A new statistical point of view to choose a better linear model for reactivity and microstructure analysis in HEMA/furfuryl acrylate copolymerization process

Gastón Fuentes Estevez[1], Oscar Valdés Lizama[1], Dionisio Zaldívar Silva[1], Lissette Agüero[1], Issa Katime[2*]

[1]*Centro de Biomateriales, Universidad de La Habana, Ave Universidad. e/ G y Ronda, Vedado, Ciudad de La Habana, 10400, Cuba*
[2]*Grupo Nuevos Materiales y Espectroscopia Supramolecular, Facultad de Ciencia y Tecnología. 48080, Bilbao, España*

*Corresponding author. Tel: (+34) 946012531; Fax: (+34) 946013500; E-mail: issa.katime@ehu.es

ABSTRACT

Copolymers of 2–hydroxyethyl methacrylate (E) and furfuryl acrylate (A) were prepared by free radical polymerization in toluene at 80°C using benzoyl peroxide as initiator. Copolymers were analyzed by ^{1}H–NMR in order to calculate the monomer composition in the copolymer. The monomer reactivity ratios were determined by four linear methods, Fineman–Röss, $r_1 = 1.33/r_2 = 0.96$; Fineman–Röss inverted, $r_1 = 1.27/r_2 = 0.92$; Kelen–Tüdos, $r_1 = 1.3/r_2 = 0.96$ and Kelen–Tüdos extended, $r_1 = 0.9982/r_2 = 1.0004$. Akaike Information Criterion was used to select the best r_1–r_2 pair of values. Dyads and triads confirm the average chain and copolymers type and lead to use a mathematical relationship to calculate a new r_1–r_2 par of values. The new values were $r_1 = 1.254/r_2 = 1.08$ from the dyads and $r_1 = 1.26/r_2 = 1.07$ from the triads. Other microstructure parameters such as run number ($R_N = 46.48$, X = 1, one A units triads) and Q–e values for A, not reported before ($e_2 = 0.10$ and $Q_2 = 1.68$) were calculated. Copyright © 2013 VBRI press.

Keywords: Copolymer; monomer reactivity; microstructure parameters; furfuryl acrylate; HEMA.

Issa Katime is Emeritus Professor of Physical Chemistry at the University of Basque Country (Spain). Obtained his Ph.D. in Chemistry in the Complutense University of Madrid with distinction "Cum Laude". He has published nearly 500 papers in scientific journals and 27 books and chapters on the field of Polymer Physical Chemistry and General Chemistry. His research interest is in the area of polymers. Prof. Katime has received the Royal Society of Chemistry and Physics Award in 1975. Editor of the spanish scientific journal: Revista Iberoamericana de Polímeros. Founder–Director of New Materials and Supramolecular Spectroscopy Group.

Dionisio Zaldivar Silva is Professor and Director of Center Biomaterials at the University of Havana, Havana, Cuba. He earned a B.S. degree in Chemical from the University of Havana and and Ph.D from the University of Havana. He has published over 50 peer reviewed articles. His research interest is in the area of polymers. Dr. Zaldivar has received several awards for his research. He has been consultant to companies in the polymer for medicine area.

MSc. Gastón Fuentes Estévez is Auxiliary Researcher at the Biomaterials Center of the Havana University, and professor of Physical Chemistry Department of the Chemistry Faculty at the same university. He earned a BSc and MSc degree in Chemistry from the University of Havana. He has published 23 peer reviewed articles in Web of Sciences and 13 peer reviewed presentations in Summary Books at international events. He has invited lecturer in two universities in Brazil and one in Spain. His research interest is in the area of composites from calcium phosphates, acrylic monomers and natural polymers, drug delivery systems from different sources and application of mathematical and statistical criteria for mechanism selection. MSc. Fuentes has received several personal and group awards for his research and he is member of the Cuban Society of Chemistry.

Introduction

Copolymers based on 2–hydroxyethyl methacrylate have found wide application in contact lenses, surgery and clinical medicine due to their ability to form biocompatible hydrogels with excellent tolerance and good stability [**1,2**]. Meanwhile, furfuryl acrylate has been used also in ophthalmic applications [**3**] and as a part of polymer mixtures in coating surfaces or for the grafting separator in electrochemical generator for the industry [**4**]. From that point of view, the study of the copolymerization process among these monomers results very interesting, because the common application in the ophthalmic field.

In the free–radical copolymerization, great emphasis has been always put on copolymer composition, appropriately considered as the most important aspect of the polymerization reaction, since it influences the properties of the resultant materials. Then, it is important to estimate the monomer reactivity ratios in a statistical correct manner [**5**]. For example, some authors have been used the Mayo–Lewis Terminal Model (MLTM) to analyze different linear and nonlinear regression approaches to estimate the monomer reactivity ratios. Although the estimation of parameters is important, the copolymer composition is often inadequate to discriminate among models such as MLTM, penultimate unit model (PUM) or complex participation model (CPM) [**6**]. The latter is much more sensitive to probe the mechanism, which best represents a particular copolymerization [**7**].

In general, non–linear models provide more reliable predictions for answers outside the observed range of the data than the linear models. It can be mechanistic, i.e. based on a (theoretical) model describing the underlying mechanism that produces the data. As a consequence, the non–linear model parameters have a more physical interpretation than the linear ones but they are more computationally intensive and require starting estimates for the fixed effect coefficients. It is important to note that it is not always easy to choose reasonable values for these estimates and poor starting values may result in calculations that do not converge [**8**]. However, even when the linear models are less accurately than nonlinear, because in essence the conclusions are only valid within the observed data range, they are more simples and require only a few resources to solve the problem [**9**]. Besides, with a good measurement and the use of adequate analytical techniques, it can be reached similar results to nonlinear methods [**10**].

The most popular linear methods are Fineman–Röss (FR) [**11**], Kelen–Tüdos (KT) [**12**] or Mayo–Lewis (ML) [**13**]. Few approximations and derivations has been emerged with the purpose of achieve the confidence of the linear methods. So, the inverted Fineman–Röss (FR$_I$) [**6, 10**] and the extended Kelen–Tüdos (KT$_E$) [**10**] equations have been applied to determine the reactivity ratios and a subsequent copolymer microstructure.

