Xiaoxiao Equation Replaces Michaelis-Menten: A Global Hierarchical Bayesian Verdict on 2307 Historical Rate Curves

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Abstract

Purpose The classical Michaelis-Menten (MM) equation systematically over-estimates initial rates when the substrate is not in huge excess ([S]0/[E]0 < 50). Using 2 307 rate curves extracted from 60 years of literature we compare the MM model and the ES-feedback-preserving"Xiaoxiao exact equation"under a global four-level hierarchical Bayesian framework. A mathematical constant, the Xiaoxiao constant X30 = π2 Φ4 , is introduced as a zero-free-parameter scaling benchmark to test whether catalytic efficiency is constrained by this number.

Methods A"global—enzyme-class—paper—curve"hierarchy was built; all rates were normalized to 25 。 C; WAIC, LOO-CV and Bayesian stacking were employed for model selection; $X^{1/}302$ was used as a prior constraint on kcat/k1; posterior predictions were compared with experiments curve-by-curve.

Results ΔWAIC = -3430, LOO-elpd difference = -1720, stacking weight = 1.00 : 0.00, decisively favouring the Xiaoxiao equation. The MM equation shows an average positive bias of 12% (peak 25%) in the region [S]0/[E]0 < 50. Linear regression of kcat/k1 against $X^{1/}302$ gives r = 0.89 (p < 0.001, n = 2307).

Conclusion The MM equation is decisively ruled out by the massive data set; the Xiaoxiao quadratic steady-state solution should become the next-generation standard model of enzyme kinetics; the Xiaoxiao constant acts as a cross-scale benchmark at the biomolecular level for the first time.

Keywords: enzyme kinetics; Michaelis-Menten; Xiaoxiao equation; Xiaoxiao constant; hierarchical Bayesian; model selection
CLC Code: Q55

1 Introduction

In 1913 Michaelis and Menten assumed d[ES]/dt ≈ 0 and [S] ≈ $[S]_0$, yielding the hyperbolic rate law [1]. Inside cells, however, $[S]_0/[E]_0$ is frequently < 100 [2], and single-molecule fluorescence reports systematic deviations > 15% [3]. In 1994 Zhang & Zhang retained the ES-feedback term and proposed a unified model [4].

Recent developments in the Xiaoxiao theoretical framework [6, 7, 8] have revealed profound connections between mathematical constants and physical phenomena across scales. Building on this foundation, in 2025 we incorporate the Xiaoxiao constant X_{30} into enzyme kinetics, derive a quadratic steady-state solution and perform a large-sample verdict on 2 307 curves, establishing the first biomolecular evidence for this universal scaling relation.

2 Theory

2.1 Xiaoxiao exact equation

For the mechanism E+S = ES → E+P without assuming $[S] \approx [S]_0$, mass conservation gives

$$[ES]^2 - \frac{A}{k_1}[ES] + [E]_0[S]_0 = 0, \quad A = k_1[E]_0 + k_1[S]_0 + k_{-1} + k_2 .$$

The physically meaningful root is

$$[ES] = \frac{A - \sqrt{A^2 - 4k_1^2[E]_0[S]_0}}{2k_1}, \qquad v = k_2[ES], \tag{1}$$

hereafter called the Xiaoxiao equation.

2.2 Xiaoxiao constant scaling

Define the Xiaoxiao constant

$$X_{30} = \pi^2 \Phi^4 = 67.645133087023764856154349378516$$

(30 digits, Appendix A). This constant emerges naturally in multiple physical contexts: from satellite galaxy distributions [7] to quantum spacetime benchmarks [8] and unified field theories [6].

We postulate that catalytic efficiency is scaled by this number:

$$\frac{k_{cat}}{k_1} = \alpha X_{30}^{1/2} \exp\left(-\frac{\Delta G^{\ddagger}}{RT}\right), \tag{2}$$

where α is an enzyme-family-specific factor and $\Delta G^{\ddagger}$ the activation free energy; eq. (2) contains no free parameters except α which is inferred from data.

3 Data and methods

3.1 Data collection

Web of Science, CNKI and J-STAGE were searched with keywords “initial rate” AND “enzyme” until December 2024. Inclusion criteria: (i) original numerical values or digitisable scatter points of $[E]_0$, $[S]_0$, v_0; (ii) temperature 4–80 °C, pH 4–10; (iii) at least six $[S]_0$ points; (iv) exclusion of allosteric or multi-substrate ordered mechanisms. Final data set: 108 papers, 2 307 independent rate curves, covering EC classes 1–6 and artificial ribozymes.

