrt{h}}$$

3 IV infusion kinetics

An intravenous infusion of a drug with concentration c_d mg/ml is started with a syringe pump. The infusion line is piggybacked to a continuously dripping carrier fluid with a three-way stopcock. The distance between the stopcock and the tip of the IV catheter is the dead volume, V. The carrier flows at a rate Q_c ml/min and the drug is infused at a rate Q_d.[1]

1. What is the steady-state drug concentration c_{ss} at the tip of the catheter?

The amount of drug, in mg/min, that is infused into V is $c_d Q_d$. Therefore in one minute, $c_d Q_d$ mg of drug have been diluted by a total of $Q_d + Q_c$ ml of fluid. Thus,

$$c_{ss} = \frac{c_d Q_d}{Q_d + Q_c}$$

2. If the drug traverses V with a discrete 'head' (*Plug-Flow*), how long does it take for the drug to reach the patient's bloodstream?

[1]Adapted from Lovich et al, The Impact of Carrier Flow Rate and Infusion Set Dead-Volume on the Dynamics of Intravenous Drug Delivery. *Anesth Analg* 2005;100:1048-55.

Since there is no mixing proximal to the head, the head itself is moving at a rate of $Q_d + Q_c$. Therefore the time to traverse V is one time constant, τ, in min:

$$\tau = \frac{V}{Q_d + Q_c}$$

3. If the drug mixes uniformly within V at all times (*Well-Mixed*), how long does it take for the drug concentration to reach 95% of steady-state?

This is similar to problem 1. Here the concentration of drug in V, like the concentration of sevo in the OR is variable. As before, the amount of drug cleared is $\frac{cV}{\tau}$. The difference here is that drug is continuously delivered to V at a rate $c_d Q_d$. This difference must be equal to the rate of change, $V\frac{dc}{dt}$. Thus,

$$V\frac{dc}{dt} = c_d Q_d - \frac{cV}{\tau}$$

$$\frac{dc}{dt} + \frac{c}{\tau} = \frac{c_d Q_d}{V}$$

Multiplying through by the integrating factor $e^{\frac{t}{\tau}}$,

$$e^{\frac{t}{\tau}}\frac{dc}{dt} + e^{\frac{t}{\tau}}\frac{c}{\tau} = \frac{c_d Q_d}{V}e^{\frac{t}{\tau}}$$

By the product rule,

$$\frac{d}{dt}(ce^{\frac{t}{\tau}}) = \frac{c_d Q_d}{V}e^{\frac{t}{\tau}}$$

Integrating both sides,

$$ce^{\frac{t}{\tau}} = \frac{c_d Q_d}{V}\int e^{\frac{t}{\tau}}dt$$

$$ce^{\frac{t}{\tau}} = \frac{c_d Q_d}{V}\tau e^{\frac{t}{\tau}} + K$$

$$ce^{\frac{t}{\tau}} = c_{ss}e^{\frac{t}{\tau}} + K$$

Therefore,

$$c(t) = c_{ss} + Ke^{-\frac{t}{\tau}}$$

But at time $t = 0$ we know that $c(t) = 0$, so $K = -c_{ss}$ and

$$c(t) = c_{ss}(1 - e^{-\frac{t}{\tau}}) \qquad \text{(Figure 2)}$$

In one time constant, $c(t)$ has increased to $1 - \frac{1}{e}$, or 63% of c_{ss}
In two time constants, $c(t)$ has increased to $1 - \frac{1}{e^2}$, or 86% of c_{ss}
In three time constants, $c(t)$ has increased to $1 - \frac{1}{e^3}$, or 95% of c_{ss}
Therefore, it takes 3τ to reach 95% of steady-state concentration.