Since many years ago, the use of various criteria to select the best model has been a problem. Some authors attack the most popular, the correlation coefficient due to the absence of a parameter related with the independent variable error [**9**]. Others suggest the application of more novel criteria taking account the computational techniques development, such as Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC) and its derivatives [**14**].

In this paper, 2–hydroxyethyl methacrylate–co–furfuryl acrylate polymerization process was studied. ^{1}H–NMR was applied in order to determine the composition of the monomers in the feed and the copolymers. Classical linear methods, Fineman Röss and Kelen–Tüdos, and its derivatives, inverted FR and extended Kelen–Tüdos were employed to calculate the reactivity ratios and the microstructure of the copolymers. Finally, the values of Q–e scheme were used to evaluate the previous conclusions above the preference to homo– or co–polymerized of both monomers. A new statistical criterion (AIC) was used to elucidate the best models.

Experimental

Materials

2–Hydroxyethyl methacrylate, monomer subscripted as 1 or E, which contain less than 0.03 wt% of hydroquinone monomethyl ether as inhibitor, was washed three times with 5% NaOH solutions, distilled under reduced pressure of nitrogen and the fraction of boiling point 88–91°C was collected.

Furfuryl acrylate (monomer subscripted as 2 or A) was prepared by transesterification of methyl acrylate with furfuryl alcohol by a procedure reported previously elsewhere [**15**]. Benzoyl peroxide (Merck, Germany) was recrystallized three times in chloroform. Solvents (toluene and methanol) were used as received without further purification.

All reagents were extra pure grade and use as purchased from Sigma–Aldrich (USA) unless it indicates other supplier.

Copolymer synthesis

Copolymerization reactions were performed in toluene solution at $(80.0 \pm 0.1)°C$, in Pyrex glass ampoules sealed off under high vacuum. Monomer and initiator concentrations were 1.0 and 0.015 mol·L^{-1}, respectively. The sealed ampoules were shaken vigorously and immersed in a water bath held at the required temperature of polymerization. After the proper reaction time, the ampoules were removed from the bath and at once the content was poured into a large excess of diethyl ether. The precipitated samples were washed with the precipitant mixture and dried under vacuum until constant weight was attained.

^{1}H NMR

The copolymers obtained from different mixtures of E and A was analyzed by ^{1}H–NMR spectroscopy with a Bruker AM–200 spectrometer working at 200 MHz. The spectra recorded at 45°C in 5% (*w/v*) deuterated dimethylsulphoxide solutions with a 2.5 kHz spectral with, flip angle of 30° (2 *ms* pulse), a pulse repetition time of 2 *s* and 128 transients. A 16 K FID was acquired and zero filled to 32 *K* before Fourier transformation. The analysis was performed by comparing the integrated intensities of resonance signals with $\delta = 3.65$ ppm and $\delta = 3.95$ ppm assigned to the oxyethylene protons of the –CH$_2$–CH$_2$–OH side residue of E units (*m$_1$*) and $\delta = 6.45$ ppm y $\delta =$

6.55 ppm, assigned to the protons in position 3 and 4 of the aromatic furfuryl ring of A (m_2) [16].

Linear methods

The linearization methods used have been reported elsewhere, but the most utilized equations are noted in Table 1 and the involved parameters to build the variables could be described as follows: $X = [E]_0/[A]_0$ or f_1/f_2 (feed) and $Y = m_1/m_2$ or F_1/F_2 (copolymer). In the specific case of Kelen–Tüdos extended equation the main idea is related with the addition of the conversion weight in the mathematical treatment of the variables. Then, the partial molar conversion of A is defined as: $\zeta_2 = C (\mu + X)/(\mu + Y)$, where C is the weight conversion of copolymerization and μ is the ratio of molar mass of A to that of E, that is $\mu = M_2/M_1$. The partial molar conversion of E is: $\zeta_1 = \zeta_2(Y/X)$. A new factor emerges from this analysis and it called conversion factor, $Z = log(1 - \zeta_1) / log(1 - \zeta_2)$. Finally the mathematical equations could be written as follows in **Table 1**.

Table 1. Linear and non–linear methods used in this work.

Method	Code	Equation	x–axis	y–axis	Ref
Fineman–Röss	FR	$G = r_1 H - r_2$	$H = \dfrac{X^2}{Y}$	$G = \dfrac{X(Y-1)}{Y}$	[11]
Fineman–Ross inverted	FR$_I$	$G/H = r_1 - (r_2/H)$			[10]
Kelen–Tüdos	KT	$\eta = \left(r_1 + \dfrac{r_2}{\alpha}\right)\xi - \dfrac{r_2}{\alpha}$	$\xi = \dfrac{H}{\alpha + H}$	$\eta = \dfrac{G}{\alpha + H}$	[12]
Kelen–Tüdos extended	KT$_E$	$\eta' = \left(r_1 + \dfrac{r_2}{\alpha}\right)\xi' - \dfrac{r_2}{\alpha}$	$\xi' = \dfrac{H'}{\alpha + H'}$	$\eta' = \dfrac{G'}{\alpha + H'}$	[10]

where $H' = Y/Z^2$, $G' = (Y-1)/Z$ and $\alpha = (H_{min} \times H_{max})^{1/2}$

Statistical criteria

In order to distinguish the models that properly described the data from those that did not correctly fit the data, the residuals sum of the squares (*RSS*, also named as Euclidean distance) was obtained and these that best explains the experimental data is the one that shows the minimal value for the *RSS*.

Table 2. AIC used at this work.

Criteria	Code	Formulae	Reference
AIC general or great	AIC$_G$	$AIC_G = 2p + n\left[\ln\left(\dfrac{2\pi(RSS)}{n}\right)+1\right]$	[14,19]
AIC smallest or short	AIC$_S$	$AIC_S = AIC_G + \dfrac{2p(p+1)}{n-p-1}$	[14,19]
AIC short corrected	AIC$_{SC}$	$AIC_{SC} = \ln\dfrac{RSS}{n} + \dfrac{n+p}{n-p-2}$	[20]
AIC new	AIC$_N$	$AIC_N = \ln\dfrac{RSS}{n-p} + \dfrac{n+p}{n-p-2}$	[20]

But, since a larger number of model parameters could lead to a higher probability of obtaining a smaller *RSS* value, it was necessary to use a new statistical approach, to elucidate the best of them, independently of the number of parameters that each model [17].

