

## The Viscosity of Degrading Polymer Solutions

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The viscosity of a polymer solution is calculated as a function of time for several simplified degradation models, assuming the validity of Staudinger's rule. It is shown how the theoretical results may be compared with measurements obtained using an Ostwald viscometer, which only give a sliding time average of the viscosity, and finally the application of the present very crude theories to enzymatic reactions is discussed. The theoretical results obtained are compared with the experiments of Andersen and Graae on the enzymatic hydrolysis of hyaluronic acid.

In his classical work on the degradation of high polymers W. Kuhn<sup>1</sup> derived an approximate expression for the molecular weight distribution in a sample which before degradation had been monodisperse and of virtually infinite molecular weight. The derivation was based on statistical considerations, and the results are only valid for samples with an average molecular weight small compared to that of the initial sample.

His results have been rederived several times. Sakurada and Okamura<sup>2</sup> used a method similar to Kuhn as did Montroll and Simha<sup>3</sup>. The latter authors, however, generalized the results to be valid for polymers with finite initial molecular weight. Simha<sup>4</sup> and Sillén<sup>5</sup> derived similar results, using a kinetic model which is essentially identical with the first model to be discussed in this paper.

Hultin<sup>6</sup> has used the results of Sillén to derive an approximate expression for the excess viscosity of a solution of a degrading polymer as a function of time. In this derivation is used a limiting process in which it is implicitly assumed that a long time  $t$  has elapsed since the start of the experiment. The result obtained, namely that the excess viscosity is proportional to  $t^{-1}$ , is therefore meaningless in the limit  $t \sim 0$ .

It is the aim of this paper to derive formulae for the viscosity for the model discussed by Sillén and for a few other models which may be relevant in connection with the work on enzymatic degradation of high polymers. To do so we shall make use of a different limiting process and obtain results which are correct for all times, in particular for  $t = 0$ . One of the formulae we obtain may be found in Sillén's work too, but there it is stated that it is only an

approximation. We shall show that the result can be derived without approximations save for the trivial one of assuming that the molecular weight of the initial sample is virtually infinite. Finally we want to discuss the applicability of the present very crude theory to systems where the degradation is caused by enzymes.

#### GENERAL ASSUMPTIONS

The usual model of a degrading polymer is a chain where each link has the same probability of breaking per unit time. Furthermore this probability is independent of the number of bonds in the molecule. It is believed that this is a fairly realistic picture, and therefore we shall first consider this model, but since there is experimental evidence that some polymers, *e. g.* hyaluronic acid<sup>7</sup> may have a preference for breaking in the middle when degraded enzymatically, we also investigate a crude model where the molecules split exclusively in the middle. In this model we can, because of its simplicity, introduce that the probability of splitting the central bond depends on the chain length.

Throughout the paper we shall assume the validity of Staudinger's rule<sup>8</sup>, *viz.*

$$\eta_n = k c_n M_n^2 \quad (1)$$

in which  $\eta_n$  is the increase in viscosity caused by a solute of molar concentration  $c_n$  and molecular weight  $M_n$ , and  $k$  is a constant. The general validity of this rule may well be questioned, and it is well to bear in mind that the following considerations apply only to polymers which follow the Staudinger rule. In the case of hyaluronic acid this has been shown experimentally<sup>9</sup>.

Furthermore we shall assume that for a solution of several species the excess viscosity is additive, *viz.*

$$\eta = \sum \eta_n = k \sum c_n M_n^2 \quad (2)$$

Our last general assumptions are that the degradation is such that the end-product is a repeated unit in the macromolecule which is the starting material, although not necessarily the smallest repeated unit, and that the initial high polymer is monodisperse. We shall indicate below, however, how this last assumption could be dispensed with.

Let the weight of the repeated unit be  $M$ . We then have  $M_n = nM$ , and

$$\eta(t) = k \sum_n c_n(t)(nM)^2 = k' \sum_n n^2 c_n(t) \quad (3)$$

so that, except for a constant factor,  $\eta(t)$  is the second moment of the molecular weight distribution.

Following Andersen and Graae<sup>10</sup> we shall denote the reduced excess viscosity  $\eta(t)/\eta(t=0)$  by  $y(t)$ . We then have  $y = 1$  for  $t = 0$  and, loosely speaking,  $1-y$  is a degree of advancement.

