

# Determination of Initial Rates for a General Class of Chemical Reactions: A Methodology

LOUIS J. PISCITELLE

*U.S. Army Natick Research Development and Engineering Center,  
Natick, Massachusetts 01760*

## Abstract

The initial rate of any general  $n$ th order ( $n$  not necessarily integer) chemical reaction can be accurately and easily computed from the slope of a chord joining two points on the progress curve. Expressions for calculating the intermediate concentration corresponding to this initial rate are provided. Examples of the technique applied to second- and third-order reactions as well as an example of a reaction with fractional order ( $n = 0.6$ ) are given.

## Introduction

Waley [1], proposed a method for determining the initial rate of an enzyme-catalyzed reaction. The technique required only the measurement of the slope of a chord joining two points on the progress curve. This technique is useful because the measurement of a tangent to the progress curve can be quite unreliable (Walter and Barrett [2]; Philo and Selwyn [3]; Nimmo and Mabood [4]; and Atkins and Nimmo [5]), but the measurement of a chord's slope can be performed simply and accurately. The formula derived by Waley [1] to determine the concentration corresponding to the rate given by the slope of the chord is based upon a reaction for which the Michaelis-Menten steady state hypothesis holds. Waley [1] states that when the integrated Michaelis-Menten equation does not hold, a differentiation rule can be useful.

The chord method introduced by Waley [1] will be extended to a general class of reactions. In particular, the technique will be shown to apply to any  $n$ th order reaction ( $n$  not necessarily an integer). This extension of the method will enable the experimentalist to determine initial rates quickly and accurately from the progress curve for a wide variety of reaction mechanisms.

## Results and Discussion

Consider a general  $n$ th order reaction for which the rate of change in the concentration of material S is given by the following differential equation. (Dot denotes differentiation with respect to time.)

$$(1) \quad \dot{s} = -ks^n, \quad s = s_0 \quad @ \quad t = 0.$$

The integrated form of eq. (1) is

$$(2(a)) \quad t = \frac{ss_0^n - s^n s_0}{k(n-1)s^n s_0^n} \quad \text{for } n \neq 1$$

and

$$(2b) \quad t = \frac{\ln\left(\frac{s_0}{s}\right)}{k} \quad \text{for } n = 1.$$

If a chord is drawn joining points  $(t_1, s_1)$  and  $(t_2, s_2)$  on a progress curve for the substrate concentration vs. time, the chord's slope is easily calculated and is given by  $(s_2 - s_1)/(t_2 - t_1)$ . By the mean value theorem for a continuously differentiable function on the open interval  $(t_1, t_2)$ , there exists at least one point  $t_3$  between  $t_1$  and  $t_2$  such that  $\dot{s}$  at  $t_3$  equals the slope of the chord (Thomas [6]). Let  $s_3$  be the intermediate substrate concentration corresponding to  $t_3$ . Using eqs. (1) and (2),  $s_3$  may be determined. First substitute  $s_3$  for  $s$  in eq. (1) and use the fact that  $\dot{s}|_{t=t_3}$  is given by  $(s_2 - s_1)/(t_2 - t_1)$ . The result is

$$(2c) \quad -ks_3^n = \frac{(s_2 - s_1)}{(t_2 - t_1)}$$

Now, eq. (2(a)) or (2(b)) may be used to write  $t_2$  and  $t_1$  in terms of  $s_2$  and  $s_1$ , respectively. These results when substituted into eq. (2(c)) yield a relationship between  $s_1$ ,  $s_2$ , and  $s_3$  which may be solved for  $s_3$  in terms of  $s_1$  and  $s_2$ . The result is independent of the rate constant  $k$  and is given by:

$$(3a) \quad s_3 = \left( \frac{(n-1)(s_1 - s_2)(s_1 s_2)^{n-1}}{s_1^{n-1} - s_2^{n-1}} \right)^{1/n} \quad \text{for } n \neq 0, 1$$

and

$$(3b) \quad s_3 = \frac{(s_1 - s_2)}{\ln\left(\frac{s_1}{s_2}\right)} \quad \text{for } n = 1.$$

Note the trivial case  $n = 0$  is neglected.

