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Molecular Weight Distribution of Linear and Multichain Polyamino Acids. Statistical Analysis

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It is shown that a statistical analysis of the molecular weight distribution of linear polyamino acids leads to results identical with those derived kinetically. The statistical treatment is extended to multichain polyamino acids synthesized by polymerizing N-carboxy-α-amino acid anhydrides in the presence of a multifunctional initiator. A general formula giving the size distribution of multichain molecules containing growing as well as terminated side chains is derived. For multichain polyamino acids obtained in the absence of a termination reaction, a sharp molecular weight distribution is predicted. It is demonstrated that the maximal value of the number average degree of polymerization which is attained in the presence of a termination reaction, when a b-functional initiator is used, is b times larger than that which is attained when the polymerization is started by a monofunctional initiator. The fact that the ratio between the weight average and number average degrees of polymerization of a multichain polymer composed of branched molecules containing terminated side chains only approaches 1, as the number of the functional groups of the initiator, b, is increased, shows that the molecular weight distribution is sharp when b is large.

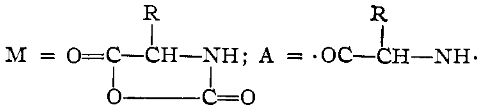
In a previous article[1] a theoretical analysis was given for the kinetics of polymerization of N-carboxy-α-amino acid anhydrides, assuming an initiation reaction (a) with a specific rate constant k_1, a propagation reaction (b) with a specific rate constant k_2, and termination reactions (c) and (d) with the rate constants k_3 and k_4, respectively. Formulas were derived for the molecular weight distribution and average degrees of polymerization of the still growing chains, characterized by free terminal amino groups, and of the terminated chains, characterized by terminal carboxyl groups.

$$\text{XH} + \text{M} \xrightarrow{k_1} \text{XAH} + \text{CO}_2 \qquad \text{(a)}$$

$$\text{XA}_i\text{H} + \text{M} \xrightarrow{k_2} \text{XA}_{i+1}\text{H} + \text{CO}_2 \qquad \text{(b)}$$

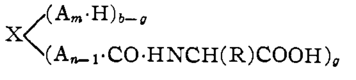
$$\text{XA}_i\text{H} + \text{M} \xrightarrow{k_3} \text{XA}_i\text{COHNCH(R)COOH} \qquad \text{(c)}$$

$$\text{XH} + \text{M} \xrightarrow{k_4} \text{XCOHNCH(R)COOH} \qquad \text{(d)}$$



$$\text{M} = \text{O}{=}\overset{}{\text{C}}{-}\overset{\text{R}}{\overset{|}{\text{CH}}}{-}\text{NH};\ \text{A} = \cdot\text{OC}{-}\overset{\text{R}}{\overset{|}{\text{CH}}}{-}\text{NH}\cdot \quad (\text{ring: C and CH of M joined through O}{-}\text{C}{=}\text{O})$$

In the present article the molecular weight distribution of the linear chains, growing and terminated, will be deduced statistically. The reactivity of the monofunctional initiator, XH, will be assumed to be similar to that of a growing chain (*i.e.*, $k_1 = k_2$ and $k_3 = k_4$). The statistical treatment will be extended to multichain polyamino acids,[2,3] synthesized recently by polymerizing N-carboxy-α-amino acid anhydrides in the presence of multifunctional initiators, XH_b. It will be assumed that each multichain molecule may contain growing, as well as terminated chains, and that it may, therefore, be represented by the formula



$$\text{X}\begin{cases}(\text{A}_m\cdot\text{H})_{b-g}\\(\text{A}_{n-1}\cdot\text{CO}\cdot\text{HNCH(R)COOH})_g\end{cases}$$

In this formula b denotes the original number of initiating groups of the multifunctional initiator, while $(b - g)$ is the number of the still growing chains, and g the number of the terminated chains. The numbers m and n determine the number of amino acid residues in the still growing and in the terminated chains, respectively.

The first synthesis of non-linear polymers of controlled structure was carried out by Schaefgen and Flory[4] who prepared multichain condensation polymers and calculated their molecular size distribution. The polymerization reaction mixture dealt with by the above authors contained multichain, as well as linear polymer molecules, and the propagation of the multichain molecules consisted of interaction with monomers as well as with linear polymers. The propagation reaction of the multichain polyamino acids, on the other hand, proceeds by interaction with monomer exclusively. Thus the theoretical treatment given below for the molecular size distribution of multichain polyamino acids differs from that discussed by Schaefgen and Flory.[4]

Linear Polyamino Acids

1. Molecular Weight Distribution of Linear Polyamino Acids Obtained in the Absence of a Termination Reaction.—When the polymerization of an N-carboxy-α-amino acid anhydride is initiated by a monofunctional initiator (*e.g.*, the amide or ester of the respective amino acid), the probability q that any specified amino acid residue will be found, at a given instant t, in a polymeric chain started by a particular initiator molecule is given by

$$q = \frac{L_0 - L_t}{L_0 I_0} \qquad (1)$$

where L_0 denotes the number of monomer molecules at the beginning of the polymerization, L_t denotes their number in the reaction mixture at time t, and I_0 denotes the number of the initiator molecules. A better understanding of the meaning of q may be obtained by making use of the identity $q = \int_{L_0}^{L_t} \mathrm{d}q$ and by elucidation of the meaning of dq derived from eq. 1.

$$\mathrm{d}q = -\frac{\mathrm{d}L_t}{L_0 I_0};\ q = \int_{L_0}^{L_t} \frac{-\mathrm{d}L_t}{L_0 I_0} \qquad (2)$$

Equation 2 shows that dq gives the increase in probability of a specified amino acid residue to be found in a polymeric chain attached to a specified initiating molecule, during the time interval between t and $t + \mathrm{d}t$, at which dL_t anhydride molecules undergo polymerization. It represents therefore the probability that a specified amino acid residue will enter a specified polymeric chain during the above mentioned time interval.

The probability that a specified amino acid residue will be found outside a specified chain is therefore $(1 - q)$. This probability consists of the probability, L_t/L_0, of the residue

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[1] E. Katchalski, I. Shalitin and M. Gehatia, THIS JOURNAL, **77**, 1925 (1955).

[2] M. Sela, *Bull. Research Council Israel*, **4**, 109 (1954).

[3] M. Sela and E. Katchalski, *Experientia*, **11**, 62 (1955).