MODELS OF DEGRADATION

We shall now study a few simple models. In each case we start by stating the additional assumptions we make for the particular model.

Model 1

Assumption: All bonds between repeated units split with equal probability ( $w$ ) per unit of time.

Notation:  $c_k$  is the concentration of molecules of molecular weight  $kM$ .  
 $NM$  is the molecular weight of the initial substance.  
 $k-1$  is the number of bonds in the molecule with concentration  $c_k$ .

The equations for the time-dependence of the concentrations are thus:

$$\begin{aligned}
 c_N &= -w(N-1)c_N \\
 \cdot &\cdot \cdot \\
 \cdot &\cdot \cdot \\
 \cdot &\cdot \cdot \\
 c_k &= 2w \sum_{i=k+1}^N c_i - (k-1)wc_k \\
 \cdot &\cdot \cdot \\
 \cdot &\cdot \cdot \\
 \cdot &\cdot \cdot \\
 c_1 &= 2w \sum_{i=2}^N c_i
 \end{aligned} \tag{4}$$

By straight-forward integration we get for  $c_k(0) = \delta_{kN}$  (that is,  $c_k = 1$  for  $k = N$ , and otherwise zero)

$$\begin{aligned}
 c_N &= e^{-(N-1)wt} \\
 c_{N-1} &= 2e^{-(N-2)wt} - 2e^{-(N-1)wt} \\
 c_{N-2} &= 3e^{-(N-3)wt} - 4e^{-(N-2)wt} + e^{-(N-1)wt} \\
 \cdot &\cdot \cdot \\
 \cdot &\cdot \cdot \\
 \cdot &\cdot \cdot \\
 c_2 &= (N-1)e^{-wt} - 2(N-2)e^{-2wt} + (N-3)e^{-3wt} \\
 c_1 &= N - 2(N-1)e^{-wt} + (N-2)e^{-2wt}
 \end{aligned} \tag{5}$$

These expressions we insert in

$$\eta = k' \sum_n n^2 c_n$$

and get

$$\eta = k' \left[ N + 2N \sum_{n=1}^{N-1} e^{-nwt} - 2 \sum_{n=1}^{N-1} ne^{-nwt} \right]$$

or

$$y = \frac{1}{N^2} \left[ N + 2N \sum_{n=1}^{N-1} e^{-nwt} - 2 \sum_{n=1}^{N-1} ne^{-nwt} \right] \quad (6)$$

which is the final expression for  $y(t)$ .

It is easily verified that these expressions for the excess viscosity are identical with the one derived by Sillén: (our notation)

$$\eta = k' \left\{ \frac{1 + e^{-wt}}{1 - e^{-wt}} - \frac{2e^{-wt}(1 - e^{-Nwt})}{N(1 - e^{-wt})^2} \right\}$$

The expression for  $y(t)$  can be simplified considerably by letting  $N \rightarrow \infty$ , but this limiting process can be carried out in different ways.

Sillén argued that for  $N \rightarrow \infty$ , one will have

$$\eta \sim \frac{1 + e^{-wt}}{1 - e^{-wt}} = \coth \frac{wt}{2}$$

since the last term on the right hand side in the expression for  $\eta$  contains  $N^{-1}$ . This limiting process corresponds to increasing the size of the molecule, keeping the size of the repeated unit constant. This leads to an infinite viscosity at  $t = 0$ , whereas the measured viscosity of course is finite, but at the same time the unnormalized probability of breaking some bond goes to infinity as  $(N-1)w$ . Therefore the viscosity calculated using this approximation is infinite at  $t = 0$ , but its rate of change is infinite also, and so the expression  $\eta \sim \coth wt/2$  may be a useful approximation at some later time.

The reason for the inconsistency in the result derived above is that one cannot let  $N$  go to infinity separately without changing  $M$  and  $w$ . What is required is to go from the discrete model to a continuous model, *i. e.*, a model where the molecule consists of infinitely many repeated units with infinitely small mass. We let  $N \rightarrow \infty$  and at the same time  $M \rightarrow 0$  so that  $NM$  stays constant. During this limiting process the number of bonds in a molecule goes to infinity too, but since  $Nw$  is an observable quantity practically equal to the rate constant in the first order expression for the disappearance of the initial polymer, we must let  $w \rightarrow 0$  such that  $Nw$  stays constant ( $= \alpha$ ).

