

The Concentration Span from First to Full Effect Is Set Not by the Effective Concentration but by Cooperativity

— the 10 % to 90 % span is $81^{1/n}$ -fold and stays at 9.000000 for $n = 2$ even when the effective concentration moves ten-thousand-fold — the separator is whether one asks about position, the concentration at which it acts, or spread, the range over which it goes from starting to full effect — [Paper 878]

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Abstract

It is easy to assume that a potent drug is simply one that acts at a low concentration. This paper counts that the span from first effect to full effect is set by a different quantity from the effective concentration. No new theorem or law is claimed. First, the span is $81^{1/n}$ -fold: solving for 10 % and 90 % effect by bisection gives 6561-fold at $n = 0.5$, 81 at 1, 9 at 2 and 3 at 4, matching $81^{1/n}$ within a relative difference of 10^{-9} (Section 2). Second, and this is the core. Moving the effective concentration does not move the span: with $n = 2$, setting the effective concentration to 0.01, 1 and 100, ten-thousand-fold apart, gives a span of 9.000000 each time (Section 2). Third, two binding sites without mutual help still give a coefficient of 1: with independent sites, $n = 1.000000$ and the span is 81-fold, the same as a single site (Section 3). Fourth, stronger help narrows the span, but not beyond the number of sites: with a help factor c of 10, $n = 1.519494$; at 100, 1.818182; at 10000, 1.980198; the span narrows only to 9.243221-fold, never below 9 (Section 3). Fifth, numerical slopes match the formula: slopes computed numerically at half binding matched $2/(1 + 1/\sqrt{c})$ within 10^{-6} (Section 3). Sixth, the separator is whether one asks about position, the concentration at which it acts, or spread, the range over which it goes from starting to full effect: position is set by the effective concentration and spread by cooperativity, and the two move independently (Section 4). **Keywords:** Hill coefficient, dose-response, cooperativity, Adair equation, effective concentration.

Scope of this paper (scope note): No new theorem or law is claimed: the Hill equation, the $81^{1/n}$ -fold span from 10 % to 90 %, the Adair equation for two binding sites, and that its coefficient does not exceed the number of sites, are all known.No real values are claimed: concentrations and coefficients are model values matching no drug and no receptor.No advice is given. What amount should be used is not stated.Mechanisms are not entered: models in which a change of shape produces the mutual help, and binding rates, are not treated.Relation to earlier papers: Paper 679 showed that a buffer does not hold the pH but only the neighbourhood of its pKa. This paper stands beside it. There the span of an equation for one proton binding at one site was seen in pH. Here the same form of equation has its coefficient varied, counted through the mutual help of two binding sites.What is added is solving the span by bisection for four values of n and matching the formula, checking that moving the effective concentration ten-thousand-fold leaves the span unchanged, measuring slope and span for each help factor with two sites, and placing the separator on position versus spread.

1. Notation and the Question

Setting: the effect R at concentration C is given by the effective concentration EC_{50} (where the effect is half) and a coefficient n .Alongside it is the Adair equation for two binding sites, where c is how much binding at one site makes binding at the other easier.

$$R = \frac{C^n}{EC_{50}^n + C^n}, \quad \frac{C_{90}}{C_{10}} = 81^{1/n}, \quad \theta = \frac{x + cx^2}{1 + 2x + cx^2}$$

x is concentration multiplied by the affinity of one site, and θ the fraction bound.The coefficient was computed numerically as the slope of $\log(\theta/(1 - \theta))$ against $\log x$ at half binding.

Question: what sets the span of concentration from first effect to full effect?

2. Coefficient and Span

Computation 2.1: the concentrations for 10 % and 90 % effect were solved by bisection ($EC_{50} = 1$).

n	concentration at 10 %	at 90 %	span (fold)	span (decades)
0.5	0.012346	81.000000	6561.000000	3.816970
1	0.111111	9.000000	81.000000	1.908485
2	0.333333	3.000000	9.000000	0.954243
4	0.577350	1.732051	3.000000	0.477121

Observation 2.2

this is the core. Moving the effective concentration does not move the span. With $n = 2$ and effective concentrations 0.01, 1 and 100, the span was 9.000000-fold each time: the effective concentration only shifts the curve left or right; it does not change how steeply it rises. What narrows the span is n , and the bisection spans matched $81^{1/n}$ within a relative difference of 10^{-9} for all four n .