[4] J. R. Schaefgen and P. J. Flory, THIS JOURNAL, **70**, 2709 (1948).

to remain as an unreacted monomer, and of the probability, $(I_0 - 1)(L_0 - L_t)/L_0I_0$, that it will be found among the amino acid residues of the other $(I_0 - 1)$ polymeric chains. Thus

$$1 - q = L_t/L_0 + (I_0 - 1)(L_0 - L_t)/L_0I_0 \qquad (3)$$

The probability P_j^* that any j-amino acid residues are attached to a specified initiator molecule is given by

$$P_j^* = \binom{L_0}{j} q^j(1 - q)^{L_0 - j} \qquad (4)$$

As L_0 is very large and $q << 1$ ($q_{\text{max.}} = 1/I_0$ at $t = \infty$), eq. 4 may be transformed into the usual Poisson formula[5]

$$P_j^* = \frac{(qL_0)^j}{j!} e^{-qL_0} \qquad (5)$$

Hence the number of the growing chains Y_j^*, composed of j-amino acid residues is given by

$$Y_j^* = I_0P_j^* = I_0 \frac{(qL_0)^j}{j!} e^{-qL_0} \qquad (6)$$

The molar concentration N_j^* of the chains composed of j-amino acid residues is then given by eq. 7

$$N_j^* = \frac{Y_j^*}{NV} = (\text{XH})_0 \frac{(qL_0)^j}{j!} e^{-qL_0} \qquad (7)$$

where V, N and $(\text{XH})_0$ denote the volume of the reaction mixture, Avogadro's number and the molar concentration of the initiator, respectively.

The kinetic derivation of the size distribution of linear polyamino acids, in the absence of a termination reaction, yielded for N_j^* (*cf.* eq. 9a[1])

$$N_j^* = (\text{XH})_0 \frac{(k_2\nu)^j}{j!} e^{-k_2\nu} \qquad (7a)$$

where the variable $\nu = \int_0^t M \, dt$, and M is the molar concentration of the free anhydride ($M = L_t/NV$). As no termination reaction occurs, and $k_1 = k_2$, the over-all rate of polymerization is given by the equation $-dM/dt = k_2(\text{XH})_0M$ or $-dM/d\nu = k_2(\text{XH})_0$. The last equation gives on integration

$$\nu = \frac{M_0 - M_t}{k_2(\text{XH})_0} = \frac{L_0 - L_t}{k_2I_0} \qquad (8)$$

The insertion of (1) into (8) leads to

$$k_2\nu = qL_0 \qquad (9)$$

which correlates the kinetic terms k_2 and ν with the probability q. Equation 9 shows the identity of eq. 7 derived statistically with eq. 7a derived kinetically.

2. Molecular Weight Distribution of Linear Polyamino Acids Obtained in the Presence of a Termination Reaction.—In the present case the attachment of an amino acid residue to a growing chain may result either in a still growing or in a terminated chain. In the calculation of the molecular weight distributions of the growing and the terminated chains two probabilities, q_1 and q_2, should therefore be taken into consideration. Their values as well as the values of their respective differentials, dq_1 and dq_2, are

$$q_1 = -\frac{\alpha}{\alpha + \beta} \frac{1}{L_0} \int_{L_0}^{L_t} \frac{dL_t}{R_t} \qquad (10)$$

$$dq_1 = -\frac{\alpha}{\alpha + \beta} \times \frac{dL_t}{L_0R_t} \qquad (11)$$

$$q_2 = -\frac{\beta}{\alpha + \beta} \times \frac{1}{L_0} \int_{L_0}^{L_t} \frac{dL_t}{R_t} \qquad (12)$$

$$dq_2 = -\frac{\beta}{\alpha + \beta} \times \frac{dL_t}{L_0R_t} \qquad (13)$$

In the above equations R_t represents the number of growing chains. The quotient $\alpha/(\alpha + \beta)$ gives, at any given time interval, the ratio between the probability of an amino acid residue to cause propagation to its total probability to undergo polymerization. $\beta/(\alpha + \beta)$ gives the similar ratio for the termination reaction.

In analogy to eq. 2, dq_1, defined in (11), represents the probability of a specified amino acid residue to attach itself by a propagation reaction to a specified growing chain at the time interval between t and $t + dt$. Similarly dq_2 defined in (13) represents the probability of a specified amino acid residue to cause a termination of a specified growing chain during the same time interval. q_1, given in (10), is the probability that a specified amino acid residue will be found in a specified growing chain at time t. Similarly, q_2, given in (12), represents the probability that a specified amino acid residue will have caused the termination of a specified growing chain during the time interval 0 to t. Obviously $1 - (q_1 + q_2)$ gives the probability that a specified residue will not be found in a specified chain at time t.

a. Distribution of Growing Chains.—The probability that, at a certain instant, a specified initiator molecule has attached to it a growing chain composed of j-amino acid residues is given by eq. 14, derived analogously to eq. 4.

$$P_j^* = \binom{L_0}{j} q_1{}^j \, [1 - (q_1 + q_2)]^{L_0 - j} \qquad (14)$$

By making approximations similar to those made in the derivation of (5), one obtains

$$P_j^* = \frac{(q_1L_0)^j}{j!} e^{-(q_1 + q_2)L_0} \qquad (15)$$

The number of growing chains, Y_j^*, composed of j-amino acid residues, is then given by eq. 16, and their molar concentration, N_j^*, by eq. 17.

$$Y_j^* = I_0P_j^* = I_0 \frac{(q_1L_0)^j}{j} e^{-(q_1 + q_2)L_0} \qquad (16)$$

$$N_j^* = (\text{XH})_0 \frac{(q_1L_0)^j}{j!} e^{-(q_1 + q_2)L_0} \qquad (17)$$

The kinetic derivation (*cf.* eq. 9c[1]) gave

$$N_j^* = (\text{XH})_0 \frac{(k_2\nu)^j}{j!} e^{-(k_2 + k_3)\nu} \qquad (17a)$$

Kinetic considerations of the type of polymerization under discussion lead to the equations

$$-dL_t' = \frac{k_2R_tL_tdt}{NV} \qquad (18)$$

$$-dL_t'' = \frac{k_3R_tL_tdt}{NV} \qquad (19)$$

$$-dL_t = -(dL_t' + dL_t'') = \frac{(k_2 + k_3)R_tL_tdt}{NV} \qquad (20)$$

where dL_t denotes the total number of monomer molecules which underwent polymerization at the time interval dt, while dL' and dL_t'' give the number of molecules which caused propagation and termination, respectively, during the same time interval. From the definitions of dq_1 and dq_2 it is obvious that

$$dq_1/dq_2 = dL_t'/dL_t'' \qquad (21)$$

Inserting the values of dq_1, dq_2, dL_t' and dL_t'', given in equations 11, 13, 18 and 19, respectively, into (21), one obtains $\alpha/\beta = k_2/k_3$, or

$$\alpha/(\alpha + \beta) = k_2/(k_2 + k_3) \qquad (22)$$

$$\beta/(\alpha + \beta) = k_3/(k_2 + k_3) \qquad (23)$$

Introducing (20) and (22) into (10) and substituting ν for $1/NV \int_0^t L_t \, dt$ yields

$$q_1L_0 = k_2\nu \qquad (24)$$

similarly on inserting (20) and (23) into (12), one obtains

$$q_2L_0 = k_3\nu \qquad (25)$$

Equations 24 and 25 show the identity of (17) derived statistically and (17a) derived kinetically.

b. Distribution of Terminated Chains.—Each terminated chain composed of j-amino acid residues is derived from a growing chain composed of $(j - 1)$ amino acid residues. Growing chains composed of $(j - 1)$ amino acid residues appear at any time, and each of them has a certain probability to turn into a terminated chain. The total number of terminated chains, composed of j-amino acid residues, at a given time t, is therefore the result of the accumulation of these chains during the whole time interval between zero and t.