We therefore have

$$\begin{aligned} y &= \lim_{\substack{N \rightarrow \infty \\ w \rightarrow 0}} \frac{1}{N^2} \left[ N + 2N \sum_{n=1}^{N-1} e^{-nwt} - 2 \sum_{n=1}^{N-1} ne^{-nwt} \right] \\ &= \frac{2(\alpha t - 1 + e^{-\alpha t})}{\alpha^2 t^2} \end{aligned} \quad (7)$$

Table 1.  $\Theta$  as a function of  $y$  (eqn. 7).

$y$	0.5	0.4	0.3	0.2	0.1
0.5 +	0.0000	0.3247	0.7101	1.1796	1.7720
0.0 +	2.5569	3.6733	5.4486	8.8732	18.9443

It is easily verified that  $y(0) = 1$  as it should be.  $\dot{y}(0) = -\alpha/3$  which can be used in fitting the expression to experimental data. For  $at \gg 1$  we have  $y \sim t^{-1}$  which is the result obtained by Hultin using the other limiting process.

When one wants to compare the theoretical result with experiments it is convenient to introduce a dimensionless quantity  $\Theta = at$ . In terms of this we have

$$y = \frac{2(\Theta - 1 + e^{-\Theta})}{\Theta^2} \quad (8)$$

Table 1 is a tabulation of  $\Theta(y)$  which can be compared with  $t(y)$  which one gets from experiments and thereby give a determination of  $\alpha$ . The data given below for hyaluronic acid do not fit this expression.

So far we have only considered the case where the initial polymer is monodisperse. Although one can in general approximate this fairly well experimentally, it would be interesting to study the case where one starts with an arbitrary initial distribution. We plan to return to this problem in a later publication, but we shall here briefly indicate how, in our mind, this problem best could be attacked. Eqn (4) is rewritten as

$$\dot{c}_k = 2Nw \sum_{i=k+1}^N c_i \frac{1}{N} - N^{-1}(k-1) Nwc_k$$

and we see that in the limit  $N \rightarrow \infty$ ,  $w \rightarrow 0$ ,  $Nw \rightarrow \alpha$  we can introduce the continuous variable  $\xi = k/N$  such that  $c = c(\xi, t)$  satisfies the integral equation

$$\frac{\partial c}{\partial t} = 2\alpha \int_{\xi}^1 c d\xi - \alpha \xi c \quad (9)$$

which can be rewritten as

$$\frac{\partial^2 c}{\partial \xi \partial t} + \alpha \xi \frac{\partial c}{\partial \xi} + 3\alpha c = 0 \quad (10)$$

after differentiation with respect to  $\xi$ . To see the influence of an initial polydispersity this equation is solved subject to the initial condition  $c(\xi, 0) = f(\xi)$  where  $f(\xi)$  is the molecular weight distribution at time zero.

The model discussed above is reasonable when we consider, for instance, a thermal degradation of the macromolecule, since Pelzer has shown<sup>11</sup> that

for a linear chain the probability of breaking a bond by a unimolecular mechanism is to a first approximation independent of the position of the bond in the molecule and of the molecular weight. When we consider a catalyzed decomposition it may no longer be a reasonable assumption. In particular when we consider an enzymatic decomposition it is in all probability a poor approximation to assume that all bonds break with equal probability, since the enzyme itself is a rather bulky molecule which has to be fitted onto a certain pattern in the degrading macromolecule.

As mentioned above<sup>7</sup> there is experimental evidence that some polymers break preferentially to give very large fragments. We shall now investigate a model where this feature has been further simplified so that we consider molecules which split exclusively in the middle.

### Model 2

Assumption: The molecules split only in the middle.

Notation:  $c_k$  is the concentration of the molecules with molecular weight  $NM2^{-k}$   
 $w_k$  is the probability that the  $k$ 'th molecule will break.

2A. (trivial case)  $w_k = w$  (all  $k$ )

We have

$$\dot{c}_n = -wc_n + 2wc_{n-1} \quad (11)$$

It is convenient to use the generating function:

$$G(x,t) = \sum_n c_n(t)x^n \quad (12)$$

since evidently  $y = G(\frac{1}{4}, t)$ . Multiplying the original differential equation with powers of  $x$  and summing we get

$$\frac{\partial G}{\partial t} = -w(1-2x)G \quad (13)$$

i. e.,  $G = e^{-w(1-2x)t}$

$$y = e^{-\frac{1}{2}wt} \quad (14)$$

This case which is in itself without any interest shows the method we shall use to get  $y$  directly from the kinetic equations in the more complicated cases.