For this reason, all the versions of the Akaike Information Criterion were used and its respective formulae as shown in **Table 2**. The $AIC = 2p - 2 \ln(L)$, where p is

the number of parameters and L is the likelihood function results a very complex equation. Assuming that the model errors are normally and independently distributed, it takes the *RSS* and *N* (the number of experimental data points) as equations parameters' taking it forms more adequately to use in mathematical analysis and statistical selections.

The model that shows the smallest value for the AIC is the one which, statistically, describes the best fitting. Additionally, we examined the fit of the predicted curve to the experimental data and the validity of the calculated parameters [14,18].

Results and discussion

Determination of monomer reactivity ratios

The data of molar composition of the initial mixtures (f_1, f_2), the resulting copolymers (F_1, F_2) and respective conversions are quoted in **Table 3**. F_1 and F_2 parameters were calculated from the ^{1}H–NMR spectra obtained and the signals above mentioned.

Table 3. Copolymer compositions determined by ^{1}H–NMR.

Feed (mol fraction)		Conversion (wt %)	Copolymer (mol fraction)	
E (f_1)	A (f_2)		E (F_1)	A (F_2)
0.15	0.85	3.3	0.164	0.836
0.20	0.80	3.4	0.227	0.773
0.30	0.70	2.9	0.313	0.687
0.40	0.60	4.2	0.413	0.587
0.50	0.50	2.4	0.555	0.445
0.60	0.40	3.7	0.632	0.368
0.70	0.30	2.8	0.761	0.239
0.80	0.20	4.3	0.836	0.164
0.85	0.15	2.7	0.879	0.121

Notice the good concordance of the values among *f–F* pairs for each monomer. This is one of the main conditions to obtain better result when linear methods were applied [10]. The parameters for all the equations used (**Table 1**) are quoted in **Table 4**.

Table 4. Linear methods parameters of the copolymers ($\alpha = 0.8409$).

| X	Y	FR		FR$_I$		KT		KT$_E$			
		H	G	1/H	G/H	ξ	η	H'	G'	ξ'	η'
0.18	0.20	0.16	–0.72	6.30	–4.56	0.16	–0.73	0.20	–0.80	0.19	–0.78
0.25	0.29	0.21	–0.60	4.70	–2.83	0.20	–0.57	0.29	–0.71	0.26	–0.62
0.43	0.46	0.40	–0.51	2.48	–1.27	0.32	–0.41	0.46	–0.54	0.35	–0.42
0.67	0.70	0.63	–0.28	1.58	–0.44	0.43	–0.19	0.70	–0.30	0.46	–0.19
1.00	1.25	0.80	0.20	1.25	0.25	0.49	0.12	1.25	0.25	0.60	0.12
1.50	1.72	1.31	0.63	0.76	0.48	0.61	0.29	1.72	0.72	0.67	0.28
2.33	3.18	1.71	1.60	0.58	0.94	0.67	0.63	3.19	2.19	0.79	0.54
4.00	5.10	3.14	3.22	0.32	1.02	0.79	0.81	5.11	4.10	0.86	0.69
5.67	7.26	4.42	4.89	0.23	1.11	0.84	0.93	7.29	6.28	0.90	0.77

The reactivity ratios evaluated through different equations showed at **Table 5** confirmed the general trend to ideal copolymer. A few comments will be added to the methods used to obtain the r_1 and r_2 in this work. In FR method as observed in **Fig. 1** (left), in most cases, the FR

straight line is plotted from several points gathered closely with one or two fairly isolated point. These last points correspond to the highest values of f_1 in the FR method and the lowest one (**Fig. 1**, right) in FR$_I$ method.

Table 5. Reactivity ratios and derived copolymerization parameters.

Code	r_1 (E)	r_2 (A)	r_1 x r_2	$1/r_1$	$1/r_2$
FR	1.33 ± 0.04	0.96 ± 0.07	1.2768	0.7519	1.0417
FR$_I$	1.27 ± 0.09	0.92 ± 0.03	1.1684	0.7874	1.0870
KT	1.3 ± 0.1	0.96 ± 0.06	1.2480	0.7692	1.0417
KT$_E$	0.9982 ± 0.0007	1.0004 ± 0.0004	0.9986	1.0018	0.9996
TM	1.42	0.93	1.3206	0.7042	1.0753
MC	1.42	0.93	1.3206	0.7042	1.0753

The contribution from these points is highly important for the slope calculus of the straight line, more specifically for r_1 in FR and $-r_2$ in FR$_I$. Since, high f_1 values are more representative of r_1 values and low ones of r_2 values the FR method is more accurate for determining r_1 and FR$_I$ method for calculating r_2 even when last one is not often applied [**21**].
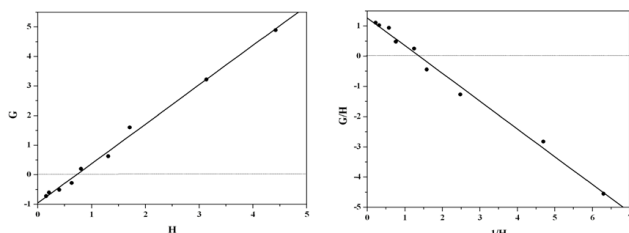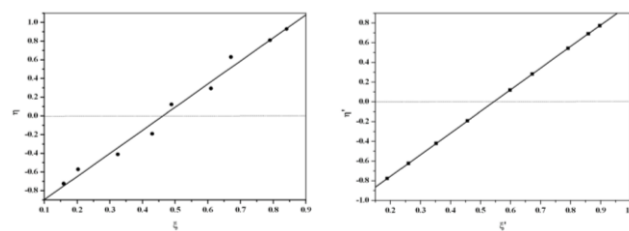

Fig. 1. Fineman–Röss plot for E/A copolymerization. Classical (left), inverted (right).