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[5] H. Margenau and G. M. Murphy, "The Mathematics of Physics and Chemistry," Van Nostrand Co., New York, N. Y., 1946, p. 425.

The probability that, at a certain instant, a specified initiator molecule has attached to it a growing chain composed of $(j - 1)$ amino acid residues is given by equation 15a derived from (15).

$$P^*_{j-1} = \frac{(q_1L_0)^{j-1}}{(j-1)!}\, e^{-(q_1+q_2)L_0} \qquad (15a)$$

The probability $\mathrm{d}P_j$ that the above specified growing chain will have undergone a termination reaction during the time interval between t and $t + \mathrm{d}t$ is given by

$$\mathrm{d}P_j = \binom{L_0}{1} P^*_{j-1}\,\mathrm{d}q_2 \qquad (26)$$

The integration of eq. 26 yields the total probability, P_j, that at a certain instant a specified initiator molecule has attached to it a terminated chain composed of j-amino acid residues.

$$P_j = L_0 \int_0^{q_2} \frac{(L_0q_1)^{j-1}}{(j-1)!}\, e^{-(q_1+q_2)L_0}\,\mathrm{d}q_2 \qquad (27)$$

The number Y_j of the terminated chains composed of j-amino acid residues will be given by eq. 28, and their molar concentration by eq. 29.

$$Y_j = I_0P_j \qquad (28)$$

$$N_j = (\mathrm{XH})_0P_j = (\mathrm{XH})_0L_0 \int_0^{q_2} \frac{(L_0q_1)^{j-1}}{(j-1)!}\, e^{-(q_1+q_2)L_0}\,\mathrm{d}q_2 \qquad (29)$$

Substituting the values of q_1 and q_2 from equations 24 and 25, respectively, into eq. 29, and changing the limits of integration accordingly, gives eq. 29a, which is identical with that derived kinetically (*cf.* eq. 25c[1]).

$$N_j = (\mathrm{XH})_0k_3 \int_0^{\nu} \frac{(k_2\nu)^{j-1}}{(j-1)!}\, e^{-(k_2+k_3)\nu}\,\mathrm{d}\nu \qquad (29a)$$

Multichain Polyamino Acids

In the following it will be assumed that a multichain polyamino acid is obtained by the polymerization of an N-carboxy-α-amino acid anhydride initiated by I_b initiator molecules containing b reactive groups each. It will be further assumed that the polymerization proceeding at each of the growing side chains is unaffected by the neighboring side chains and that the chemical reactivity of the initiating groups toward the monomers is identical with that of the growing chains.

In the absence of a termination reaction each multichain molecule will obviously contain growing chains only. On the other hand, in the presence of a termination reaction the reaction mixture will contain multichain molecules composed of growing chains only, molecules composed of terminated chains only, and molecules composed of growing as well as terminated chains. The concentrations of all the above mentioned types of molecules will be deduced statistically below.

3. Molecular Weight Distribution of Multichain Polyamino Acids Obtained in the Absence of a Termination Reaction.—The probability that a multichain molecule contains m_1 amino acid residues in its first side chain, m_2 amino acid residues in its second side chain, m_r in its rth side chain and m_b in its last side chain, may be deduced from (5) and is given by the product $\prod_{r=1}^{b} \frac{(L_0q)^{m_r}}{m_r!} e^{-L_0q}$, where $q = (L_0 - L_t)/L_0bI_b$. The probability P^{b*}_{bj} that a multichain molecule contains $j = \sum_{r=1}^{b} m_r$ amino acid residues, distributed in any possible distribution among the b side chains, therefore is given by eq. 30

$$P^{b*}_{bj} = \sum_{m_1m_2\ldots m_b} \prod_{r=1}^{b} \frac{(L_0q)^{m_r}}{m_r!}\, e^{-L_0q} = \frac{(L_0q)^j}{j!}\, e^{-bL_0q} \sum_{m_1m_2\ldots m_b} \frac{j!}{m_1!m_2!\ldots m_b!} \qquad (30)$$

where the summation is taken over all possible values of $m_r (m_r = 0, 1, 2 \ldots . j)$. As each term of the summation represents a term in the multinomial $(1 + 1 + \ldots . + 1)^j$, in which the number of unities is b.

$$\sum_{m_1m_2\ldots m_b} \frac{j!}{m_1!m_2!\ldots m_b!} = b^j \qquad (31)$$

Inserting (31) into (30) one obtains

$$P^{b*}_{bj} = \frac{(bL_0q)^j}{j!}\, e^{-bL_0q} \qquad (32)$$

The total number, Y^{b*}_{bj}, of multichain molecules containing j-amino acid residues is therefore

$$Y^{b*}_b = I_b\, \frac{(bL_0q)^j}{j!}\, e^{-bL_0q} \qquad (33)$$

and their molar concentrations, N^{b*}_{bj}, is

$$N^{b*}_{bj} = (\mathrm{XH}_b)_0\, \frac{(bL_0q)^j}{j!}\, e^{-bL_0q} \qquad (34)$$

where $(\mathrm{XH}_b)_0$ is the molar concentration of the multifunctional initiator.

Since L_0q equals $k_2\nu$ also in the present case, the kinetic expression for N^{b*}_{bj} is given by

$$N^{b*}_{bj} = (\mathrm{XH}_b)_0\, \frac{(bk_2\nu)^j}{j!}\, e^{-bk_2\nu} \qquad (34a)$$

Equation 34a solves equations 35 and 36 describing the kinetics of polymerization of an N-carboxy-α-amino acid anhydride started by a multifunctional initiator in the absence of a termination reaction.

$$-\frac{\mathrm{d}(\mathrm{XH}_b)}{\mathrm{d}\nu} = k_2b(\mathrm{XH}_b) \qquad (35)$$

$$\frac{dN^{b*}_{bj}}{\mathrm{d}\nu} = k_2bN^{b*}_{b(j-1)} - k_2bN^{b*}_{bj} \qquad (36)$$

The value of (XH_b) as a function of time may be derived from (34a) assuming $j = 0$ and $(\mathrm{XH}_b) = N^{b*}_{b0}$.

In our previous article[1] it was shown that, in the absence of a termination reaction, when a monofunctional initiator is used (*i.e.*, $b = 1$) and $k_2\nu >> 1$, the number average degree of polymerization as well as the weight average degree of polymerization are given by $k_2\nu$ (*cf.* eq. 12a[1] and 15a[1]). Analogously in the present case, when $bk_2\nu >> 1$

$$P_n = P_w = bk_2\nu \qquad (37)$$

Equation 37 shows that the number average degree of polymerization, P_n, as well as the weight average degree of polymerization, P_w, of the multichain polymer, increases with ν. At equal time values ν the average degree of polymerization of the multichain polymer is b times greater than that of a polymer obtained when a monofunctional initiator is used. The Poisson distribution, given in eq. 34, as well as the equality of P_n and P_w, show that the multichain polymer has, in the absence of a termination reaction, a very narrow molecular weight distribution.