We shall now let  $w_k$  depend on  $k$ . For an enzymatic decomposition it is reasonable to assume that this dependence is such that  $w_k$  decreases when  $k$  increases, since supposedly the enzyme is one suited for decomposition of the original macromolecule. By introducing this in the model we hope to be able to account, for instance, for the rapid initial decrease in viscosity which is

characteristic of the degradation of hyaluronic acid. The initial decrease during which the excess viscosity drops to about one third of its initial value is followed by a very slow decrease.

The simplest dependence is  $w_k = w 2^{-k}$  ( $w$  being a constant) so that  $w_k$  is proportional to the molecular weight of the molecule to which it belongs. This model therefore resembles model 1 somewhat, only here all the probability of breaking a bond is located at one particular bond.

2B. Assumption:  $w_k = w 2^{-k}$  ( $w$  constant)

This gives the following equation for  $c_k$ :

$$\dot{c}_k = -w 2^{-k} c_k + 2w 2^{-k+1} c_{k-1} \tag{15}$$

From this we get the equation for the generating function:

$$\frac{\partial}{\partial t} G(x,t) = -w(1 - 2x)G\left(\frac{x}{2}, t\right) \tag{16}$$

To solve this we use the Laplace transformation, introducing

$$g(x,s) = \int_0^\infty e^{-st} G(x,t) dt$$

We have then

$$s g(x,s) - 1 = -w(1 - 2x)g\left(\frac{x}{2}, s\right) \tag{17}$$

and making a power series expansion of  $g$

$$g(x, s) = \sum_{n=0}^\infty S_n(s) x^n \tag{18}$$

we get by comparing terms

$$\begin{aligned} S_0 &= \frac{1}{w + s} \\ \vdots & \\ S_n &= \frac{w}{2^{n-2} \left( s + \frac{w}{2^n} \right)} S_{n-1} \\ \vdots & \end{aligned} \tag{19}$$

Transforming back we obtain

$$y = \sum_{n=0}^{\infty} A_n e^{-wt/2^n} \quad (20)$$

$$\text{with } A_0 = \frac{1}{3} - \frac{1}{3 \cdot 7} + \frac{1}{3 \cdot 7 \cdot 15} - \frac{1}{3 \cdot 7 \cdot 15 \cdot 31} + \dots \quad (21)$$

$$\text{and } A_n = 2^{(n^2-n)/2} \prod_{k=1}^n \frac{1}{2^k - 1} A_0 \quad (22)$$

Since  $A_{n+1}/A_n \sim 1/2$ , the series for  $y$  converges for all fixed  $t$ . It is convenient to consider  $y$  as a function of  $\Theta = wt$ . We have

$$\left[ \frac{dy}{d\Theta} \right]_{\Theta=0} = - \sum 2^{-n} A_n = - \frac{1}{2} \quad (23)$$

which can be used in fitting the theory to experimental data. Because of the rapid convergence of the above series it is easy to calculate a sufficient number of points.

It is interesting to note that this complicated expression gives values for  $y(\Theta)$  which almost coincide with those given by the expression derived for model 2A, *viz.*  $y = \exp(-\frac{1}{2} \Theta)$ . The slopes for  $\Theta = 0$  are the same, and in the range  $1 < y < 0.35$  the difference  $y_B - y_A$  is only 1–2 %. For smaller  $y$  this difference increases rapidly, being about 20 % for  $y \sim 0.2$ . This shows clearly how accurately one must measure in order to be able to decide between two models of this kind. Furthermore it shows that the last mentioned theory does not give any abrupt change in  $y$  as we might have hoped.

If we want to keep the idea of molecules breaking in the middle only and obtain the above mentioned abrupt change in viscosity we must change the dependence of  $w_k$  on  $k$  rather drastically. The only simple relationship we have been able to find which gives a reasonable result is one where  $w_k$  has a constant value for all molecules above a certain size and another constant value for molecules with smaller molecular weight. If we consider an enzymatic process, this corresponds to an enzyme which has a selective catalytic effect on large, resp. small molecules.!

