

# The role played by head–tail configuration on the molecular weight distribution of $\alpha$ -cyclodextrin tubes

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**Abstract** Supramolecular complexes consisting of cyclic molecules, such as cyclodextrins (CD), and polymeric chains have attracted considerable attention, being addressed in literature as novel molecular assembly. The so-called molecular tube (MT), synthesized by cross-linking adjacent  $\alpha$ -CD in a polyrotaxane, is expected to act as host for large molecules in inclusion processes. In addition, these tubes can also be used as building-blocks in the formulation of novel materials. Molecular tubes constructed with  $\alpha$ -cyclodextrin are obtained as a mixture containing entities with various molecular weights, and the molecular features determining the tube size distribution are not completely understood. In this paper, we propose the use of a statistical procedure based on binary numbers to examine the MT formation process. A complete analysis of the distinct orientations between cyclodextrin's units was made and, in the light of the approximations of our model, we pointed out, on quantitative basis, that the molecular weight distribution of  $\alpha$ -cyclodextrin MTs can

be explained assuming imperfections in the cross-linking process due to the existence of head-to-tail (HT) arrangements in the polyrotaxanes employed in synthesis.

**Keywords** Cyclodextrin · Molecular necklace · Molecular tube · Binary numbers · Supramolecular chemistry

## Introduction

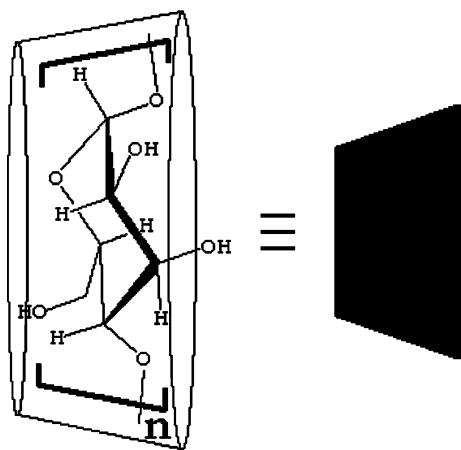
Molecules can be assembled together by means of noncovalent bonding to give supramolecular entities. Those nonbonding interactions play a fundamental role in supramolecular chemistry [1, 2], one of the most interesting and promising areas of modern science. A detailed understanding of the intermolecular interactions, specially the hydrogen bonds, is important for obtaining insight into the nature of most supramolecular systems, where selective molecular interactions are fundamentally requested [3]. Supramolecular chemistry is a highly interdisciplinary field and has attracted the interest of several researchers working with host compounds that fall under this important branch of chemistry, such as the cyclodextrins (CD).

Cyclodextrin is a cyclic oligomer of  $\alpha$ -D-glucose structured by the action of certain enzymes on starch. Generally described as shallow truncated cones, CD present a hydrophobic cavity of different sizes, depending on the number of elementary glucose units, and two different rims, a wider (head) containing all secondary hydroxyl groups and a narrower (tail) containing all primary hydroxyl groups. There are three CD readily available having six, seven or eight glucose units named  $\alpha$ -CD,  $\beta$ -CD and  $\gamma$ -CD, respectively, as depicted in Fig. 1 [4]. CD applications in supramolecular chemistry have been widely

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**Fig. 1** General structure of  $\alpha$ -CD,  $\beta$ -CD and  $\gamma$ -CD cyclodextrins, for  $n = 6, 7$  or  $8$  glucose units, respectively and the schematic representation used in this work

addressed in the literature. Due to its unique architecture, these molecules can be used in a large number of molecular devices such as molecular reactors, molecular nanotubes and molecular wires [5–13]. In the supramolecular context CD are also used in molecular recognition process [14–16].

The applicability of CD is closely related to the ability of this class of carbohydrate to form inclusion complexes with a very wide range of guest species in aqueous solutions. The inclusion complexation comprises secondary interactions often of solvophobic nature. In general, each weak interaction such as van der Waals, hydrophobic or hydrogen-bonding, is not sufficient enough individually to lead inclusion complex formation. Thus, the driving force responsible for the inclusion phenomena is the sum of such interactions. Depending on the structure of the guest molecules, hydrogen-bonding can play a fundamental role in the stabilization of the host-guest complex [17, 18].