4. Molecular Weight Distribution of Multichain Polyamino Acids Obtained in the Presence of a Termination Reaction. a. Distribution of Molecules Containing Growing Side Chains Only.—When a termination reaction occurs, usually only a small part of the multichain molecules present in the reaction mixture will contain growing side chains exclusively. Their amount may be calculated by making use of the equations, derived in section 2a, giving the distribution of growing linear polymeric chains in the presence of a termination reaction. The probability that a reactive group of a multifunctional initiator molecule has attached to it a growing side chain containing j-amino acid residues is given by (15); q_1 and q_2 are defined also in the present case by equations 10 and 12, respectively, provided that R_t denotes the total number of reactive groups of the multichain molecules present in the reaction mixture. The probability, P^{b*}_{bj}, that a b-functional initiator will form a branched molecule composed of b growing side chains, and containing j-amino acid residues arranged in any possible way, may be calculated with the help of (15) in a manner analogous to that given in section 3.

$$P^{b*}_{bj} = \frac{(bq_1L_0)^j}{j!}\, e^{-b(q_1+q_2)L_0} \qquad (38)$$

The total number of molecules, Y^{b*}_{bj}, containing growing chains exclusively, and composed of j-amino acid residues, is given by eq. 39, while their concentration, N^{b*}_{bj}, is given by eq. 40.

$$Y^{b*}_{bj} = I_b \frac{(bq_1L_0)^j}{j!} e^{-b(q_1+q_2)L_0} \tag{39}$$

$$N^{b*}_{bj} = (\mathrm{XH_b})_0 \frac{(bq_1L_0)^j}{j!} e^{-b(q_1+q_2)L_0} \tag{40}$$

Substitution of the values of q_1L_0 and q_2L_0, given in equations 24 and 25, respectively, into eq. 40 yields the analogous kinetic equation

$$N^{b*}_{j} = (\mathrm{XH_b})_0 \frac{(bk_2\nu)^j}{j!} e^{-b(k_2+k_3)\nu} \tag{40a}$$

Obviously when $k_3 = 0$, *i.e.*, when the polymerization is void of a termination reaction, eq. 40a reduces to 34a.

By a treatment analogous to that given in the previous paper (*cf.* eq. 12c[1] and eq. 14c[1]), it can easily be shown that when $bk_2\nu >> 1$, both the number average and the weight average degrees of polymerization of the multichain polymeric fraction now discussed are equal to $bk_2\nu$. Hence the polymeric fraction composed of branched molecules containing only growing chains represents a fraction with a sharp molecular weight distribution, just as in the case where no termination reaction occurred (*cf.* section 3).

b. Distribution of Molecules Containing Terminated Side Chains Only.—In the following the concentration N_{bj} of the multichain molecules composed of b terminated chains and containing j-amino acid residues will be derived statistically. Since each of the functional groups of the initiator reacts independently, the probability that such a functional group has attached to it a terminated side chain composed of n-amino acid residues will be given by eq. 27 substituting n for j and defining q_1 and q_2 as in section 4a. The probability that the first functional group of an initiator molecule carries a terminated side chain composed of n_1-amino acid residues, the second functional group—a terminated side chain composed of n_2-amino acid residues, the ith—a terminated side chain of n_i-amino acids and the last, *i.e.*, the bth functional group—a terminated side chain of n_b-residues, is given by the product

$$\prod_{i=1}^{b} P_{ni} = \prod_{i=1}^{b} L_0 \int_0^{q_2} \frac{(L_0q_1)^{n_i-1}}{(n_i-1)!} e^{-(q_1+q_2)L_0}\, \mathrm{d}q_2 \tag{41}$$

Finally the probability, P_{bj}, that a specified b-functional initiator molecule has attached to it j-amino acid residues distributed in any possible way between the b terminated chains, is given by

$$P_{bj} = L_0{}^b \sum_{n_1n_2\ldots n} \prod_{i=1}^{b} \int_0^{q_2} \frac{(L_0q_1)^{n_i-1}}{(n_i-1)!} e^{-(q_1+q_2)L_0}\, \mathrm{d}q_2 \tag{42}$$

where the summation is carried out over all possible values of $n_1, n_2, \ldots n_b$; *i.e.*, $n_i = 1, 2, 3 \ldots. j - b + 1$, provided that $\sum_{i=1}^{b} n_i = j$. The concentration N_{bj} of the multichain molecules containing j-amino acid residues distributed among b terminated chains will therefore be given by

$$N_{bj} = (\mathrm{XH_b})_0L_0{}^b \sum_{n_1n_2\ldots n_b} \prod_{i=1}^{b} \int_0^{q_2} \frac{(L_0q)^{n_i-1}}{(n_i-1)!} e^{-(q_1+q_2)L_0}\, \mathrm{d}q_2 \tag{43}$$

where $\sum_{i=1}^{b} n_i = j$ and $n_i = 1, 2, \ldots j - b + 1$.

Inserting equations 24 and 25 in eq. 43 yields the kinetic equation 43a

$$N_{bj} = (\mathrm{XH_b})_0k_3{}^b \sum_{n_1n_2\ldots n_b} \prod_{i=1}^{b} \int_0^{\nu} \frac{(k_2\nu)^{n_i-1}}{(n_i-1)!} e^{-(k_2+k_3)\nu}\, \mathrm{d}\nu \tag{43a}$$

When the polymerization is brought to a stage at which all the growing chains of all the multichain molecules have suffered termination, the molecular weight distribution of the polymer will be determined by eq. 43 or eq. 43a. If it is assumed that $k_2 >> k_3$ (or, $q_1 >> q_2$), the following equations hold as $\nu \rightarrow \infty$ (*cf.* Appendix 1).

$$\sum_{j=b}^{\infty} N_{bj} = (\mathrm{XH_b})_0 \tag{44}$$

$$\sum_{j=b}^{\infty} jN_{bj} = (\mathrm{XH_b})_0b(k_2/k_3) \tag{45}$$

$$\sum_{j=b}^{\infty} j^2N_{bj} = (\mathrm{XH_b})_0b(b+1)(k_2/k_3)^2 \tag{46}$$

Equations 44, 45 and 46 permit the calculation of the number average degree of polymerization, P_n, as well as the weight average degree of polymerization, P_w, of the completely terminated polymer

$$P_n = \frac{\sum_{j=b}^{\infty} jN_{bj}}{\sum_{j=b}^{\infty} N_{bj}} = b(k_2/k_3) \tag{47}$$

$$P_w = \frac{\sum_{j=b}^{\infty} j^2N_{bj}}{\sum_{j=b}^{\infty} jN_{bj}} = (b+1)(k_2/k_3) \tag{48}$$

In our previous paper,[1] it was shown that when the polymerization reaction of N-carboxy-α-amino acid anhydrides is initiated by a monofunctional initiator, the maximal average degree of polymerization which can be attained in the presence of a termination reaction equals k_2/k_3. Equation 47 shows that the use of a b-functional initiator enables the preparation of a polymer with a number average degree of polymerization b times larger than the one obtained when a monofunctional initiator was used.