### Model 3

- Assumptions: 1. Molecules break in the middle only  
 2. For molecules with a molecular weight  $> M^*$  the rate-constant is  $w_1$ , for molecules with molecular weight  $\leq M^*$  the rate-constant is  $w_2$ .

Notation:  $w_2 = \frac{1}{2} \overline{w_2}$   
 $c_k$  is the concentration of molecules with molecular weight  $NM2^{-k}$



$$3A. \quad M^* = \frac{N}{2} M$$

$$\begin{aligned} \dot{c}_0 &= -w_1 c_0 \\ \dot{c}_1 &= -\overline{w_2} c_1 + 2w_1 c_0 \\ \dot{c}_2 &= -\overline{w_2} c_2 + 2\overline{w_2} c_1 \\ &\text{etc.} \end{aligned} \quad (24)$$

We solve the first equation to get  $c_0 = e^{-w_1 t}$  and use this to get an equation for the generating function

$$\frac{\partial G}{\partial t} + \overline{w_2}(1-2x)G = -(w_1 - \overline{w_2})(1-2x)e^{-w_1 t} \quad (25)$$

from which we get

$$G = \frac{1}{w_1 - (1-2x)\overline{w_2}} \left[ (w_1 - \overline{w_2})(1-2x)e^{-w_1 t} + 2w_1 x e^{-(1-2x)\overline{w_2} t} \right] \quad (26)$$

and

$$y = \frac{w_1 - 2w_2}{2(w_1 - w_2)} e^{-w_1 t} + \frac{w_1}{2(w_1 - w_2)} e^{-w_2 t} \quad (27)$$

$$3B. \quad M^* = \frac{N}{4} M$$

Using a similar technique we get:

$$y = (a_0 + a_1 t)e^{-w_1 t} + b e^{-w_2 t} \quad (28)$$

with

$$\begin{aligned} a_0 &= \frac{w_1 - 2w_2}{2(w_1 - w_2)} + \frac{w_1(w_1 - 2w_2)}{4(w_1 - w_2)^2} \\ a_1 &= \frac{w_1(w_1 - 2w_2)}{4(w_1 - w_2)} \end{aligned} \quad (29)$$

$$b = 1 - a_0$$

It is easy to see that the general form is

$$y = \left[ \sum_{n=0}^k a_n t^n \right] e^{-w_1 t} + b e^{-w_2 t} \quad (30)$$

for  $M^* = NM2^{-k-1}$ . The most important general feature of these equations is that  $b$  is smaller the higher  $n$  is. If in these models we put  $w_2 \ll w_1$ , *i. e.*, if the selectivity of the enzyme is pronounced, we get a sharp change in  $y$ .

For model 3B this change occurs at  $y \approx \frac{1}{4}$ , which is fairly close to what one can

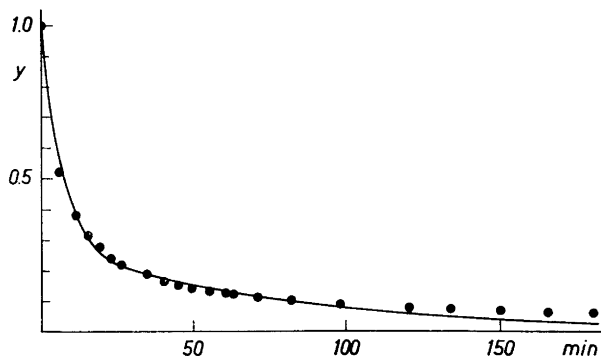


Fig. 1. Relative excess viscosity  $y$  as a function of time. The theoretical curve is calculated from eqn. 28, and the points are the experimental results of Andersen and Graae.

observe experimentally for hyaluronic acid. Fig. 1 shows the shape of the curve using  $w_1 = 0.2019$  and  $w_2 = 0.0130$  and the experimental points of Andersen and Graae<sup>10</sup>. The values for  $w_1$  and  $w_2$  have been calculated from the experimental data using an iterative least square procedure as described by Bond<sup>15</sup>. The agreement is not nearly as good as is the agreement with the empirical formula suggested by Andersen and Graae, but the expression used here has the advantage that it is derived from a specific model.