When the experimental error is reasonably small and the data have been taken under the appropriate conditions, the approximation can be remarkably good as it can be seen not only in **Fig. 1** but **Fig. 2** too [**15**]. Notice in **Fig. 2**, the precise fitting of the experimental data to extended Kelen–Tüdos equation where the effect of conversion is considered. But, the values of r_1 and r_2 obtained by KT$_E$ method do not have the same absolute value of the other methods, near to TM and MC results, as it know more precise methods by the origin of its mathematical treatments, non–linear and randomize, respectively [**15**]. It could be explained by the general copolymerization equation, because all the linear methods are applicable when the conversion is low (< 15%). The KT$_E$ equation is an approximation in order to calculate the reactivity ratios from high conversion experimental data due to the long, precise, meticulous and detailed work to obtain low conversion data.

The increasing of reaction time produces an enhancement of viscosity of the reaction media, while the latter changes the monomer diffusion to macro radicals. In other words, at high conversions both the propagation constant and the monomer collision to macro radicals are lowered. In this situation the effect of penultimate bulky group is considerable and the system tends to adopt second–order Markov statistics (so called penultimate model reactivity ratios), thus affecting the reactivity ratios

[**10, 22**]. For that reason, the KT$_E$ equation results non applicable to low conversion although their use will allows us to predict the high conversions behaviour of the copolymer system.

Fig. 2. Kelen–Tüdos plot for E/A copolymerization. Classical (left), extended (right).

The r_1 x r_2 products for our system from KT$_E$ equation are closely to unity. It is generally believed that r_1 x $r_2 = 1$ represents the upper limit for proper copolymerization. The value of r_1 x $r_2 > 1$ (slightly) may be plausible for polarity and bulky groups of E in our systems. Considering the above effect, our reactivity ratios should be taken as apparent reactivity ratios. It is worth noting that there are many systems in the literature, including free radical copolymerizations, which contradict the belief, that r_1 x $r_2 = 1$ represents the upper limit for proper copolymerization. More precisely, when $r_1 = r_2 \approx 1$, (with both ratios around the unity as our case), monomer 1 (E) will react as fast with another monomer 1 or the other (monomer 2) and a random copolymer results [**23, 24**], to which lead to the same conclusion about the utility of the KT$_E$ model to predict the ending behavior of the copolymeric system even to low conversions. Perhaps, it will be important to note that r_1 is slightly bigger than 1, which mark at begin of the copolymerization process a higher probability find HH units than rest of possible combinations, but this fact will be decreased with time and the progress of copolymerization rapidly because r_1 is not so bigger than 1. A plot of the mole fractions of E in the copolymer (F_1) versus that in the feed (f_1) is shown in the **Fig. 3**, calculated through the general copolymerization equation from Mayo and Lewis [**13,15–16**].
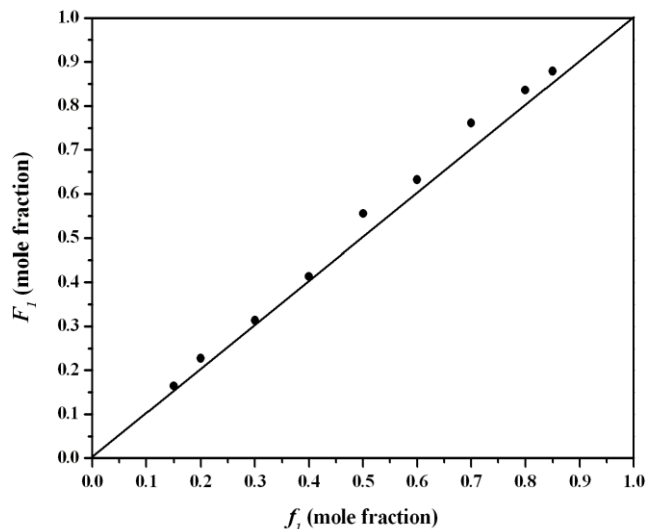
Fig. 3. Composition diagram for copolymerization of E with A.

It can be observed that the copolymers tend towards an almost ideal behavior which matches with the r_1–r_2 pairs obtained by the KT_E equation and the general theory of the copolymerization [23]. In terms of the r_1–r_2 pairs of values more closely to the TM and MC (see **Table 5**), the reactivity of growing radicals with E ends was measured by the ratio $1/r_1$ and the reactivity of growing radicals with A ends was measured by the ratio $1/r_2$. As the $1/r_1 < 1/r_2$ it can be concluded that there is more growing radicals with A ends than E ends due to $r_1 > r_2$, which define what monomer is more reactive than other (E > A).

Statistical discussion to select the best model

It was very important to know that any statistical discussion, independent of the result, required of the physical sense. Statistics is a very powerful tool in order to elucidate through many formulae, criteria, parameters, etc., but the election could be based on the statistical criteria and the possible explanation that it offers subsequently of the selected model.

In **Table 6** are shown the classical statistical parameters of each linear model used in this work (except KT_E, for the differences among the r_1–r_2 pairs of values with TM and MC reported) [15, 25].

Table 6. Classical statistical parameters.

Code	R	R^2	RSS
FR	0.99745	99.49 %	0.1556
FR_I	0.99586	99.17 %	0.2552
KT	0.99261	98.53 %	0.0440

The values of r_1 and r_2 confirm that FR method fit better than FR_I to the experimental data. In fact the FR method has the better values of R (correlation coefficient) and R^2 (determination coefficient) but if it look to the RSS criteria, then the best method was KT, more agree with literature. What is the apparent contradiction between these results? Akaike use the statistical probability function for the evaluation of models, including in his criterion, the number of parameters. This fact makes more precise and exact the election, joined to the inclusion of the experimental data size. Finally, any of them, that is to say AIC and its derivatives (**Table 2**) make easier the selection of any model as it can see in **Table 7**.

Table 7. Novel statistical parameters with $p = 2$ (linear methods) and $n = 9$.