Hence, if the reaction were to begin with  $s_0 = s_3$ , the initial rate would be  $(s_2 - s_1)/(t_2 - t_1)$ . To obtain the actual initial rate one more simple step is required. Assuming the points  $(t_1, s_1)$ ,  $(t_2, s_2)$  have been taken far enough apart to reduce the error introduced by any scatter in the data, the previously calculated chord slope  $(s_2 - s_1)/(t_2 - t_1)$  and the corresponding concentration  $s_3$  (obtained from eq. (3(a)) or (3(b))) may now be used to compute the actual initial rate. By eq. (1),

$$(4a) \quad \dot{s}|_{t=t_0} = -ks_0^n$$

and

$$(4b) \quad \dot{s}|_{t=t_3} = -ks_3^n$$

Dividing eq. (4(a)) by eq. (4(b)) and simplifying gives

$$(4c) \quad \dot{s}|_{t=t_0} = \dot{s}|_{t=t_3} \left( \frac{s_0}{s_3} \right)^n$$

or

$$(4d) \quad \dot{s}|_{t=t_0} = \frac{(s_2 - s_1)}{(t_2 - t_1)} \left( \frac{s_0}{s_3} \right)^n$$

It is interesting to observe that the relationship of  $s_3$  to  $s_1$  and  $s_2$  given by eq. (3(b)) for a first order reaction is identical to the result Waley [1] obtains when the Michaelis-Menten equation is obeyed. In one sense, this fact is obvious. The differential equation for Michaelis-Menten kinetics is:

$$(5(a)) \quad \dot{s} = -\frac{Vs}{K_m + s}$$

It is well known that when  $s \ll K_m$ , eq. (5(a)) is identical to eq. (1) with  $n = 1$  and  $k = V/K_m$ , that is, first order. Hence one would "expect" the observed result. However if one looks at the integrated form of the Michaelis-Menten equation:

$$(5(b)) \quad t = \frac{(s_0 - s)}{V} + \frac{K_m}{V} \ln\left(\frac{s_0}{s}\right)$$

and compares this with eq. (2(b)), it is not quite so obvious a result. The result may be shown by considering the chord's slope  $(s_2 - s_1)/(t_2 - t_1)$  and using eq. (5(b)) to compute the denominator:

$$(6) \quad t_2 - t_1 = \frac{K_m}{V} \ln\left(\frac{s_1}{s_2}\right) + \frac{(s_1 - s_2)}{V}$$

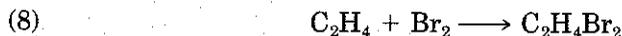
When  $s_1, s_2 \ll K_m$ , the first term on the right hand side of eq. (6) is dominant since  $s_1 > s_2$  causes  $\ln(s_1/s_2) > 1$ . This is exactly the result for  $t_2 - t_1$ , which eq. (2(b)) gives with  $k = V/K_m$ . Since eqs. (5(a)) and (6) hold for the entire time the reaction is proceeding and approach the respective equations for a first order reaction as  $s$  goes to zero, the result is proved.

Waley [1] does not observe this result and in fact states that if the reaction does not obey the Michaelis-Menten equation a numerical scheme may be useful. The chord method is merely the application of the mean value theorem of calculus and as such should be expected to work for a variety of common reactions, as has just been demonstrated.

The result for a second order reaction is given by:

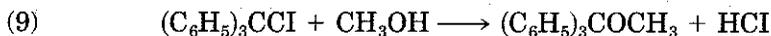
$$(7) \quad s_3 = (s_1 s_2)^{1/2}$$

An important observation concerning the extension of the method is its application to the kinetics of heterogeneous gas reactions. The bromination of ethylene at the walls of a glass vessel:



is a reaction where both reactants are weakly absorbed and the rate expression for the bimolecular heterogeneous reaction is second order in the gas pressure (Stevens [7]). Hence for this case, with the gas pressure being a measure of concentration, eq. (7) would be applicable. Stevens [7] also states that when the reactants are moderately absorbed (as in the case for the decomposition of  $\text{SbH}_3$  on an antimony surface at  $20^\circ\text{C}$ ), the rate expression is given by eq. (1) with  $n = 0.6$ . The resulting value of the intermediate gas pressure, at which the reaction velocity is that given by the slope of the chord to the progress curve, may be obtained from eq. 3(a) with  $n = 0.6$ . If the chord is chosen so that the gas pressure at the right end of the chord  $p_2$  is half that at the left end, the intermediate pressure  $p_3$  is very simply given by  $p_3 \approx 1.454p_2$ .

As a last example, consider the reaction of triphenylmethyl chloride with methanol. Emanuel [8] gives the following stoichiometric equation



and states that the reaction is third-order since one more  $\text{CH}_3\text{OH}$  molecule is involved and acts as a catalyst. Emanuel [8] gives the rate equation for the product as:

$$(10) \quad \dot{x} = k(A_{1o} - x)(A_{2o} - x)^2,$$

where the concentrations of triphenylmethyl chloride and methanol are denoted by  $A_1$  and  $A_2$ , respectively. As before, subscript  $o$  represents initial values. While this rate equation appears different from eq. (1), the same technique applies. If the initial concentrations of the reactants are equal, then with a simple linear transformation on  $x$ , the equation becomes equivalent to eq. (1). If as in Emanuel [8] the concentrations are not equal, the modified chord method may still be applied but the algebra becomes more involved. To simplify the work, the product and initial concentrations are transformed by:

$$(11(a),(b)) \quad z = A_{2o} - x \quad \text{and} \quad A_3 = A_{1o} - A_{2o}.$$

Substituting eqs. 11(a) and 11(b) into eq. (10) and integrating, we can compute the concentration  $z_3$ , at which the reaction would have a rate equal to that given by the slope of a chord to the progress curve, which is given by:

$$(12) \quad z_3^2(z_3 + A_3) = \frac{z_1 A_3^2 z_2 (z_2 - z_1)}{z_2 \left( z_1 \ln \left( \frac{z_1 A_3 + z_1 z_2}{z_2 A_3 + z_1 z_2} \right) + A_3 \right) - z_1 A_3}.$$

When appropriate values for the initial concentrations of triphenylmethyl chloride and methanol and chord endpoints are used in eq. (12), the cubic is easily solved for  $z_3$ . Emanuel [8] gives experimental data for the production of product based upon  $A_{1o} = 0.106$  mol/l and  $A_{2o} = 0.054$  mol/l. The concentration of product is given as 0.0207 mol/l and 0.0318 mol/l at 444 min and 1150 min, respectively. Based upon these values eq. (12) gives a value for  $z_3$ , which corresponds to a product concentration of 0.0268 mol/l. At this concentration the reaction rate is equal to the slope of the chord (marked A in Fig. 1) connecting these two points on the progress curve.

This information may now be used to compute the initial rate of reaction. From eq. (10);

$$(13) \quad \dot{x}|_{t=t_0} = kA_{1o}A_{2o}^2$$

and

$$(13(a)) \quad \frac{(x_2 - x_1)}{(t_2 - t_1)} = \dot{x}|_{t=t_3} = k(A_{1o} - x_3)(A_{2o} - x_3)^2$$

Thus using the same procedure as was previously demonstrated for a general  $n^{\text{th}}$  order reaction (eqs. (4(a)–(d)) one obtains

$$(14) \quad \dot{x}|_{t=t_0} = \frac{A_{1o}A_{2o}^2}{(A_{1o} - x_3)(A_{2o} - x_3)^2} \frac{(x_2 - x_1)}{(t_2 - t_1)}$$