#### COMPARISON WITH EXPERIMENTAL DATA

Usually the viscosity of the polymer solution is measured with an Ostwald viscometer, while the degradation is going on, and in that case if the measurement takes  $2\tau$  seconds, the measured "viscosity"  $\eta$  is related to the true viscosity  $y$  by the equation

$$\eta^{-1}(t) = \frac{1}{2\tau} \int_{-\tau}^{+\tau} y^{-1}(t + t') dt' \quad (31)$$

This equation is obtained by expressing the length of the capillary in the viscometer in terms of  $\eta$  and  $y$  and equating the two expressions. If  $\tau$  is constant, it is easy to find  $y$  from the given function<sup>12</sup>  $\eta(t)$ . But unfortunately  $\tau$  is not constant, it is proportional to  $\eta$ , so that the equation reads

$$\eta^{-1}(t) = \frac{1}{2k\eta} \int_{-k\eta}^{+k\eta} y^{-1}(t + t') dt' \quad (32)$$

We have not been able to solve this equation, but by finding  $\eta$  using different expressions for  $y$  we have been able to estimate the error one makes in using  $\eta$  for  $y$ . In the experiments published by Andersen and Graae the error (for

$y \sim 0.52$ ,  $t \sim 6$  min.) is approximately 2 % for the most reasonable shapes of  $y = y(t)$ . For  $t \rightarrow 0$  the error becomes very large. Even within the measurable range the error can amount to about 10 %.

If experimental data have to be corrected by some iterative procedure using the above integral equation, they have to be extremely accurate in order that one may draw any conclusions whatsoever from the corrected data, and we believe that no such data have been published so far.

If one could measure the viscosity in such a way that each measurement took the same time, or if the measurements were almost instantaneous such as for instance in the case in the Couette viscometer, the correction would be much easier, and in the latter case actually superfluous.

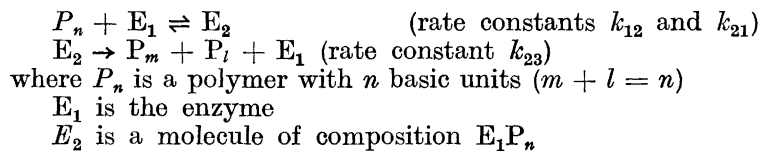
As mentioned above, we have tried to fit the expression derived for model 3B to the uncorrected data given by Andersen and Graae; Fig. 1 shows the agreement obtained. Not too much importance should be attached to the experimental points for small  $t$  (where the correction is large) nor to the values for large  $t$  (where transglucosidation may be the dominating reaction).

It is easy to make a better fit by adding an extra term or by letting the pre-exponential factors be parameters which can be varied to get a better fit, but these additions would not be explicable in terms of a molecular mechanism.

#### APPLICATION OF THE THEORY TO CATALYZED PROCESSES

So far we have assumed that the degradation can be described in terms of monomolecular rate constants  $w_k$ . When we consider a thermal degradation this seems very reasonable, but it is not at all clear that the same considerations apply to a reaction catalyzed for instance by an enzyme.

In order to see to what extent it may still be a good approximation we shall have to consider the detailed mechanism of the enzymatic degradation. We consider the simplest possible mechanism:



Using steady state kinetics<sup>13</sup> we have readily:

$$[E] \frac{dt}{d[P_n]} = \frac{1}{k_{12}} \left( 1 + \frac{k_{21}}{k_{23}} \right) \frac{1}{[P_n]} + \frac{1}{k_{23}} \quad (33)$$

letting  $[P_n]$  denote the concentration of  $P_n$  and  $[E]$  denote the concentration of  $E_1 + E_2$ .

If  $k_{23}$  is large, so that the last term on the right hand side is small, we have a first order degradation of  $P_n$ . Furthermore, since in this case the concentration of  $E_2$  is low, only very small amounts of the enzyme is bound in the substrate-complex, and the different first order degradations of P-molecules are therefore effectively independent. In that case the previous considerations

therefore are valid, and a "local stationarity" exists in which all the separate first order reactions are in steady states, but not in steady states with respect to each other.

If  $k_{23}$  is small so that the term  $k_{23}^{-1}$  cannot be neglected, one will usually find that the first term is negligibly small<sup>14</sup>, and that the concentration of  $E_2$  is comparatively high. In that case, therefore, the degradation of the macromolecule must be considered as a large number of zero order reactions competing to form complexes with the enzyme, and thereby degrading P-molecules. In this case, as in the rare case where both terms will have to be considered, the previous considerations are not valid.

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