What Sets a Dosing Interval Is Two Things: the Half-Life and the Width of the Therapeutic Window

— at steady state the ratio of peak to trough is $2^{\tau/t_{1/2}}$, **256.000000** for a one-hour half-life taken every eight hours and only **1.515717** for a 40-hour half-life taken every 24 — a window only twofold wide requires an interval no longer than the half-life — [Paper 578]

Yuuki YAMAGISHI (山岸 勇輝)
Yamagishi Complexity Torus Lab, Japan
September 2026

— From thinking to syncing. —

Abstract

Medicines come with an interval: three times a day, once a day.What this paper shows is that what sets the interval is only two things, the half-life and the width of the therapeutic window; that for the same daily dose the mean concentration does not depend on the interval; and that what the interval changes is only the ratio of peak to trough.No new theorem or law is claimed. First, at steady state the ratio of peak to trough is $2^{\tau/t_{1/2}}$——256.000000 for a one-hour half-life taken every eight hours and 1.515717 for a 40-hour half-life taken every 24 (Section 2). **Second, accumulation is $1/(1-2^{-\tau/t_{1/2}})$——a short half-life at a long interval hardly accumulates (1.003922), while a 40-hour half-life every 24 hours accumulates 2.939050 times** (Section 2). **Third, and this is the core.To stay within a therapeutic window of width W requires $\tau \le t_{1/2}\log_2 W$——for a twofold window the interval can be at most 1.000000 half-lives, for threefold 1.584963, for tenfold 3.321928** (Section 3). **Fourth, for the same daily dose, the mean does not depend on the interval——with an eight-hour half-life, intervals of 4, 8, 12 and 24 hours all give a mean of 0.480898, while the ratio of peak to trough widens from 1.414214 to 8.000000** (Section 4). **Fifth, the approach to steady state is set by the number of half-lives——0.937500 of steady state after four half-lives and 0.968750 after five, independent of the interval and the dose** (Section 5). **Sixth, the separator is mean against swing ——the mean is set by the daily dose and the swing by $\tau/t_{1/2}$; the two knobs are separate** (Section 6). **Keywords**: pharmacokinetics, half-life, therapeutic window, dosing interval, steady state.

Scope of this paper (scope note): **No new theorem or law is claimed——the formulae for repeated dosing in a one-compartment model are all standard.Only the simplest model is used——the body is one box, elimination is first order and absorption instantaneous. For oral drugs absorption takes time and lowers the peak, which is not included.First-order elimination is assumed——for drugs whose elimination saturates and stops being first order, these formulae do not apply.Differences between people are not treated——the half-life varies with age, kidney and liver function and other drugs taken.The width of the therapeutic window is set as a ratio——which drug has which width is not stated, and no drug is named.The mean concentration is in units where the daily dose and the volume are 1.No dosing is prescribed——how to take a medicine is for doctors and pharmacists to decide; this paper looks only at the form of the formulae.Relation to earlier papers**: **Paper 346 showed that for two of the three reaction orders a half-life is not even a property of the substance——every formula here stands on first-order elimination; because it is first order, the half-life is one number and the ratio of peak to trough takes the closed form $2^{\tau/t_{1/2}}$.Paper 386 stated in its scope note that it designed no drug——it dealt with the speed of dissolving, the way into the body; this paper deals with the speed of elimination, the way out.Paper 300 showed that sharing a root is decidable——"the mean does not move" and "the swing changes with the interval" have distinct roots.**What is added is **setting out the ratios of peak to trough and the accumulation**, **placing the condition for staying within the window in the closed form $\tau \le t_{1/2}\log_2 W$ and confirming that at that interval the ratio returns exactly to W, confirming by numerical integration and by the closed form that for the same daily dose the mean does not depend on the interval**, and **placing the separator on the distinction between mean and swing**.

1. Notation and the Question

Setting: **take the body as one box, with the drug eliminated at first order (rate constant $k = \ln 2/t_{1/2}$).Giving a dose D repeatedly at interval τ, the steady-state concentration is**

$$C(t) = \frac{D}{V}\,\frac{e^{-kt}}{1-e^{-k\tau}} \quad (0 \le t < \tau),$$

and the ratio of peak to trough, the accumulation and the mean are

$$\frac{C_{\max}}{C_{\min}} = 2^{\tau/t_{1/2}}, \qquad R = \frac{1}{1-2^{-\tau/t_{1/2}}}, \qquad \bar{C} = \frac{D}{Vk\tau}.$$

Observation 1.1

medicines come with an interval, three times a day or once a day.The number of times seems to be set by the strength of the drug or the dose——what sets the interval, and what changing it changes, can be read from the form of the formulae.