Over several decades, inclusion of low molecular weight compounds by CD attracted the attention of the scientific community and has been the subject of numerous investigations [18, 19]. Polyrotaxanes are formed when threadlike molecules penetrate the cavities of cyclic molecules. Linear chain cyclodextrin-based polyrotaxanes can be prepared either by the polymerisation of a monomer complexed inside a cyclodextrin or by threading of cyclodextrin rings onto polymer chain [18]. In the beginning of the 1990s, there were a limited number of observations concerning the threading of polymers with CD. The number of related publications displayed an increasing after the independent and pioneering works of Harada and Kamachi [20] and Wenz and Keller [21].

Cyclodextrin necklace also named molecular necklace, has a polyrotaxane structure obtained when the carbohydrate units are threaded on a polymer chain [19, 22]. In sequential supramolecular structures as necklaces, CD can

be assembled in three possible conformations. These alignments are defined depending on whether two equal or two different rims are faced each other and are named head-to-head (HH), tail-to-tail (TT) or head-to-tail (HT). CD form inclusion complexes with various polymers in high yields. It has been shown that the threading process is chain-length selective, the yields usually depend on the degree of polymerisation of the included polymer used, and present different dependencies for  $\alpha$ -,  $\beta$ - and  $\gamma$ -CD. Another important factor affecting the complex formation is the correlation between the relative sizes of the cavities of CD and the cross-sectional areas of the polymers [23].

Despite the differences due to the nature of the CD and the polymers used in the threading process, some common features reported remain the same, independently of the necklace obtained. One of these features is related with X-ray studies, which indicates that the complexes have a column structure also named channel type structure. Other common features are related with the role played by hydrogen-bonding between CD units, which are thought to be responsible for the complex formation. In addition, in the earlier experimental papers an overall arrangement for adjacent CD exclusively formed by HH and TT, thought to be the most probable structures, has been proposed for necklaces of  $\alpha$ -,  $\beta$ - and  $\gamma$ -CDs [24–29].

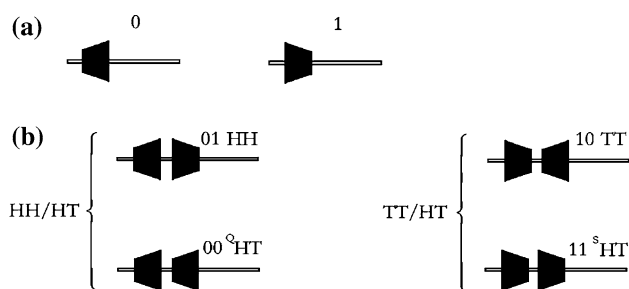
Recently, by means of scanning tunnelling microscopy (STM), the first experimental quantitative determination of the intramolecular conformations of  $\alpha$ -CD's units in a molecular necklace was made [30]. In that paper, Miyake and co-workers pointed out that, about 20% of HT arrangements were found to exist in the supramolecular structure, contrary to the current model which indicates that all CDs are arranged in HH or TT conformation, in the molecular necklace synthesized according to the method described in ref. [22]. The condensation of  $\alpha$ -CD threaded on a polymer chain, with epichlorohydrin, results in the formation of the so-called molecular tubes (MTs) [31]. In the synthesis of MT, bulk ends prevents the unthreading of cyclodextrin's units, before the cross-linking process. The number of  $\alpha$ -CD units existent in the MT and in the polyrotaxanes employed in the synthesis, should be, in principle, the same, because cyclodextrin's units are almost closely packed from end to end on the polymer chain. Therefore, the length of the polymer employed as template in the polyrotaxane synthesis, should determine the length of the synthesized MT. In fact, the maximum number of CDs threaded depends on the length of the polymer, nevertheless the MT synthesized according to Harada's procedure is obtained with a wide range of molecular weight [32–34]. The orientations of CD's units are supposed to play an important role in the synthesis of polyrotaxane derivatives, such as MT. As firstly suggested by Boogaard [35], the tube length distribution might be explained considering

insufficient cross-linking between adjacent CD's units in the polyrotaxanes employed in the synthesis. This was attributed to the existence of HT conformations in the linear structure of such polyrotaxanes. However, we feel that the ideas and suggestions presented so far have not been completely proven based on solid arguments, and also the explanations given may not look quite sound.