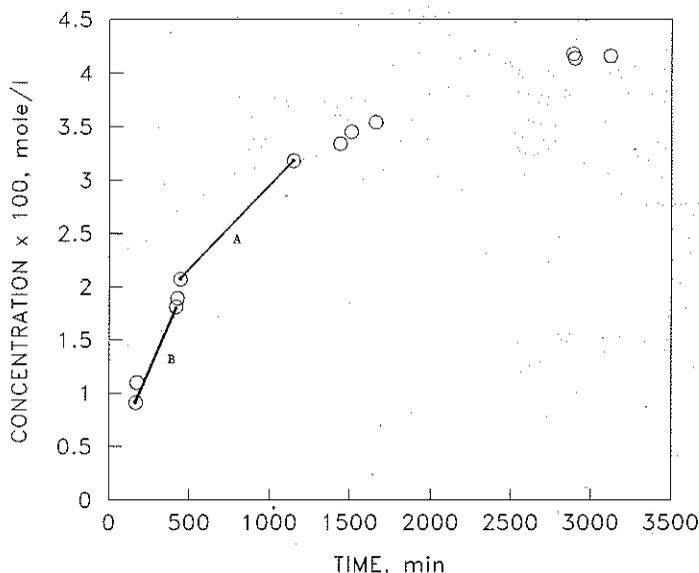


Figure 1. Reaction of Triphenylmethyl chloride with methanol.

Thus, for  $x_3 = 0.0268$ , the initial rate obtained from eq. (14) is  $0.0000833 \text{ mol}/(l - \text{min})$ . Emanuel [8], experimentally determined an initial rate of  $0.0000807 \text{ mol}/(l - \text{min})$ . Hence, the initial rate computed by the chord method is within 3% of Emanuel's value.

In all of the cases described in this article, the results obtained may be used to compute the value of  $k$ . Note that one may simply use the computed chord slope and the calculated concentration corresponding to this rate to compute the  $k$  for the reaction. This may be repeated at a number of places along the progress curve to obtain an average value in the event there exists scatter in the progress curve data.

This idea may be easily illustrated for the reaction described by the rate eq. (10). Based upon the previous calculation in which a product concentration of  $0.0268 \text{ mol}/l$  was computed,  $k$  the third order rate constant may be evaluated. The resulting  $k$  is  $.2967 \text{ l}^2/(\text{mol}^2 - \text{min})$ . Earlier in the reaction the concentration of product is given as  $0.0091 \text{ mol}/l$  and  $0.0181 \text{ mol}/l$  at 168 and 418 min, respectively. Based upon the slope of the chord marked B in Figure 1 and the  $z_3$  calculated from eq. (12), eqs. (10) and (11) give a  $k$  value of  $0.2428 \text{ l}^2/(\text{mol}^2 - \text{min})$ . The average  $k$  value based upon these two results is  $0.2698 \text{ l}^2/(\text{mol}^2 - \text{min})$  which is in good agreement with the calculated average of  $0.261 \text{ l}^2/(\text{mol}^2 - \text{min})$  obtained by Emanuel [8].

In conclusion, it has been demonstrated that the chord method (Waley [1]) may be extended to reactions of arbitrary order  $n$ . Examples of reactions with fractional order, second, and third order have been presented to demonstrate the versatility and simplicity of the extended chord method.

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### Bibliography

- [1] S. G. Waley, *Biochem. J.*, **193**, 1009 (1981).
- [2] C. Walter and M. J. Barrett, *Biochem. Biophys. Acta*, **480**, 1 (1970).
- [3] R. D. Philo and M. J. Selwyn, *Biochem. J.*, **135**, 525 (1973).
- [4] I. A. Nimmo and S. F. Mabood, *Anal. Biochem.*, **94**, 265 (1979).
- [5] G. L. Atkins and I. A. Nimmo, *Anal. Biochem. Soc. Trans.*, **6**, 545 (1980).
- [6] G. B. Thomas, *Calculus and Analytic Geometry*, Addison-Wesley Publishing Co., Reading, Massachusetts, 1986, p. 132.
- [7] B. Stevens, *Chemical Kinetics*, Chapman & Hall, London, 1961, p. 64.
- [8] N. M. Emanuel, *Chemical Kinetics*, John Wiley & Sons, New York, 1973, p. 184.

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