An estimate of the spread of the molecular weight distribution of the completely terminated multichain polymer may be obtained from the ratio of the weight average to the number average degrees of polymerization. Dividing (48) by (47) one obtains

$$P_w/P_n = 1 + \frac{1}{b} \tag{49}$$

When $b = 1$, *i.e.*, when a monofunctional initiator is used, $P_w/P_n = 2$, and the molecular weights are spread over a wide range. On the other hand, as the number of functional groups on the multifunctional initiator increases, the ratio P_w/P_n approaches unity, and a relatively sharp distribution of molecular weights is obtained. The use of a multifunctional initiator, therefore, does not only increase the average molecular weight of the polymer obtained, but it also narrows its molecular weight distribution. Schaefgen and Flory[4] and Schulz[6] arrived at a similar conclusion concerning multichain polymers obtained by another polymerization mechanism.

c. Distribution of Molecules Containing Growing as well as Terminated Side Chains.—In the following a general formula will be derived for the concentration $N^{(b-g)*}_{bj}$ of b-branched polyamino acids composed of j-amino acid residues and possessing g-terminated and $(b - g)$ growing chains. As in the previous cases, it will be assumed that the polymerization is initiated by a homogeneous b-functional catalyst.

The probability that the first functional group of an initiator molecule is attached to a terminated side chain composed of n_1-amino acid residues, the second functional group—to a terminated side chain composed of n_2-amino acid residues, the ith—to a terminated chain composed of n_i-residues and the gth functional group—to a terminated side chain of n_g-residues, is given by the product $\prod_{i=1}^{g} P_{ni}$, obtained by substituting g for b in eq. 41. The probability that the remaining $(b - g)$ functional groups of the initiator are attached to growing chains containing a total number

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(6) G. V. Schulz, *Z. physik. Chem.*, **B43**, 25 (1939).

of $j - \sum_{i=1}^{g} n_i$ amino acid residues may be deduced from eq. 38 and is given by eq. 38a

$$P^{(b-g)*}_{(b-g),j-\sum_{i=1}^{g} n_i} = \frac{\left[(b-g)q_1L_0\right]^{j-\sum_{i=1}^{g} n_i}}{\left(j - \sum_{i=1}^{g} n_i\right)!} e^{-(b-g)(q_1+q_2)L_0} \tag{38a}$$

Hence the probability that a b-functional initiator will form a multichain molecule of j-amino acid residues, and will carry on its first g-functional group—terminated chains containing n_1, n_2 .... n_g amino acids, respectively, and on the remaining $(b - g)$ functional groups—growing chains containing in total $j\text{-}\sum_{i=1}^{g} n_i$ amino acid residues, is given by the product $P^{(b-g)*}_{(b-g),j-\sum_{i=1}^{g} n_i} \prod_{i=1}^{g} Pn_i$. As g may be chosen from b by $\binom{b}{g}$ ways, the probability that a b-functional initiator carries g terminated chains as above, but irrespective of the order on the b-functional groups of the initiator, is

$$\binom{b}{g} P^{(b-g)*}_{(b-g),j-\sum_{i=1}^{g} n_i} \prod_{i=1}^{g} Pn_i$$

Finally the probability, $P^{(b-g)*}_{bj}$, has to be evaluated, that a multichain molecule contains g terminated and $(b - g)$ growing chains, and be composed of j-amino acid residues distributed in any possible way among the terminated and the growing chains. In the calculation of this probability it should be borne in mind that $\sum_{i=1}^{g} n_i$ may take each of the following values: g, $g + 1$, $g + 2$, ... j; and each of the n_i's may have the values 1, 2, 3, ... $j - g + 1$. The total probability $P^{(b-g)*}_{bj}$ is thus given by (50), where the summation should be carried out over all the permitted sets of values of n_1, n_2, ... n_g

$$P^{(b-g)*}_{bj} = \sum_{n_1n_2\ldots n_g} \binom{b}{g} P^{(b-g)*}_{(b-g),j-\sum_{i=1}^{g} n_i} \prod_{i=1}^{g} P_{n_i} \tag{50}$$

The concentration, $N^{(b-g)*}_{bj}$, of multichain molecules containing j-amino acid residues and possessing g terminated and $(b - g)$ growing chains, is obtained from eq. 50 by multiplying with $(\mathrm{XH_b})_0$ and by substituting the values of $P^{(b-g)*}_{(b-g),j-\sum_{i=1}^{g} n_i}$ and of $\prod_{i=1}^{g} P_{n_i}$ from equations 38a and 41, respectively.

$$N^{(b-g)*}_{bj} = (\mathrm{XH_b})_0 P^{(b-g)*}_{bj} = (\mathrm{XH_b})_0 L_0{}^g \binom{b}{g} e^{-(b-g)(q_1+q_2)L_0} \sum_{n_1\ldots n_g} \frac{\left[(b-g)q_1L_0\right]^{j-\sum_{i=1}^{g} n_i}}{\left(j-\sum_{i=1}^{g} n_i\right)!} \prod_{i=1}^{g} \int_0^{q_2} \frac{(L_0q_1)^{n_i-1}}{(n_i-1)!} e^{-(q_1+q_2)L_0} \mathrm{d}q_2 \tag{51}$$

where $\sum_{i=1}^{g} n_i = g, g + 1, \ldots j$; and $n_i = 1, 2, \ldots j - g + 1$.

Equation 51 gives the size distribution of the most general type of multichain polyamino acid and should obviously reduce to the size distribution of the various special types of polyamino acids deduced in the previous sections. Thus the concentration of the multichain molecules, N_{bj}, containing terminated chains only, given by (43), may be derived from (51) by putting $g = b$ and $\sum_{i=1}^{b} n_i = j$. The concentration of the multichain molecules, N^{b*}_{bj}, containing growing chains only and obtained in the presence of a termination reaction, may be derived from (51) by putting $g = 0$. In this case $n_i = 0$ and $\sum_{i=1}^{b} n_i = 0$, and the product of integrals appearing in this equation reduces to unity. As each $n_i = 0$, the summation is taken over one set of variables $n_1 = n_2 = n_3 = \ldots . n_g = 0$ only; and the complicated term under the summation reduces to $(bq_1L_0)^j/j!$ With this, and remembering that $g = 0$, one obtains from (51) eq. 40 for N^{b*}_{bj} derived previously. When no termination reaction takes place, $g = 0$ and $q_2 = 0$, and thus (51) reduces to (34).

The concentration, N_j, of the terminated linear polymer molecules is given by (29). This equation may be obtained from (51) by putting $b = 1$; $g = 1$, and reducing the set of variables n_1n_2 .... n_g, to the one variable $n = j$ only. The concentration of the linear growing chains, $N_j{}^*$, in the presence of a termination reaction, given by (17), may be derived from (51) by putting $b = 1$, $g = 0$ and $n_i = 0$. In the absence of a termination reaction $q_2 = 0$, and eq. 17 becomes eq. 7.