In this paper, we propose the use of a statistical procedure based on binary numbers to examine the MT formation process. A complete analysis of the distinct orientations between cyclodextrin's units was made and, in the light of the approximations of our model, we pointed out that the molecular weight distribution of  $\alpha$ -CD MTs can be quantitatively explained assuming imperfections in the cross-linking process due to the existence of HT conformations in the polyrotaxanes employed in the synthesis. A nice agreement between our theoretical approach and the experimental characterization of MT was obtained providing, for the first time, strong support to the relevance of the HT conformation to the MT synthesized by the Harada's procedure. We believe that our approach to this problem can make a contribution to our better understanding of the  $\alpha$ -CD MT formation process.

### Theoretical details

Binary numbers can completely represent the three possible cyclodextrin conformations formed in the threading process. As depicted in Fig. 2a, adopting the left side as reference, the digits 0 and 1 are related to ring units included onto a polymer chain with distinct orientation. In our model, cyclodextrin's associations have been correlated with pairs of binary numbers. Therefore, HH was represented by the pair 01 and TT by the pair 10. The HT conformations have to be related with more than one binary



**Fig. 2** (a) Binary representation of cyclodextrin's units included with distinct orientations. (b) Molecular conformations and related binary pair for cyclodextrins in supramolecular sequential structures named head-to-head (HH), tail-to-tail (TT) and head-to-tail (HT), respectively. The superscripts stand for HT obtained from distinct disputes,  $^Q$ HT represents the head-to-tail conformations from dispute HH/HT and  $^S$ HT represents the head-to-tail conformations from dispute TT/HT

pair. In necklace formation, independently of the side which cyclodextrin rings are included onto a polymer chain, two distinguished competitions should be taken into account in the threading process: one concern to the HH/HT dispute and the other to the TT/HT dispute. Thus, the HT conformation was taken into account two times, one concerning the HT conformation formed from HH/HT dispute, named  $^Q$ HT, represented by 00, and another concerning the HT conformation formed from TT/HT dispute, named  $^S$ HT, represented by 11. The four associations, related to the two disputes, are depicted in Fig. 2b. Independently of the number of cyclodextrin units used in the simulations, all possible necklaces can be regarded as binary sequences. We focus on such binary sequences in order to correlate probability and supramolecular conformational analysis.

The number of cyclodextrin rings of a given necklace ( $n_{CD}$ ) corresponds to the number of binary digits of the sequences analysed where the number of pairs in each necklace is equal to  $n_{CD}-1$ . The possible necklaces are limited by the number of cyclodextrin units considered. Thus, there are  $2^{n_{CD}}$  possibilities. In our approach, the HH conformation is introduced with a probability equals to  $P$  and the  $^Q$ HT is introduced with probability equal to  $Q$ , where  $Q = 1 - P$ . Similarly, the TT conformation is introduced with a probability equals to  $R$  and the  $^S$ HT, which disputes with TT, is introduced with probability equal to  $S$ , where  $S = 1 - R$ . From the analysis of Fig. 2 it becomes clear that there is no way of evaluating the four probabilities simultaneously. Once the HH/HT dispute is established it eliminates the occurrence of the TT/HT dispute, and vice-versa. Therefore, the two disputes are independent and so, mutually excluding.