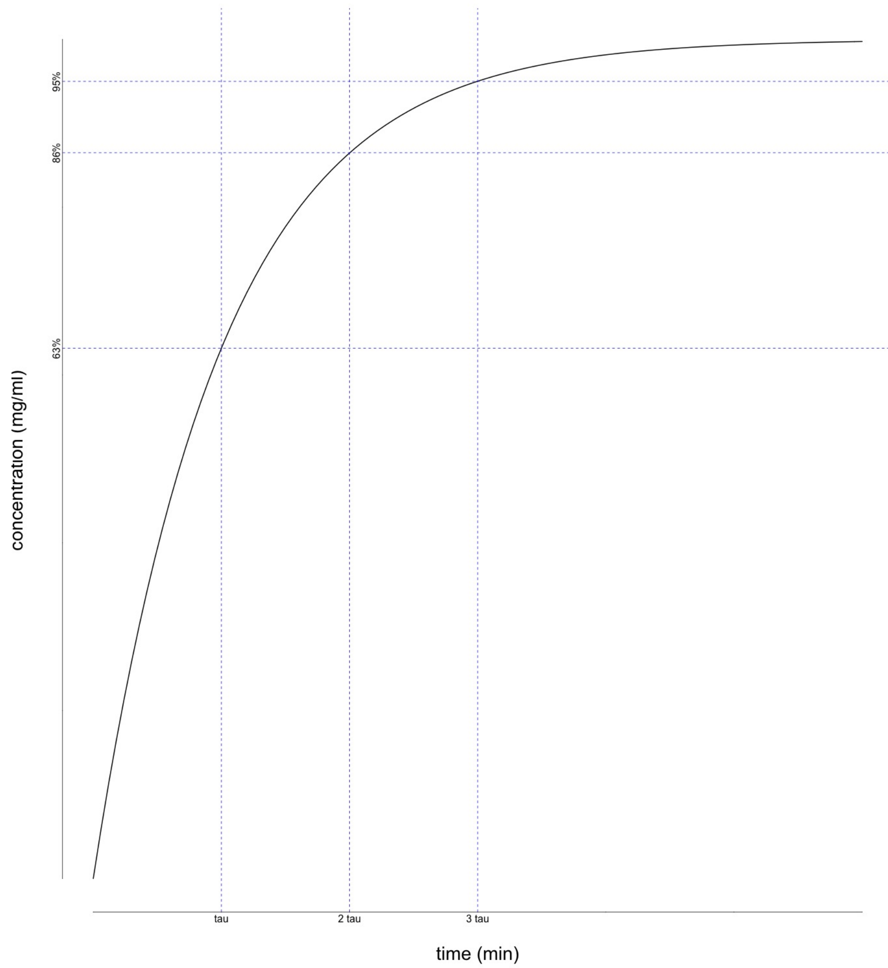

Figure 2: Infusion delivery vs time

4 I smell sevo!

An anesthesia delivery system at steady-state is delivering 8% sevoflurane with a total fresh gas flow Q. Prior to intubation, the mask is taken off the patient and exposed to the environment. Let V be the dead volume of the breathing system (includes the breathing circuit, breathing bag, and internal plumbing distal to the vaporizer).

1. How much wasted sevoflurane gas, W, is delivered into the OR environment in t minutes?

$$W = (.08)Qt \qquad \text{(Figure 3, RED)}$$

2. As you take off the mask you turn the sevoflurane vaporizer off. Now how much sevoflurane gas, W, is delivered into the OR environment in t minutes?

Here the concentration is variable, and just as in problem 1, is given by

$$c(t) = (.08)e^{-\frac{t}{\tau}}$$

where

$$\tau = \frac{V}{Q}$$

Therefore, the delivery $d(t)$ of sevo is

$$d(t) = (.08)Qe^{-\frac{t}{\tau}}$$

And so

$$W = \int_0^t (.08)Qe^{-\frac{t}{\tau}}dt$$

$$W = (.08)Q\tau(1 - e^{-\frac{t}{\tau}})$$

$$W = (.08)V(1 - e^{-\frac{t}{\tau}}) \qquad \text{(Figure 3, BLACK)}$$

3. Now, instead of turning off the vaporizer, you turn off the fresh gas flow. How much sevoflurane gas, W, is delivered into the OR environment in t minutes?

Here $Q = 0$ so it follows that $W = 0$ independent of t. (Figure 3, GREEN)