Code	*RSS*	AIC_G	AIC_S	AIC_{SC}	AIC_N
FR	0.1556	4.98	6.98	−1.86	−1.61
FR_I	0.2552	5.47	7.47	−1.36	−1.11
KT	0.0440	3.71	5.71	−3.12	−2.87

The distances between any of *AIC* criteria are wider than the difference between the correlations and/or determination coefficients as it can see in **Table 6** and **7**. In fact, the r_1–r_2 pairs of values of FR and KT are more closely between them than any other combination that

include FR_I. Besides, even when AIC_G solves the problem with accuracy, it can be included the rest of criteria (AIC_S, AIC_{SC} and AIC_N) because usually, the border among the small and larger data size tends to be confuse.

The derivatives of AIC attributed to McQuarrie and Tsai (AIC_{SC} and AIC_N) [20] were developed in order to take account data size mainly from the first correction made by Akaike himself [19]. At the end, when can you consider a data size smaller o greater than other, according to evaluated model and physical phenomena that it explains. For the rest of this work and being consequent with the statistical proposition, it will work with $r_1 = 1.31$ (average among FR and KT) and $r_2 = 0.96$ in order to determine the microstructure of the copolymers.

Copolymer microstructure

From the reactivity ratios of monomers, we determined the *run number*, R_N (Eq. (1)), defined by Harwood and Ritchey (and reported elsewhere [26]) as the average number of monomer alternations per 100 monomeric units in a copolymer chain.

$$R_N = \frac{200}{2 + r_1 X + r_2 / X} \qquad (1)$$

The value of R_N can give us a view of sequence distributions in copolymer chains and help us to estimate the relationship between physical properties of copolymers and their compositions. The value of R_N can be calculated by reactivity ratios and probability statistics for different monomer feeds. The variation of R_N with the X parameter (f_1 / f_2) is shown in **Fig. 4**.
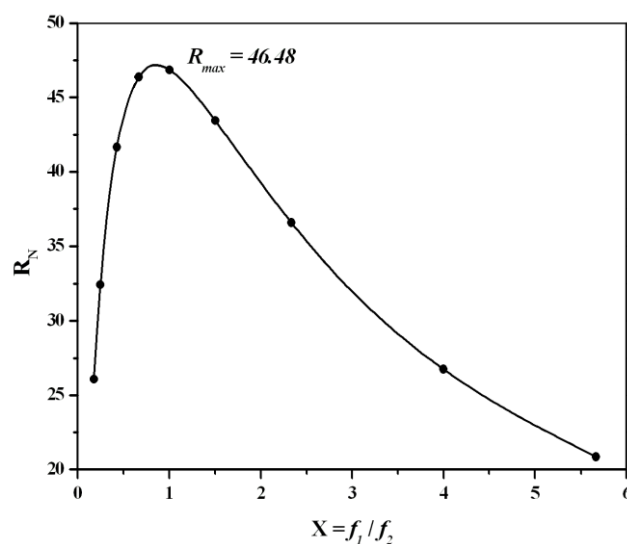
Fig. 4. Variation of run number with the ratio of monomer concentrations in the feed (*X*).

The maximum value of R_N is about 46.48 at X = 1 for the poly(E–co–A) system. To gain further information about the copolymer structure, the formation probabilities of dyad fractions as a function of the molar fraction of monomeric units in the copolymer can be calculated from the monomer feed compositions and reactivity ratios. The equations used were show at **Table 8**.

Table 8. Dyads and triads equations.

Dyads	$P_{EA} = 1 - P_{EE} = \dfrac{1}{1 + r_1 X}$	$P_{AE} = 1 - P_{AA} = \dfrac{1}{1 + r_2/X}$
Triads	$[EEE] = \dfrac{P_{AE}(1-P_{EA})^2}{P_{EA}+P_{AE}}$	$[AAA] = \dfrac{P_{EA}(1-P_{AE})^2}{P_{EA}+P_{AE}}$
	$[EAE] = \dfrac{P_{EA}P_{AE}^2}{P_{EA}+P_{AE}}$	$[AEA] = \dfrac{P_{AE}P_{EA}^2}{P_{EA}+P_{AE}}$
	$[EEA] = [AEE] = \dfrac{P_{EA}P_{AE}(1-P_{EA})}{P_{EA}+P_{AE}}$	$[EAA] = [AAE] = \dfrac{P_{EA}P_{AE}(1-P_{AE})}{P_{EA}+P_{AE}}$

Fig. 5 shows clearly the full agreement of the copolymer dyads with the first conclusions of this work. For example, there is a coincident point at $X = 1$, where $f_1 = f_2$. It is indicate the high probability to find a random copolymer with small blocks of EE homopolymers due to a value of r_1. As it can be discussed above, the r_1 value, slightly bigger than 1, does more probable the mixture of HH units (increasing with time, $r_1 = k_{11}/k_{12} > 1$, homopolymerization) combined to AE (E ending) units at the beginning of polymerization, that is to say with values of $X < 1$.

But, consequently with the increasing of X value, the possibility to combine EA (A ending) units diminishes sharply at the same time of AA because the A monomer is less reactive than E and just lead to process of random copolymerization to high conversions or in this case, to the mixture of radical with E endings according to $1/r_2$ value.
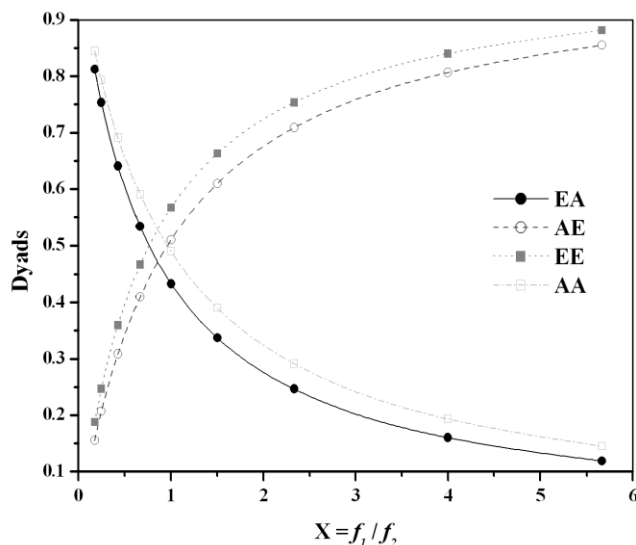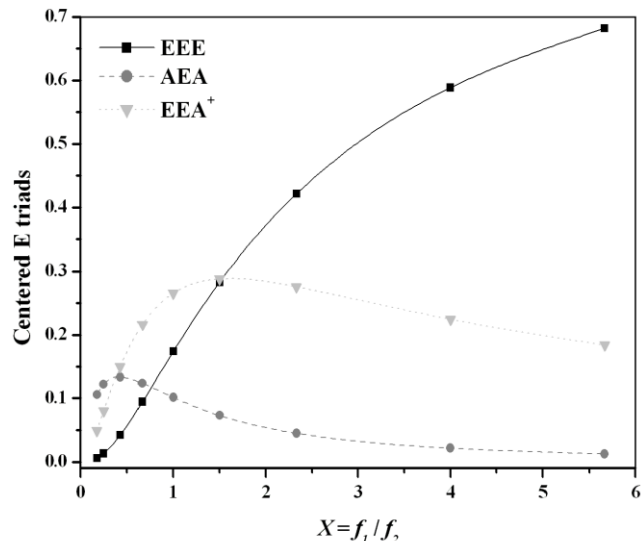