Inserting into (51) the values of q_1L_0 and q_2L_0 given in (24) and (25), respectively, one obtains an expression giving the concentration of $N^{(b-g)*}_{bj}$ in terms of the propagation constant k_2, the termination constant k_3 and the time variable ν.

$$N^{(b-g)*}_{bj} = (\mathrm{XH_b})_0 k_3{}^g \binom{b}{g} e^{-(b-g)(k_2+k_3)\nu} \sum_{n_1n_2\ldots n_g} \frac{\left[(b-g)k_2\nu\right]^{j-\sum_{i=1}^{g} n_i}}{\left(j-\sum_{i=1}^{g} n_i\right)} \prod_{i=1}^{g} \int_0^{\nu} \frac{(k_2\nu)^{n_i-1}}{(n_i-1)!} e^{-(k_2+k_3)\nu}\, \mathrm{d}\nu \tag{51a}$$

$$n_i = 1, 2, \ldots . j - g + 1 \text{ and } \sum_{i=1}^{g} n_i = g, g + 1, \ldots . j$$

It is of interest to note that eq. 51a solves the differential equation 52 describing kinetically the rate of formation of $N^{(b-g)*}_{bj}$ (*cf.* Appendix 2).

$$\frac{\mathrm{d}N^{(b-g)*}_{bj}}{\mathrm{d}\nu} = -(k_2 + k_3)(b - g)N^{(b-g)*}_{bj} + k_2(b - g)N^{(b-g)*}_{b(j-1)} + k_3(b - g + 1)N^{(b-g+1)*}_{b(j-1)} \tag{52}$$

Discussion

The statistical treatment given above for the growing and the terminated chains of linear polyamino acids yielded an expected molecular weight distribution identical with that derived kinetically and discussed in a previous article.[1] The following discussion will deal therefore mainly with multichain polyamino acids.

In the derivation of the general eq. 51, as well as in all the other equations dealing with multichain polyamino acids, it was assumed that all the molecules of the multifunctional initiator are equal. It should be borne in mind, however, that similar formulas will hold also when the multifunctional initiator is a high molecular weight material with a molecular weight distribution of its own. The polymer will consist in the latter case of multichain molecules containing different numbers of side chains, and the concentration $N_{bj}^{(b-g)*}$ of molecules having $(b - g)$ growing and g terminated chains, and composed of j-amino acid residues will again be given by eq. 51, where $(\mathrm{XH_b})_0$ denotes the initial concentration of the fraction of the initiator possessing b-functional groups. The total concentration of molecules having a constant number of j-amino acid residues as well as g-terminated chains and a varying number of side chains b, will be given in this case by the sum $\sum\limits_{b=g}^{\infty} N_{bj}^{(b-g)*}$.

In the preparation of most of the multichain polyamino acids described,[3] polylysine was used as initiator. Since polylysine prepared in the absence of a termination reaction has a Poisson molecular size distribution,[1] it is of interest to evaluate the molecular weight distribution of a multichain polyamino acid in this particular case. If the concentration of initiator molecules containing b functional groups is given by

$$N_b^* = (\mathrm{XH})_0' \frac{(k'\nu')^b}{b!} e^{-k'\nu'}$$

an equation identical with that given in equation 7a, and if the polymerization leading to the formation of a multichain polymer is not accompanied by a termination reaction, it can easily be verified that the number average degree of polymerization of the multichain polymer, defined by $P_n = \dfrac{\sum\limits_{b=1}^{\infty}\sum\limits_{j=0}^{\infty} jN_{bj}^{b*}}{\sum\limits_{b=1}^{\infty}\sum\limits_{j=0}^{\infty} N_{bj}^{b*}}$ as well as the weight average degree of polymerization, defined by

$$P_w = \frac{\sum\limits_{b=1}^{\infty}\sum\limits_{j=0}^{\infty} j^2N_{bj}^{b*}}{\sum\limits_{b=1}^{\infty}\sum\limits_{j=0}^{\infty} jN_{bj}^{b*}}$$

will both approximately equal $(k'\nu')$ $(k_2\nu)$, when $k'\nu' >> 1$. This expression is similar to equation 37, since $(k'\nu')$ is the average degree of polymerization of the multifunctional initiator used. By an analogous calculation it can be shown that when the same multifunctional initiator is used, but the polymerization reaction leading to the formation of the multichain polymer is composed of a propagation as well as a termination reaction, the number average and the weight average degrees of polymerization of a polymer containing terminated chains only will be given approximately by $(k'\nu')$ (k_2/k_3), when $k_2 >> k_3$, $\nu \rightarrow \infty$ and $k'\nu' >> 1$. The last expression is similar to equations 47 and 48 derived for a homogeneous initiator.

Equations 34 and 34a show that, in the absence of a termination reaction, polymers with high molecular weights may be obtained by making use of initiators with a great number of functional groups, and by continuing the polymerization for long periods in the presence of an excess of N-carboxy-α-amino acid anhydride. In the presence of a termination reaction the polymerization is brought to completion when all the side chains of the multichain molecules become terminated. For such a case the number average degree of polymerization equals $b(k_2/k_3)$ (*cf.* eq. 47). In our previous work[1] it was indicated that the magnitude of the termination constant k_3 does not exceed a few percentage of the propagation constant k_2. If it is assumed that k_2/k_3 equals 10 to 100 and the branched polymer grown on a multifunctional initiator, such as polylysine, with an average number of functional groups of $b = 10$ to 50, a maximal average degree of polymerization of 100 to 5000 will be expected. As the average molecular weight of an α-amino acid residue is about 100, maximal average molecular weights of 10,000 to 500,000 may be obtained.

Multichain polyamino acids may be prepared in aqueous media.[2,3,7] A part of the anhydride molecules decompose in such media to yield the corresponding amino acids as well as short peptides.[8,9] Obviously the value of ν will depend on these side reactions which diminish considerably the amount of the N-carboxy anhydride available for polymerization. The equations derived for the molecular weight distribution of the various forms of multichain polyamino acids will hold, however, also in the presence of side reactions, provided that the experimental values of ν are used.

The polymerization of N-carboxy-α-amino acid anhydrides in aqueous media, using proteins as homogeneous multifunctional initiators,[2,7,10] seems of particular interest, since the attachment of various peptidic chains to the protein under mild conditions leads to modified proteins with new chemical and biological properties. From the formulas derived it can be predicted that the attachment of polyamino acid chains to the proteins under the above conditions will not change very significantly the homogeneity of the protein molecule.

Among the homogeneous initiators which could be used in the preparation of multichain polyaminoacids, tri-, tetra-, penta- and higher polyamines as well as glycerol and other polyalcohols might be mentioned. The basic polyamino acids, polylysine and polyornithine, as well as other synthetic polymers such as polyvinylamine and polyvinyl alcohol may serve as possible high molecular weight multifunctional initiators with a molecular weight distribution of their own.

Although our discussion of the molecular weight distribution was devoted entirely to multichain polyamino acids, other multichain polymers may be included in the same category. Thus from the study of the polymerization of ethylene oxide[11] it seems that its polymerization initiated by polyalcohol (*e.g.*, polyvinyl alcohol), will lead to the formation of multichain polymers with a molecular size distribution similar to that given for multichain polyamino acids obtained in the absence of a termination reaction.