Assuming that the first inclusion of a cyclodextrin molecule is introduced with a probability of 1/2 and also that the two mentioned competitions are mutually excluding, as well as, the two possible outcomes obtained from those competitions, a general expression for the probability of each necklace can be written. Therefore, the probability of each necklace is given by Eq. 1, where the superscripts stand for the number of arrangements related with probabilities  $P$ ,  $Q$ ,  $R$  and  $S$ , of each possible necklace, respectively. As should be expected, the total probability equals to unity. The reason for the factor 1/2 in Eq. 1 is due to the fact that the first inclusion, for example digit 0, excludes the possibility of having digit 1. In our approach digits 0 and 1 both have the same weight (1/2) since the total probability is normalized to unity.

$$p_i = (1/2)P^{n_{HH_i}}Q^{n_{^QHT_i}}R^{n_{TT_i}}S^{n_{^SHT_i}} \quad (1)$$

$$\sum_{i=1}^{2^{n_{CD}}} p_i = 1 \quad (2)$$

In addition, based on the set of  $2^{n_{\text{CD}}}$  possible necklaces, the probability of obtaining a number  $x$  of HT associations ( ${}^Q\text{HT} + {}^S\text{HT}$ ), denoted by  $P^{\text{HT}}(x)$ , can be calculated by Eq. 3 where the variable  $\delta$  is defined in Eq. 4. It is possible to determine the probability of obtaining necklaces with particular number of HT from each of the two disputes mentioned separately, but  $P^{\text{HT}}(x)$  indicates the probability of obtaining a necklace with  $x$  HT associations in its structure independently of the dispute it came from

$$P^{\text{HT}}(x) = \sum_{i=1}^{2^{n_{\text{CD}}}} p_i \delta \quad \text{for } x = 0, 1, 2, 3, \dots, n_{\text{CD}} - 1 \quad (3)$$

$$\delta = \begin{cases} 0 & \text{if } (n^Q\text{HT}_i + n^S\text{HT}_i) \neq x \\ 1 & \text{if } (n^Q\text{HT}_i + n^S\text{HT}_i) = x \end{cases} \quad (4)$$

It is important to bear in mind that the number of a particular association (HH, TT or HT) is distributed in a range of distinct necklaces, possessing equal or different probabilities, and there is a direct relationship between the total number of those associations and experimental data. With our approach, histograms can be constructed to study how the different necklaces are distributed. Therefore, it is possible to correlate the quantities  $P$ ,  $Q$ ,  $R$  and  $S$  with those distributions. In order to compare directly the number of HT associations with experimental data we use the Eq. 5 where the HT percentage can be calculated.

$$\% \text{HT} = \frac{100}{n_{\text{CD}} - 1} \sum_{x=1}^{n_{\text{CD}}-1} x P^{\text{HT}}(x) \quad (5)$$

Taking these five equations into account and the related assumptions described, we wrote a computer simulation program to quantitatively study necklaces obtained by the threading process. All possible necklaces are allocated as binary sequences in a matrix with predefined dimension. In the computer program, written in *FORTRAN* computational language, values for the constants  $P$ ,  $Q$ ,  $R$  and  $S$  can be readily assigned allowing probability calculations. The steps implemented will be discussed later, when the fundamental aspects concerning the model applied to the MTs will be presented.

## Results and discussion

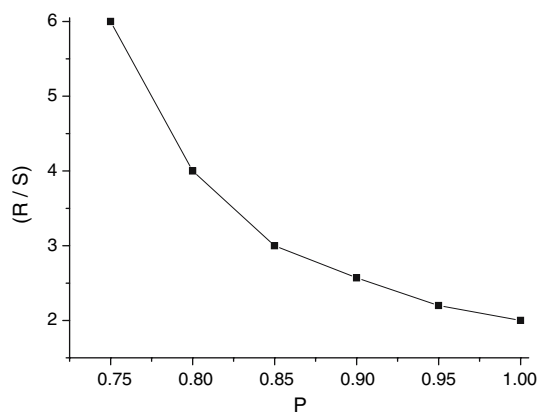
### Modelling necklace formation

For practical purpose, the number of cyclodextrin's units of the necklaces modelled, have to be specified. The number of digits is related to the number of possible associations of each necklace. In general, the size of the polymer chain can determine the number of cyclodextrin constituting the

molecular necklace. In spite of that, in our approximation, adequate values for  $P$ ,  $Q$ ,  $R$  and  $S$  constants can be determined independently of the size of the binary numbers employed in calculations but, in order to compare results properly, it is necessary to handle binary sequences compatible with the number of CD of the necklace modelled.