Question: what sets the dosing interval?What changes when the interval changes, and what does not?

2. Peak and Trough

Computation 2.1: ratio of peak to trough and accumulation at steady state for pairs of half-life and interval.

half-life	interval	peak to trough	accumulation
1 h	8 h	**256.000000**	**1.003922**
4 h	8 h	**4.000000**	**1.333333**
8 h	8 h	**2.000000**	**2.000000**
8 h	24 h	**8.000000**	**1.142857**
40 h	24 h	**1.515717**	**2.939050**

> **Observation 2.2**
>
> a short half-life at a long interval makes peak and trough differ by orders of magnitude.A one-hour half-life every eight hours swings 256 times——too strong at the peak, nearly ineffective at the trough; and since almost all is gone before the next dose, nothing accumulates (1.003922).

> **Observation 2.3**
>
> when the interval equals the half-life, both the ratio and the accumulation are exactly 2.The accumulation $1/(1-2^{-1})$ returns exactly to 2 (to 10^{-12})——at each dose, half of the previous amount remains.

3. Staying Within the Window

Computation 3.1: let the width W of the therapeutic window be the ratio of the concentration at which harm begins to the lowest effective one.The longest interval for which the ratio of peak to trough stays within W is $\tau/t_{1/2} = \log_2 W$.

window width W	longest interval (in half-lives)
1.5	**0.584963**
2	**1.000000**
3	**1.584963**
10	**3.321928**

> **Observation 3.2**
>
> **at that interval the ratio of peak to trough returns exactly to W (all four to 10^{-12}).The condition $\tau \le t_{1/2} \log_2 W$ contains only two things, the half-life and the width of the window——this is the core. What sets the dosing interval is neither the strength of the drug nor the size of a dose, but only the half-life and the width of the window.**

> **Observation 3.3**
>
> **a drug with a narrow window cannot have its interval stretched.With a window only twofold wide, the interval cannot exceed the half-life——a tenfold window allows a little over three half-lives (3.321928).**

4. The Mean Does Not Move

Computation 4.1: **with an eight-hour half-life, the daily dose and the volume fixed at 1, only the number of portions was changed.The steady-state mean was computed both by numerical integration and by the closed form (all four agree to 10^{-9}).**

interval	mean concentration	peak to trough
4 h	**0.480898**	**1.414214**
8 h	**0.480898**	**2.000000**
12 h	**0.480898**	**2.828427**
24 h	**0.480898**	**8.000000**

Observation 4.2

for the same daily dose, the mean does not depend on the interval.The closed-form mean $1/(24k) = 0.480898$ contains no interval——the mean settles where the amount entering in a day balances the amount eliminated in a day. The interval changes only the ratio of peak to trough.

Observation 4.3

“more doses work better” is half wrong.Dividing the same daily dose more finely does not raise the mean ——it only shrinks the swing, making the trough less likely to fall below the window.

5. The Approach to Steady State

Computation 5.1: **how close to steady state the concentration is after a given number of half-lives from the first dose.**

time elapsed	fraction of steady state
1 half-life	**0.500000**
2 half-lives	**0.750000**
3 half-lives	**0.875000**
4 half-lives	**0.937500**
5 half-lives	**0.968750**

Observation 5.2

the approach to steady state is set by the number of half-lives.It depends neither on the interval nor on the dose——a drug with a 40-hour half-life takes about a week to reach some ninety-four per cent of steady state, however it is divided.

6. The Separator

Observation 6.1

the separator is mean against swing.The mean is set by the daily dose and the speed of elimination; the swing (ratio of peak to trough) by $\tau/t_{1/2}$——the two knobs are separate: changing the daily dose does not change the swing, and changing the interval does not change the mean.

Observation 6.2

standing on Paper 346.It showed that for two of the three reaction orders a half-life is not even a property of the substance——the formulae here take closed forms because elimination is first order. If elimination saturated and approached zeroth order, $2^{\tau/t_{1/2}}$ would not hold.

Observation 6.3

a counterpart to Paper 386, entrance and exit.It dealt with the speed of dissolving, the way into the body, and its scope note designed no drug——this paper deals with the speed of elimination, the way out. As “hard to dissolve” pointed at two quantities there, “the effect lasts” points at two here, the mean and the swing.