3. Two Binding Sites

Computation 3.1: varying the help factor c between two sites, the coefficient at half binding and the span from 10 % to 90 % were computed.

c	numerical coefficient	formula $2/(1 + 1/\sqrt{c})$	span (fold)
1	1.000000	1.000000	81.000000
10	1.519494	1.519494	20.436504
100	1.818182	1.818182	11.741239
10000	1.980198	1.980198	9.243221

Observation 3.2

the number of sites only caps the coefficient; mutual help sets it. With independent sites ($c = 1$) the coefficient is 1.000000 and the span 81-fold, the same as one site: stronger help raises the coefficient to 1.519494, 1.818182 and 1.980198 but never beyond 2, and the span narrows only to 9.243221-fold, not below the 9 of $n = 2$. Numerical coefficients matched the formula within 10^{-6} .

4. The Separator

Observation 4.1

the separator is whether one asks about position, the concentration at which it acts, or spread, the range over which it goes from starting to full effect. Position is set by the effective concentration, which shifts the curve: spread is set by cooperativity, which steepens its rise. The two move independently, so acting at a low concentration and changing effect sharply with a small change in concentration are different properties.

Observation 4.2

placed beside Paper 679.679 showed that a buffer holds only the neighbourhood of its pKa. There the span of an equation for one proton at one site was seen in pH. That equation has coefficient 1, taking 1.908485 decades from 10 % to 90 %. Here the coefficient of the same form was varied, counting that mutual help is what narrows the span.

Observation 4.3

what is not said. Real drug or receptor values, amounts to use, and mechanisms of help through shape change are not treated. What is shown is that the span of concentration is set not by the effective concentration but by cooperativity.

5. Census and Closing

1. span $81^{1/n}$ -fold (Section 1): **the Hill equation.**
2. **81-fold at $n = 1$** (Computation 2.1): **1.908485 decades.**
3. **9 at $n = 2$, 3 at $n = 4$** (Computation 2.1): **steeper.**
4. **9.000000 despite a ten-thousand-fold shift** (Observation 2.2): **the core.**
5. **bisection matches the formula** (Observation 2.2): **within 10^{-9} .**
6. **coefficient 1 with two independent sites** (Computation 3.1): **span 81.**
7. **1.519494 at $c = 10$** (Computation 3.1): **help raises it.**
8. **1.980198 at $c = 10000$** (Computation 3.1): **not beyond 2.**

9. **span down to 9.243221** (Observation 3.2): **not below 9.**

10. **position, or spread** (Observation 4.1): **the separator; Paper 679.**

Closing: The span of concentration from first effect to full effect is set not by the effective concentration but by the degree of cooperativity. The span from 10 % to 90 % is $81^{1/n}$ -fold, and with $n = 2$ it stays 9.000000-fold even when the effective concentration moves ten-thousand-fold, because the effective concentration only shifts the curve and does not change how steeply it rises. Even with two binding sites, without mutual help the coefficient is 1 and the span 81-fold, and however strong the help, the coefficient reaches only 1.980198 and the span does not narrow below 9.243221-fold: the number of sites only caps it; mutual help sets it. Placed among the earlier papers: beside the span of single-site binding that Paper 679 saw in pH, we placed what narrows the span in the same form of equation. To be honest: concentrations and coefficients are model values, and neither the mechanism of help nor binding rates are included.

References

1. Brunton, L. L., Hilal-Dandan, R., & Knollmann, B. C. (Eds.). (2018). *Goodman & Gilman's The Pharmacological Basis of Therapeutics* (13th ed.). McGraw-Hill.
2. Hill, A. V. (1910). The Possible Effects of the Aggregation of the Molecules of Haemoglobin on Its Dissociation Curves. *The Journal of Physiology*.
3. Yamagishi, Y. (2026). *A Buffer Does Not Hold the pH; It Holds Only the Neighbourhood of Its pKa* [Paper 679]. YOI: <https://www.yamagishiyuuki.com/yoi/679>; DOI: 10.5281/zenodo.23014789

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