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Appendix I

When the polymerization reaction is brought to completion and the multichain molecules contain terminated chains only, the total molar concentration of the terminated multichains, $\sum\limits_{j=b}^{\infty} N_{bj}$, obviously equals the initial concentration $(\mathrm{XH_b})_0$ of the multifunctional initiator. Equation 44 is thus self evident. It is instructive, however, to show that (43a) satisfies this equation. Defining a new function, Φ_{n_i}, eq. 1*, and inserting it into (43a), one obtains eq. 2*

$$\Phi_{n_i} = (\mathrm{XH_b})_0{}^{1/b}\, k_3 \int_0^{\nu} \frac{(k_2\nu)^{n_i - 1}}{(n_i - 1)!}\, e^{-(k_2+k_3)\nu}\, \mathrm{d}\nu \qquad (1^*)$$

where $n_i = 1, 2, 3, \ldots . j - b + 1$; and $\sum\limits_{i=1}^{b} n_i = j$

$$N_{bj} = \sum_{n_1 n_2 \ldots n_b} \prod_{i=1}^{b} \Phi_{n_i} \qquad (2^*)$$

Hence

$$\sum_{j=b}^{\infty} N_{bj} = \sum_{j=b}^{\infty} \sum_{n_1 n_2 \ldots n_b} \prod_{i=1}^{b} \Phi_{n_i} \qquad (3^*)$$

The identity given in eq. 4* can be easily verified

$$\sum_{j=b}^{\infty} \sum_{n_1 \ldots n_b} \prod_{i=1}^{b} \Phi_{n_i} = \sum_{n_1 \ldots n_b} \prod_{i=1}^{b} \Phi_{n_i} = \left(\sum_{n_i=1}^{\infty} \Phi_{n_i}\right)^b \qquad (4^*)$$

where

$$n_i = 1,2,3 \ldots j - b + 1 \qquad n_i = 1,2,3 \ldots \infty$$

$$\sum_{i=1}^{b} n_i = j \qquad \sum_{i=1}^{b} n_i = b,\, b + 1,\, b + 2 \ldots \infty$$

From our previous article[1] (*cf.* eq. 26c there) it can be deduced that as $\nu \rightarrow \infty$

$$\sum_{n_i=1}^{\infty} \Phi_{n_i} = (\mathrm{XH_b})_0{}^{1/b} \qquad (5^*)$$

Finally, from equations 5*, 4* and 3* we obtain eq. 6* identical with (44)

$$\sum_{j=b}^{\infty} N_{bj} = (\mathrm{XH_b})_0 \qquad (6^*)$$

Putting $\sum\limits_{i=1}^{b} n_i$ for j and (2*) for N_{bj} one obtains

$$\sum_{j=b}^{\infty} jN_{bj} = \sum_{j=b}^{\infty}\left(\sum_{i=1}^{b} n_i\right)\left(\sum_{n_1 n_2 \ldots n_b} \prod_{i=1}^{b} \Phi_{n_i}\right) \qquad (7^*)$$

where $n_i = 1,2,3 \ldots j - b + 1$ and $\sum\limits_{i=1}^{b} n_i = j$. Proceeding with a treatment analogous to the one given above and taking into consideration the symmetry of the terms on the right-hand side of the last equation, (7*) becomes

$$\sum_{j=b}^{\infty} jN_{bj} = b\left(\sum_{n_i=1}^{\infty} n_i\, \Phi_{n_i}\right)\left(\sum_{n_i=1}^{\infty} \Phi_{n_i}\right)^{b-1} \qquad (8^*)$$

The value of $\sum\limits_{n_i=1}^{\infty} n_i \Phi_{n_i}$ for the limiting case $k_2 >> k_3$ and for $\nu \rightarrow \infty$ may be derived from eq. 33 of our previous paper[1].

$$\sum_{n_i=1}^{\infty} n_i \Phi_{n_i} = (\mathrm{XH_b})_0{}^{1/b}\, (k_2/k_3) \qquad (9^*)$$

Equation 10*, identical with eq. 45, is finally obtained on inserting (5*) and (9*) into (8*).

$$\sum_{j=b}^{\infty} jN_{bj} = (\mathrm{XH_b})_0 b(k_2/k_3) \qquad (10^*)$$

By a treatment similar to the one given above we obtain for $\sum\limits_{j=b}^{\infty} j^2 N_{bj}$

$$\sum_{j=b}^{\infty} j^2 N_{bj} = \sum_{j=b}^{\infty}\left(\sum_{i=1}^{\infty} n_i\right)^2\left(\sum_{n_1 \ldots n_b} \prod_{i=1}^{b} \Phi_{n_i}\right) =$$

$$b\left(\sum_{n_i=1}^{\infty} n_i{}^2 \Phi_{n_i}\right)\left(\sum_{n_i=1}^{\infty} \Phi_{n_i}\right)^{b-1} +$$

$$(b^2 - b)\left(\sum_{n_i=1}^{\infty} n_i \Phi_{n_i}\right)^2\left(\sum_{n_i=1}^{\infty} \Phi_{n_i}\right)^{b-2} \qquad (11^*)$$

The value of $\sum\limits_{n_i=1}^{\infty} n_i{}^2 \Phi_{n_i}$ for the limiting case $k_2 >> k_3$ and $\nu \rightarrow \infty$ may be derived from eq. 35 of our previous article[1]

$$\sum_{n_i=1}^{\infty} n_i{}^2 \Phi_{n_i} = (\mathrm{XH_b})_0{}^{1/b}\, 2(k_2/k_3)^2 \qquad (12^*)$$

Equation 13* identical with (46) is finally obtained on inserting (5*), (9*) and (12*) into (11*)

$$\sum_{j=b}^{\infty} j^2 N_{bj} = (\mathrm{XH_o})_0 b(b + 1)(k_2/k_3)^2 \qquad (13^*)$$

Appendix II

Defining new functions, U_1, U_2 and U_3, equations 15*, 16* and 17*, respectively, and introducing into eq. 51a, one obtains eq. 14*

$$N_{bj}^{(b - g)*} = U_1 \sum_{n_1 \ldots n_g} U_2 U_3 \qquad (14^*)$$

$$U_1 = (\mathrm{XH}_b)_0 k_3^g \binom{b}{g} e^{-(b-g)(k_2+k_3)\nu} \qquad (15^*)$$

$$U_2 = \frac{\Big[(b - g)k_2\nu\Big]^{j - \sum\limits_{i=1}^{g} n_i}}{\left(j - \sum\limits_{i=1}^{g} n_i\right)!} \qquad (16^*)$$

$$U_3 = \prod_{i=1}^{g} \int_0^{\nu} \frac{(k_2\nu)^{n_i - 1}}{(n_i - 1)!}\, e^{-(k_2+k_3)\nu}\, \mathrm{d}\nu \qquad (17^*)$$

Differentiating (14*) with respect to ν one finds

$$\frac{\mathrm{d}N_{bj}^{(b - g)*}}{\mathrm{d}\nu} = \frac{\mathrm{d}U_1}{\mathrm{d}\nu} \sum_{n_1 \ldots n_g} U_2 U_3 +$$

$$U_1 \sum_{n_1 \ldots n_g} \frac{\mathrm{d}U_2}{\mathrm{d}\nu} U_3 + U_1 \sum_{n_1 \ldots n_g} U_2 \frac{\mathrm{d}U_3}{\mathrm{d}\nu} \qquad (18^*)$$

Eq. 15* becomes on differentiation with respect to ν

$$\frac{\mathrm{d}U_1}{\mathrm{d}\nu} = -(b - g)(k_2 + k_3)U_1$$

Thus

$$\frac{\mathrm{d}U_1}{\mathrm{d}\nu} \sum_{n_1 \ldots n_g} U_2 U_3 = -(b - g)(k_2 + k_3) N_{bj}^{(b - g)*} \qquad (19^*)$$

Equation 19* proves the equality of the first term on the right side of (18*) with the corresponding term on the right side of (52).