Fig. 5. Dyads of E–A systems.

The molar fraction of E–centered sequences can be determined by the application of well-known statistical relationships. Most accurately, the **Fig. 6** shows the diagram of the statistical distribution of E centered triads along the copolymer chains, as function of the molar concentration ratio of both monomers in the feed. However the molar fraction of heterotriads, that has one A unit, $EEA^+ = EEA + AEE$ reaches a maximum of almost 0.3 at $X = 1.5$.

The obtained diagram corresponds to statistical sequences with a random distribution of comonomeric units in the sequences considered. Therefore, the concentration

of an individual sequence, i.e. *iii, jii* or *iij* and *jij* $(i,j = E, A)$ can be regulated by controlling the composition of the monomer feed.

Fig. 6. Homo– and heterotriads of E–A systems centered on E monomer.

According to the relative proximity of r_1 and r_2 to unity, it can be expected that the average composition of the monomer feed does not change drastically with conversion and therefore the distribution diagram E–centered sequences drawn in **Fig. 6** and a similar one obtained for the A–centered sequences are valid as a first approximation for copolymers prepared in a wide interval of conversions [**27**].

Reactivity ratios calculation by dyads and triads methods

In many cases, it is more efficient to assume a general copolymerization model and calculate the average number sequence length of each monomer in terms of this model and the measured distribution by techniques such as NMR. The terminal copolymer model is used in this article because it fits all the sequence distribution data which were available at the time of writing [**13**]. Extension to more complicated copolymerization models is straightforward, in any case. Knowledge of the monomer feed composition and the corresponding average sequence lengths provides a value of the reactivity ratio, r. Each copolymerization experiment can produce estimates of r_1 and r_2. Dyads and triads measurements to calculate reactivity ratios have also employed simple methods recently. Finally, the equations used for the calculus and reported elsewhere [**28, 29**]:

$$\frac{P_{EE}}{P_{EA}} = r_1 \frac{F_E}{F_A} \tag{2}$$

$$\frac{P_{AA}}{P_{AE}} = r_2 \frac{F_A}{F_E} \tag{3}$$

$$\frac{T_{EEE} + 2T_{EEA} + T_{AEA}}{T_{EEA} + T_{AEA}} = r_1 \frac{F_E}{F_A} + 1 \tag{4}$$

$$\frac{T_{AAA} + 2T_{EAA} + T_{EAE}}{T_{EAA} + T_{EAE}} = r_2 \frac{F_A}{F_E} + 1 \qquad (5)$$

Graphs of the all fitting models to obtain data are shown at Fig 7. The values of r_1 and r_2 were calculated from the linear plot of dyads molar fraction ratios (Eqs. (2) and (3)) and triads molar fraction ratios (Eqs. (4) and (5)), both cases, vs (F_1/F_2) or inverse (F_2/F_1) when is necessary. At **Fig. 7** (left), it can be determined r_1 (E–based) and r_2 (A–based) from slope due to is the value of dyads molar fraction ratios when (F_1/F_2) = 1. The mathematical model demands that intercept of straight line be zero and the graph shows the good agreement with it.

On the other hand, **Fig. 7** (right), r_1 (E–centered) and r_2 (A–centered) can be determined from slope due to is the value of triads molar fraction ratios when (F_1/F_2) = 1, although in this case it could be rest 1 (from intercept) according to Eqs (4) and (5). The mathematical model demands that intercept of straight line be one and the graph shows the good agreement with it. Both r_1–r_2 pairs of values and both demands can be confirm by the classical statistical ANOVA showed at **Table 9**.
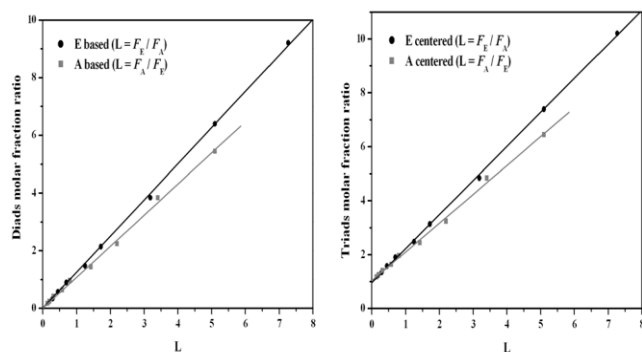

Fig. 7. Dyads and triads molar fraction ratios vs monomer in copolymers.

Table 9. Classical ANOVA parameters and fitting model results from **Fig. 7.**

Model (y–axis)	Slope (r_m)	Intercept	R^2	RSS
E–based dyad ratio	1.254 ± 0.008	$3.0 \times 10^{-16} \approx 0^a$	99.96 %	0.0429
A–based dyad ratio	1.08 ± 0.01	$2.6 \times 10^{-16} \approx 0^a$	99.74 %	0.0719
E–centered triad ratio	1.26 ± 0.01	0.96 ± 0.03	99.96 %	0.0336
A–centered triad ratio	1.07 ± 0.02	1.03 ± 0.05	99.74 %	0.0685

where [a]not significant statically, $m = 1$ (E based or centered) and $m = 2$ (A based or centered)

Notice the likeness among the r_1–r_2 pairs of values between them and respect to the obtained r_1 and r_2 with linear methods above discussed. It can be observed the outstanding fitting of these models for the high percentage of determination coefficients, which define that the models explain in those percentages the variability in y–axis. Besides, the RSS parameter confirms the last affirmation, even smaller than the obtained by linear methods. It can be consider not using the novel AIC and derivatives criteria in this analysis because these models were used as alternative to determine r_1–r_2 pairs of values through dyads and triads molar fraction ratio, taking into account the possibility to determine these ratios by spectroscopic techniques [28–30].

