A formula for the cummulative drug level from repeated dosing

Assumptions: Dosing at a regular interval. At each dose, drug blood (or system) level increases by the same amount. At the first dose this amount will then be the same as the total blood level which we call L_1. Let r be the fraction of L_1 remaining by the second dose—which depends only on the dosing interval and the half-life of the drug. The blood level just after the second dose is then $L_1 + rL_1$ which we call L_2.

The accumulated level just after the third dose, called L_3, will be

$$\begin{aligned} L_3 &= L_1 + rL_2 \\ &= L_1 + r(L_1 + rL_1) \\ &= L_1 + rL_1 + r^2L_1 \end{aligned}$$

Continuing in this manner, we get the accumulated level just after the n^{th} dose, called L_n:

$$L_n = L_1 + rL_1 + r^2L_1 + r^3L_1 + \ \ ... \ + r^{n-1}L_1$$

multiplying by r gives

$$rL_n = \qquad rL_1 + r^2L_1 + r^3L_1 + \ \ ... \ + r^{n-1}L_1 + r^nL_1$$

Subtracting:

$$\begin{aligned} L_n - rL_n &= L_1 - r^nL_1 \\ (1-r)L_n &= L_1 - r^nL_1 \end{aligned}$$

Dividing:

$$L_n = \tfrac{L_1}{(1-r)} - r^n \tfrac{L_1}{(1-r)}$$

Since the drug does decay (it has a real half-life), r is less than 1. Therefore r^n goes to zero as n gets arbitrarily large. So the entire second term in the right side of the equation above goes to zero, and L_n approaches a limit (call it L), which is just $\frac{L_1}{(1-r)}$. That is, L is the repeated peak value that we get after we have been dosing for a while. Since r is the fraction of the drug remaining, $1 - r$ (call it f) is the fraction that has decayed (metabolized). Since $f = 1 - r$,

$$L = \tfrac{1}{f} L_1$$

In words: As we continue to dose, the limit of the peak values we get just after dosing is the reciprocal of the fraction *lost* between doses multiplied by the peak value after the first dose.

Since L is the peak value right after a dose (in the long run), $L - L_1$ is the value just before a dose. This represents the cummulative drug level that is always present.

Examples:

Let $r = \frac{3}{4}$ be the fraction of the first dose remaining at dose number two. Then $\frac{1}{4}$ was lost (metabolized). The reciprocal of $\frac{1}{4}$ is 4, so $L = 4L_1$. And $L - L_1 = 4L_1 - L_1 = 3L_1$.

Fluctuation: Blood (or system) levels then fluctuate between $3L_1$ (just before dosing) to $4L_1$ (just after dosing). The increase from low to high is 33%.

Suppose dosing is at 24 hour intervals, and the half life is 12 hours. Then as we go from dose 1 to dose 2, we lose half of the blood level by 12 hours, and half of the remaining half by the 24 hours. Thus we lose 75% or $\frac{3}{4}$ of the blood level. The reciprocal of $\frac{3}{4}$ is $\frac{4}{3}$ so $L = \frac{4}{3}L_1$. The limiting peak level is only $\frac{4}{3}$ of the original level L_1. Since $L - L_1 = \frac{1}{3}L_1$, the fluctuation is from $\frac{1}{3}$ to $\frac{4}{3}$ or 400%.