Differentiation of (16*) with respect to ν gives

$$\frac{\mathrm{d}U_2}{\mathrm{d}\nu} = (b-g)k_2 \frac{\left[(b-g)k_2\nu\right]^{j-1-\sum\limits_{i=1}^{g} n_i}}{\left(j-1-\sum\limits_{i=1}^{g} n_i\right)!} \qquad (20^*)$$

In this equation $\sum\limits_{i=1}^{g} n_i = g, g+1, \ldots (j-1)$ and $n_i = 1, 2, \ldots (j-g)$. Hence

$$U_1 \sum_{n_1 \ldots n_g} \frac{\mathrm{d}U_2}{\mathrm{d}\nu} U_3 = k_2(b-g)U_1 \sum_{n_1 \ldots n_g} \frac{\left[(b-g)k_2\nu\right]^{j-1-\sum\limits_{i=1}^{g} n_i}}{\left(j-1-\sum\limits_{i=1}^{g} n_i\right)!} U_3 = k_2(b-g)N_{b(j-1)}^{(b-g)*} \qquad (21^*)$$

where $N_{b(j-1)}^{(b-g)*}$ is derived from (51a) by replacing j by $j-1$.

Equation 21* proves the equality of the second term of the right side of (18*) with the corresponding term of the kinetic equation 52.

Differentiation of (17*) with respect to ν gives

$$\frac{\mathrm{d}U_3}{\mathrm{d}\nu} = e^{-(k_2+k_3)\nu} \sum_{i=1}^{g} \frac{(k_2\nu)^{n_i-1}}{(n_i-1)!} \prod_{\substack{r=1\\ r\neq i}}^{g}{}' \int_0^{\nu} \frac{(k_2\nu)^{n_r-1}}{(n_r-1)!} e^{-(k_2+k_3)\nu}\,\mathrm{d}\nu \qquad (22^*)$$

where Π' denotes a product of all the integrals corresponding to the integral values $r = 1, 2, \ldots g$, except for the particular integral for which $r = i$. In the following a prime (′) will denote operations in which a specified term is omitted.

From (22*) and (16*) we obtain

$$\sum_{n_1 \ldots n_g} U_2 \frac{\mathrm{d}U_3}{\mathrm{d}\nu} = e^{-(k_2+k_3)\nu} \sum_{n_1 \ldots n_g} \frac{\left[(b-g)k_2\nu\right]^{j-\sum\limits_{i=1}^{g} n_i}}{\left(j-\sum\limits_{i=1}^{g} n_i\right)!} \sum_{i=1}^{g} \frac{(k_2\nu)^{n_i-1}}{(n_i-1)!} \prod_{r=1}^{g}{}' F_r \qquad (23^*)$$

where

$$F_r = \int_0^{\nu} \frac{(k_2\nu)^{n_r-1}}{(n_r-1)!} e^{-(k_2+k_3)\nu}\,\mathrm{d}\nu$$

Because of symmetry (each n_i and n_r equals 1, 2, 3, . . . $j-g+1$), g equal terms are obtained when the second summation, carried out over $i = 1$ to g, written explicitly. Hence

$$\sum_{n_1 \ldots n_g} U_2 \frac{\mathrm{d}U_3}{\mathrm{d}\nu} = g e^{-(k_2+k_3)\nu} \sum_{n_1 \ldots n_g} \frac{\left[(b-g)k_2\nu\right]^{j-\sum\limits_{i=1}^{g} n_i}}{\left(j-\sum\limits_{i=1}^{g} n_i\right)!} \frac{(k_2\nu)^{n_i-1}}{(n_i-1)!} \prod_{\substack{r=1\\ r\neq i}}^{g}{}' F_r \qquad (24^*)$$

Equation 24* may be written in the form

$$\sum_{n_1 \ldots n_g} U_2 \frac{\mathrm{d}U_3}{\mathrm{d}\nu} = g e^{-(k_2+k_3)\nu} \sum_{\substack{n_1 \ldots n_g\\ n_r \neq n_i}}{}' \frac{(k_2\nu)^{g-1-\sum\limits_{r=1}^{g}{}' n_r}}{\left(j-1-\sum\limits_{r=1}^{g}{}' n_r\right)!} \sum_{n_i=1}^{j-g+1} \frac{(b-g)^{\left(j-1-\sum\limits_{r=1}^{g}{}' n_r\right)-(n_i-1)} \left(j-1-\sum\limits_{r=1}^{g}{}' n_r\right)!}{\left[\left(j-1-\sum\limits_{r=1}^{g}{}' n_r\right)-(n_i-1)\right]!\,(n_i-1)!} \prod_{\substack{r=1\\ r\neq i}}^{g}{}' F_r \qquad (25^*)$$

As the sum over n_i in the last equations represents the sum of terms of a multinomial, eq. 25* gives

$$\sum_{n_1 \ldots n_g} U_2 \frac{\mathrm{d}U_3}{\mathrm{d}\nu} = g e^{-(k_2+k_3)\nu} \sum_{\substack{n_1 \ldots n_g\\ n_r \neq n_i}}{}' \frac{(k_2\nu)^{j-1-\sum\limits_{r=1}^{g}{}' n_r}}{\left(j-1-\sum\limits_{r=1}^{g}{}' n_r\right)!} (b-g+1)^{j-1-\sum\limits_{r=1}^{g}{}' n_r} \prod_{\substack{r=1\\ r\neq i}}^{g}{}' F_r =$$

$$g e^{-(k_2+k_3)\nu} \sum_{\substack{n_1 \ldots n_g\\ n_r \neq n_i}}{}' \frac{\left[(b-g+1)k_2\nu\right]^{j-1-\sum\limits_{r=1}^{g}{}' n_r}}{\left(j-1-\sum\limits_{i=1}^{g}{}' n_r\right)!} \prod_{\substack{r=1\\ r\neq i}}^{g}{}' F_r \qquad (26^*)$$

It should be noted that the total number of variables n_r in the last equation is only $(g-1)$.

From (15*), (26*) and (14*) it finally can be shown that the last term of (18*) is

$$U_1 \sum_{n_1 \ldots n_g} U_2 \frac{\mathrm{d}U_3}{\mathrm{d}\nu} = k_3(b-g+1)N_{(b-1)}^{(b-jg+1)*} \qquad (27^*)$$

Equations 19*, 21*, 27* and 18* prove that (51a) satisfies the kinetic equation 52.

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