Q–e schemes

There is a selective factor in copolymerization that was qualitatively recognized from the phenomenon of heteropolymerization, involving the successful polymerization of two monomers, such as maleic anhydride and stilbene or fumarates and simple olefins, neither of which would polymerize successfully alone. It is thus obvious that, to account for such observations, there must be a selective factor greatly promoting addition of one radical to the second monomer and the second radical to the first monomer. This factor has been interpreted on the basis of polarity in the radical and the monomer [31].

In addition to this selective polar factor, there is another important influence on the copolymerization tendency related to the general ease with which a specific radical will add to a particular double bond, regardless of polarity. It has presented extensive experimental data in support of this factor and has termed it the "general monomer reactivity" factor. It has further pointed out that it seems to be closely related to the possibilities for resonance stabilization of the radical adduct formed. Sometimes this must be of considerable importance, particularly for monomers substituted at both ends of the double bond, such as maleic anhydride, stilbene, maleates and fumarates, and may even be of some importance in monomers containing two bulky substituents at one end of the double bond, such as o–methyl styrene, diphenylethylene and even methyl methacrylate or 2–hydroxyethyl methacrylate.

It has recently been possible, at least for those cases where steric factors are not disturbing, to derive an equation for the copolymerization ratio expressing the monomer reactivity factor (Q_1 or Q_2) in more precise terms These equations were derived from the expression for a rate constant on the basis of the assumption that the activation energy could be split into an "energy" factor and an "electrical" factor. The latter is considered to be a simple coulombic charge interaction between charges of the two monomers [31].

$$e_2 = e_1 \pm \sqrt{|\ln r_1 r_2|} \qquad (6)$$

$$Q_2 = \frac{Q_1}{r_1 e^{e_1(e_1 - e_2)}} \qquad (7)$$

From this point of view and taking as Q–e values of E, those reported by Rainaldi et al. [33] and Young [34], the Q–e values of A were calculated (**Table 10**).

Table 10. Q–e values of E–A system.

e_1	Q_1	Ref	e_2	Q_2
-0.39	1.78	[33]	0.10 ± 0.06	1.68 ± 0.07
0.2	0.8	[34]	0.69 ± 0.06	0.57 ± 0.01

Since, to the best of our knowledge, the obtained results are consistent with these data: the order of magnitude is the same and the reactivity ratio of a methacrylate type monomer (as 1–E) is slightly greater than the reactivity ratio of an acrylate type monomer (as 2–A) [33]. The calculated reactivity ratios are in good agreement with the experimental ones in the case of E ($1.25 < r_1 < 1.42$, [15,

25, 34]) while the values range differs in the case that A was $0.92 < r_2 < 1.08$. The "Q–e scheme" has to be considered as a useful approximation rather than a rigorous method, since only the electrostatic interactions between permanent charges due to the mutual polarization of monomers and radicals are taken into account whereas the steric effects are completely neglected due to the similarity of the structure of both monomers, just differentiated by the furfuryl ring in case of furfuryl acrylate.

From the obtained results it can be drawn that the acrylic monomer has a preferential tendency to copolymerize with 2–hydroxyethyl methacrylate (cross polymerization) while the latter shows a greater tendency to the auto–propagation. In practice a growing radical with methacrylic final unit mostly reacts with an E molecule thus favoring the formation of sequences of methacrylate units. From the Q–e scheme point of view, the copolymer reported by Rainaldi et al [**33**], has likeness with the system of this work. Then the most probable values of Q–e in these conditions are: $e_1 = -0.39$, $Q_1 = 1.78$, $e_2 = 0.10$ and $Q_2 = 1.68$.

It should be pointed out that, on the basis of Q–e scheme equations, Q and e are not independent variables and unique values for e cannot be derived from any amount of data on copolymerization ratios alone. The assumption that the average charge on the monomers without cycles be zero is perfectly acceptable. This seems to give fairly reasonable values for Q and e, in agreement with the qualitative concept that Q, the monomer reactivity factor, is related to resonance stabilization and that e, the electrical factor, parallels the charge induced by a given substituent in the cycles ring. Due to, one of the monomers of this work has a furfuryl ring, the e factor must be a different electric charge than the reported for the E (see e_1 and e_2 values) and the proximity of Q values confirm the proximity of the r_1–r_2 pair of values. Both reactivity ratios, near to unity, describe a random copolymerization there, although in principle, as higher probability of homopolymerization of E units and preference to copolymerization of A units [**33**].

Conclusion

Copolymers of HEMA and furfuryl acrylate were synthesized by free radical polymerization in toluene at 80°C using benzoyl peroxide as initiator. It was possible to calculate the reactivity ratios for this system using different methods. Comparing linearization methods, Fineman–Röss and Kelen–Tüdos give better values of r_1–r_2. However, the reactivity ratios are similar (almost independent of the calculation method) due to the accuracy of the measurement.

A Kelen–Tüdos extended model, KT_E shows good agreement to determine reactivity ratios to high conversion due to the tendency of the system according to reactivity ratios relationships. The microstructure characterization shows a behavior according to predicted by reactivity ratios values with R = 46.48 at X = 1 for one A units triads and a very good agreement among r_1–r_2 pairs of values obtained from the mathematical relations involved dyads and triads. The values of the Q–e scheme (not reported before for furfuryl acrylate) confirm the possible kind of copolymer in good concordance with the previous analysis by reactivity ratios and microstructure.