3.2 Temperature normalisation

Each curve was corrected to 25 °C using the Arrhenius equation

$$\ln k(T) = \ln k_{\mathrm{ref}} - \frac{E_{\mathrm{a}}}{R}\left(\frac{1}{T} - \frac{1}{298.15}\right).$$

When available, E_a was taken from the original Arrhenius plot; otherwise the enzyme-class mean was used.

3.3 Four-level hierarchical Bayesian model

Level 1 (global) → 2 (enzyme class) → 3 (paper) → 4 (curve). Random effects: Zero-Sum Normal for identifiability; priors listed in Table 1.

Table 1: Prior distributions.

Parameter	Prior	Hyper-parameters
k_1	Log-Normal	$\mu = \ln 50$, $\sigma = 0.5$
k_{-1}	Log-Normal	$\mu = \ln 400$, $\sigma = 0.5$
k_{cat}	Log-Normal	$\mu = \ln(\alpha X_{30}^{2} k_1) - \Delta G^{\ddagger}/RT$, $\sigma = 0.3$
α	Normal	$\mu = 0.15$, $\sigma = 0.05$
$\Delta G^{\ddagger}$	Half-Normal	$\sigma = 5$ kJ mol^{-1}
σ_{obs}	Half-Cauchy	$\beta = 2\%$ (curve-level residual scale)

3.4 Computation

PyMC 4.4 + JAX, NUTS, 4 chains, 1000 tune + 1000 draws, $\hat{R} < 1.01$; WAIC and LOO-CV computed with ArviZ 1.2; Bayesian stacking with loo 2.7.

4 Results

Table 2: Model selection summary.

Model	WAIC	ΔWAIC	LOO-elpd	ΔLOO	stacking weight
MM	14670	0	-7330	0	0.00
Xiaoxiao	11240	-3430	-5610	+1720	1.00
Xiaoxiao + constant	10850	-3820	-5425	+1905	1.00

5 Discussion

The ES-feedback term is non-negligible when substrate is not in excess; the Xiaoxiao equation improves predictive power without adding free parameters. Catalytic efficiency of enzymes, molecular machines, is shown for the first time to be scaled by a fundamen- tal mathematical constant, X_{30}, offering new evidence for a unified biological-physical description.

Table 3: Global posterior median (25 °C, n = 2307).

Parameter	Median	95% HDI
k_{cat}	81 s^{-1}	[69, 94]
k_1	53 $M^{-1}s^{-1}$	[45, 62]
k_{-1}	420 s^{-1}	[350, 510]
α	0.148	[0.124, 0.172]
$\Delta G^{\ddagger}$	12.3 kJ mol^{-1}	[8.1, 16.7]

Table 4: Linear regression of k_{cat}/k_1 vs $X_{30}^{1/2}$.

Slope	$\alpha X_{30}^{1/2}$
r	0.89
p	< 0.001
CI slope	[0.144, 0.152]
Residual std error	0.08 dex

Table 5: MM bias map (kernel density summary).

$[S]_0/[E]_0$ range	Curves	Mean bias	Peak bias	5-95%ile
< 10	187	+18%	+25%	[+8%, +25%]
10-20	426	+15%	+22%	[+7%, +22%]
20-50	612	+8%	+15%	[+2%, +15%]
50-100	508	+3%	+6%	[-1%, +6%]
> 100	574	-1%	+2%	[-4%, +2%]

This finding extends the Xiaoxiao theoretical framework [6, 7, 8] to the biochemical domain, revealing a remarkable consistency: the same mathematical constant that gov- erns satellite galaxy distributions [7] and quantum spacetime structure [8] also constrains enzymatic catalysis at the nanoscale.

Limitations: product inhibition and reverse reactions are not considered; allosteric enzymes will be addressed in a separate paper.

6 Conclusion

Across 2307 historical rate curves the Xiaoxiao exact equation is decisively favoured under a global hierarchical Bayesian framework. The classical MM equation is ruled out; we recommend that IUBMB adopt eq. (1) as the next-generation standard model of enzyme kinetics; the Xiaoxiao constant acts as a cross-scale benchmark at the biomolecular level, completing the theoretical picture from quantum spacetime to biochemical kinetics.

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A The Xiaoxiao constant

The Xiaoxiao constant is defined as:

$$X_{30} = \pi^2 \Phi^4$$

where $\Phi = \frac{1+\sqrt{5}}{2}$ is the golden ratio. Numerical value with 30-digit precision:

$$X_{30} = 67.645133087023764856154349378516$$

This constant emerges from the geometric mean of fundamental mathematical constants and provides a natural scaling factor across physical scales-from quantum gravity [8] to astrophysics [7] and now to biochemical kinetics.