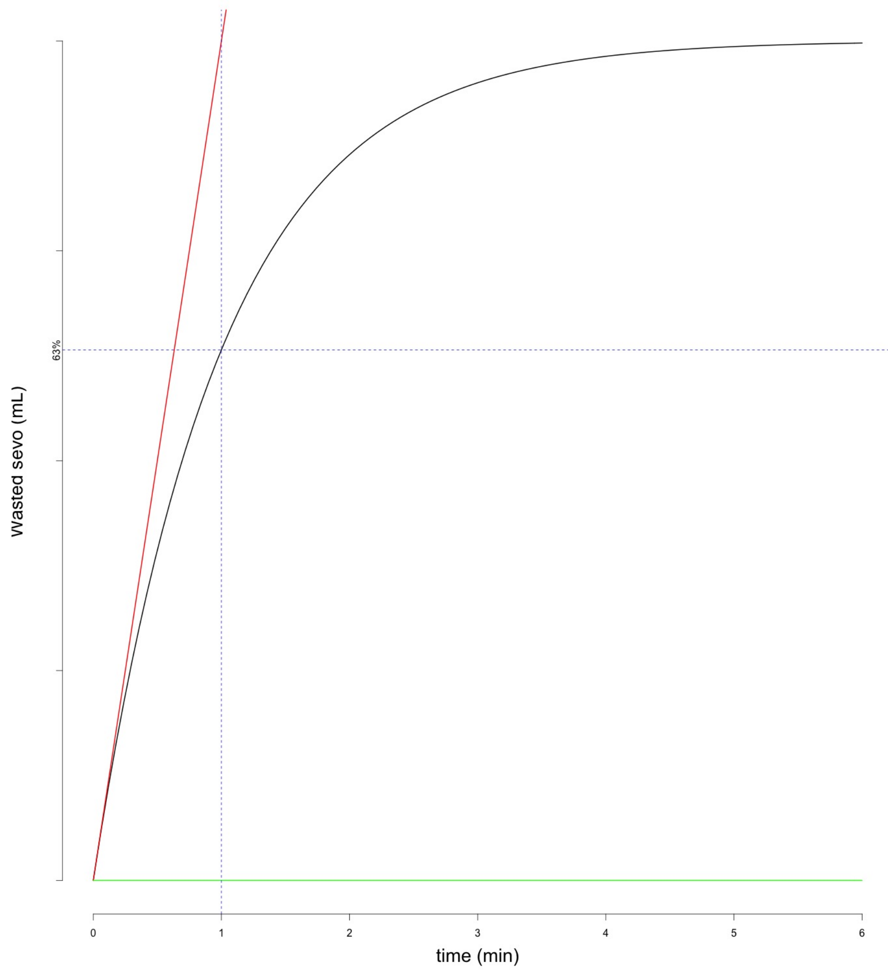

Figure 3: Wasted sevo vs time, assuming V = 10 L and Q = 10 lpm. RED - Vaporizer and flows on. BLACK - Vaporizer off and flows on. GREEN - Vaporizer on or off and flows off.

5 Anesthesia at high altitude

You take an anesthesia machine up to 10,000 ft (P_{atm} = 500 mmHg) and set the vaporizer (calibrated at sea level) to deliver 2.1% sevoflurane (vapor pressure 160 mm). What concentration of sevoflurane gets delivered? What is the relative potency?

How does the sevo vaporizer deliver a 2.1% concentration? At sea level, the saturated vapor concentration of sevoflurane equals $\frac{160}{760} = 21\%$. The vaporizer must dilute this saturated vapor with enough fresh gas to reduce the concentration by a factor of 10.

Modern vaporizers accomplish this by diverting the fresh gas into two streams, a bypass stream which does not contact anesthetic liquid, Q_{bypass}, and a vaporizing chamber stream, $Q_{chamber}$ which becomes saturated with sevoflurane vapor, Q_{sevo}.

If Q_{sevo} is the amount of sevoflurane gas produced from vaporization, then

$$\frac{Q_{sevo}}{Q_{bypass} + Q_{chamber} + Q_{sevo}} = 2.1\%$$

The vaporizing chamber stream completely saturates with sevoflurane, i.e.

$$\frac{Q_{sevo}}{Q_{chamber} + Q_{sevo}} = 21\%$$

and so

$$Q_{chamber} = 3.8 Q_{sevo}$$

which means

$$Q_{bypass} = 42.9 Q_{sevo}$$

So the vaporizer must split the fresh gas flow using a ratio of

$$\frac{Q_{bypass}}{Q_{chamber}} = 11.3$$

At $P_{atm} = 500$, the splitting ratio is unchanged but now

$$\frac{Q_{sevo}}{Q_{chamber} + Q_{sevo}} = \frac{160}{500} = 32\%$$

Working backward,

$Q_{chamber} = 2.1 Q_{sevo}$ and since $Q_{bypass} = 11.3 Q_{chamber}$, we find $Q_{bypass} = 23.7 Q_{sevo}$,

The output concentration is

$$\frac{Q_{sevo}}{Q_{bypass} + Q_{chamber} + Q_{sevo}} = 3.7\%$$

How much more potent is this? Potency depends on partial pressure, not concentration. 3.7% of 500 is 18.7 mm. 1 MAC at sea level is equivalent to (2.1%)(760 mm) = 16 mm. Therefore at $P_{atm} = 500$, the potency increases by a factor of $\frac{18.7}{16} = 1.2$