Reference

1. Brar, A.S., Hooda; S.; Goyal A.K. *J. Molecular Structure* **2007**, 828, 25.
   DOI: 10.106/j.molstruc.2006.05.031
2. Gallardo, A.; *Polymer* **1993**, 34(3), 567. DOI: 10.1016/0032–3861(93)90552–L
3. Mentak, K.; Keslinke, A.; Phan, K. Nanohybrid polymers for ophthalmic applications. US Patent WO/2006/063139, **2006**.
4. Gineste, J.L.; Pourcelly, G.; Brunea, J.; Perton, F.; Broussely, M. U.S. Patent 5578400, 1996.
5. López, E. *Prog Polym Sci*. **2002**, 27, 1879.
6. O'Driscoll, K.F.; Reilly, P.M. *Makromol Chem Macromol. Symp.* **1987**, 10/11, 355.
   DOI: 10.1002/masy.19870100118
7. Hill, D.J.T.; O'Donnell, J.H. *Makromol Chem Macromol. Symp*. **1987**, 10/11, 375.
   DOI: 10.1002/masy.19870100119
8. Adams, A.; Coomans, D.; Smeyers, J.; Massart, D.L. *Int. J. Pharm.* **2002**, 240, 37.
   DOI: 10.1016/s0378–5173(02)00127–8
9. Pinheiro, J.C.; Bates, D.M. "*Mixed–Effects Models in S and S–plus, Statistics and Computing*". Springer–Verlag, New York **2002**, (Chapters I & II)
10. Ziaee, F.; Nekoomanesh, M. *Polymer* **1998**, 39(1), 203.
    DOI: 10.1016/S00032–3861(97)00249–8
11. Fineman, M.; Röss, S.D. *J. Polym. Sci*. **1975**, 5(2), 259.
12. Kelen, T, Tüdos F. *J. Macromol. Sci. Chem*. A. **1975**, 9(1), 1.
    DOI: 10.1080/00222337508068644
13. Mayo, F.R.; Lewis, F.M. *J. Am. Chem. Soc*. 1**944**, 66, 1594.
    DOI: 10.1021/ja01237a052
14. Burnham, K.; Ardenson, D. "*Model Selection and Multi–Model Inference: A Practical Information–Theoretic Approach*", **2004**, Spring–Verlag, (Chapter 2, pp 49–95 & Chapter 8, pp. 437–454)
15. Zaldívar, D.; Fuentes, G.; Monett, D.; Peniche, C.; Arcís, R.W., Soto, A. *Polímeros: Ciência e Tecnologia* **1999**, 9(1), 35.
    DOI: 10.1590/S0104–14281999000100005
16. Zaldívar, D.; Fuentes, G.; Monett, D.; Peniche, C.; Arcís, R.W.; Soto, A. *Latin Am App Res*. **2002**, 32(2), 117.
17. Serra, L.; Doménech, J.; Peppas, N.A. *Biomaterials* **2006**, 27(31), 5440.
    DOI: 10.1016/j.biomaterials.2006.06.011
18. Fuentes, G.; Peón E.; Campos Y.; López N.; Resende C.X.; Soares. G.A. *Application of New Statistical Approach to Study Drug Release from OCP Coating on Titanium Sheets*. 21 BIOCERAMICS'2008, Buzios, Rio Janeiro, Brazil **2008**
19. Akaike, H. *IEEE Trans Autom Contr*. **1974**, 19(6), 716.
    DOI: 10.1109/TAC.1974.1100707
20. McQuarrie, A.D.R.; Tsai, C.L. "*Regression and time series model selection*", World Scientific Publishing Corp, New Jersey, USA **1998**.
21. Deen, GR.; Gan, L.H. *Polymer* **2006**, 47(14), 5025.
    DOI: 10.1016/j.polymer.2006.05.003
22. Deb, P.C.; *Polymer* **2007**, 48(2), 432.
    DOI: 10.1016/j.polymer.2006.11.027
23. Odian, G. *Principles of Polymerization*. 4th edition. John Wiley & Sons, NJ, 2004, pp.480–515.
24. Yong Feng, Yi Yi.; Xinghe, F.; Xiaofang, C.; Xinhua, W.; Qi–Feng, Z. *J. Polym. Sci. Part A: Polymer Chemistry* **2005**, 43(12), 2666.
    DOI: 10.1002/pola.20742.
25. Zaldívar, D.; Peniche, C.; Bulay, A. *J. Polymer* **1992**, 33(21), 4625.
    DOI: 10.1016/0032-3861(92)90423–T.
26. Semchikov, Y.D.; Smirnova, L.A.; Kopylova, N.A.; Izvolenskii, V.V. *Eur. Polym. J.* **1996**, 32(10), 1213.
    DOI: 10.1016/S0014-3057(96)00054–7
27. Gallardo, A. *J. Polymer* **1994**, 35(12), 2501.
    DOI: 10.1016/0032-3861(94)90370–0
28. Moritani, T.; Iwasaki, H. *Macromolecules* **1978**, 11(6):1251.

DOI: 10.1021/ma60066a036

29. Rudin, A.; O'Driscoll, K.F.; Rumack, M.S. *Polymer* **1981**, 22 (6), 740.
    DOI: 10.1016/0032–3861(81)90007–0

30. Xiaoqin, Z. "*Evaluation of instantaneous and cumulative models for reactivity ratio estimation with multiresponse scenarios*". Master of Applied Science in Chemical Engineering dissertation. University of Waterloo, **2004**, Ontario, Canada.

31. Alfrey, T.; Price, C.C. *J. Polymer Sci*. **1947**, 2(1), 101.
    DOI: 10.1002/pol.1947.120020112

32. Price, C.C. *Chem. Rev*. **1941**, 29(1), 37.
    DOI: 10.1021/cr60092a002

33. Rainaldi, I.; Cristallini, C.; Ciardelli, G.; Giusti, P. *Macromol. Chem. Phys.* **2000**, 201(17), 2424.
    DOI: 10.1002/1521–3935(20001101)201:17<2424::AID–MACP2424>3.0.CO;2–8

34. Young, L. *Q–e values*. In: Brandrup, J.; Immergut, E.H. (editors). In *Polymer Handbook*, 3rd edition, vol. 1. John Wiley & Sons, New York. **1989**, pp II–398/II–401