Observation 6.4

distinct roots, under Paper 300.“The mean does not move” comes from the balance of what enters and what is eliminated——“the swing changes with the interval” comes from the shape of first-order decay. With different roots, moving one does not move the other.

Observation 6.5

what is not said.No dosing is prescribed——how to take a medicine is for doctors and pharmacists to decide. What is shown is only the two numbers that set the interval, and the distinction between what the interval changes and what it does not.

7. Roll Call and Closing

1. **peak to trough $2^{\tau/t_{1/2}}$** (Computation 2.1): **256.000000 at half-life 1, interval 8.**
2. **1.515717 at half-life 40, interval 24** (Computation 2.1): **accumulation 2.939050.**
3. **interval equal to half-life gives 2 and 2** (Observation 2.3): **half the previous dose remains.**
4. **the window condition $\tau \le t_{1/2} \log_2 W$** (Computation 3.1): **the core.**
5. **1.000000 for $W = 2$, 3.321928 for $W = 10$** (Computation 3.1): **how many half-lives an interval may be.**
6. **the mean stays at 0.480898** (Computation 4.1): **independent of the interval.**
7. **only the swing moves, 1.414214 to 8.000000** (Computation 4.1): **what the interval changes.**
8. **0.937500 after four half-lives** (Computation 5.1): **the approach is counted in half-lives.**
9. **the separator is mean against swing** (Observation 6.1): **two separate knobs.**
10. **standing on Paper 346** (Observation 6.2): **first order makes the forms closed.**

Closing: **Medicines come with an interval: three times a day, once a day.What sets that interval is only two things, the half-life and the width of the therapeutic window——at steady state the ratio of peak to trough is $2^{\tau/t_{1/2}}$, 256.000000 for a one-hour half-life every eight hours and 1.515717 for a 40-hour half-life every 24. Accumulation is $1/(1 - 2^{-\tau/t_{1/2}})$, ranging from 1.003922 to 2.939050, and when the interval equals the half-life both ratio and accumulation are exactly 2. The condition for staying within a window of width W is $\tau \le t_{1/2} \log_2 W$: at most 1.000000 half-lives for $W = 2$ and 3.321928 for $W = 10$.For the same daily dose, the mean concentration does not depend on the interval——with an eight-hour half-life and intervals from 4 to 24 hours the mean stays at 0.480898, numerical integration and closed form agreeing; only the ratio of peak to trough changes, from 1.414214 to 8.000000. More doses do not raise the mean; they only shrink the swing. The approach to steady state is counted in half-lives, 0.937500 after four, independent of the interval and the dose.The separator is mean against swing——the mean is set by the daily dose, the swing by $\tau/t_{1/2}$; under Paper 300 the two have distinct roots, and moving one does not move the other.Placed among the earlier papers——the formulae stand on Paper 346: because elimination is first order, the half-life is one number and the ratio takes a closed form. Where Paper 386 looked at the way in, the speed of dissolving, this paper looks at the way out, the speed of elimination.To be honest——this is the simplest model, one box with instantaneous absorption and first-order elimination. The delay of oral absorption, saturable elimination and differences between people are not included; the window was set only as a ratio and no drug is named. And no dosing is prescribed: how to take a medicine is for doctors and pharmacists to decide.**

References

1. Gibaldi, M., & Perrier, D. (1982). *Pharmacokinetics* (2nd ed.). Marcel Dekker.

2. Rowland, M., & Tozer, T. N. (2011). *Clinical Pharmacokinetics and Pharmacodynamics: Concepts and Applications* (4th ed.). Lippincott Williams & Wilkins.

3. Yamagishi, Y. (2026). *The Three Hundredth Census: Whether Two Things Share a Root Is Decidable* [Paper 300]. Zenodo. 10.5281/zenodo.22171914

4. Yamagishi, Y. (2026). *For Two of the Three Reaction Orders, "Half-Life" Is Not Even a Property of the Substance* [Paper 346]. Zenodo. 10.5281/zenodo.22682323

5. Yamagishi, Y. (2026). *The Solubility Did Not Move at All, and the Dissolution Became a Thousand Times Faster* [Paper 386]. Zenodo. 10.5281/zenodo.22699119

— From thinking to syncing. —

Yuuki YAMAGISHI (山岸 勇輝)

© 2026 Yamagishi Complexity Torus Lab, Japan · Licensed under Creative Commons Attribution 4.0 International (CC BY 4.0)