As mentioned previously, by means of scanning tunnelling microscopy (STM), 20% of HT conformation was found to exist in  $\alpha$ -cyclodextrin necklaces obtained by the threading process with poly(ethylene glycol). The other 80% of the conformation are distributed over HH or TT arrangements [30]. Those percentages are closely related to the formation ratio of the conformations based on strength differences between secondary–secondary, primary–primary and primary–secondary hydrogen bonding considering both, the HH/HT and the TT/HT disputes [36]. Such differences are expressed, in our approach, by the constants  $P$ ,  $Q$ ,  $R$  and  $S$ , which are used as input in our model. Thus, a set of specific values for those constants determines the HT conformation percentage. Based on such constant dependencies, only two parameters can be used to apply the model. Therefore, in order to direct compare the experimental formation ratio of the TT and HT conformations previously reported [30], we choose to work with  $P$  and the  $(R/S)$  ratio. Once one of the four constants has been determined, or specified, the others can be found by a search program based on the assumptions previously established and focusing on the percentage obtained experimentally. Therefore, we modified our original computer simulation program to search for the formation ratio of TT/HT based on a pre-defined value for  $P$ . The computer program found the ratio  $(R/S)$  in accordance with a defined HT percentage (for instance 20%). We used binary sequences with 15 digits based on experimental data from ref. [30].

For distinct  $P$  values, different  $(R/S)$  ratio can be found in accordance with HT experimental percentage. For example, we can define  $P$  as one ( $P = 1$ ), supposing that only HH conformation is obtained from the dispute HH/HT. This assumption implies in a specific value for the  $(R/S)$  ratio. Using our program we found the values  $2/3$  and  $1/3$  for  $R$  and  $S$ , respectively, which are exactly the same relation reported in ref. [30]. There is a determined HT percentage for any given  $P$  and  $(R/S)$  value and more than one value for  $P$  and the ration  $(R/S)$  can determine the same HT percentage, what reveal a non unique character (more than one solution is possible). In accordance with the existence of 20% of the HT conformation, a set of  $(R/S)$  ratios has been determined for distinct values of  $P$ , as depicted in Fig. 3. The percentage of HT is achieved considering the contributions of the two disputes. Therefore, different  $(R/S)$  ratios stand for the different contributions of each dispute. The increase of HT from



**Fig. 3** Some values for  $P$  constant in accordance with the existence of 20% of the HT conformation

HH/HT dispute (smaller value for  $P$ ) produces the decreasing of HT from TT/HT dispute in order to maintain the specified percentage. But there is a limit for  $P$  that must be  $>0.65$ , because if we consider as zero the contribution from TT/HT dispute, what is equivalent to assume  $R = 1$ , and assumes a value for  $P < 0.65$ , we find a percentage  $>20\%$  for HT conformations. In order to determine the correct  $P$  value, additional information has to be supplied by, for example, another experimental observation.

The binary model can be adapted in order to study the MT formation, numerically. The additional information can be supplied by data related to the characterization of tubes synthesized by the Harada's procedure, as addressed in the literature [32–34]. Therefore, the correct  $P$  value can be estimated. This is described in the next section.

### Modelling MT formation

In the synthesis of MT, two hydroxyl groups closed to each other are covalently connected by the action of the cross-linking agent, which contains in its structure two functional groups with comparable reactivity, in order to avoid the formation of dangling cross-linking groups. However, the primary and secondary hydroxyl groups present different reactivity [37]. Thus, it is reasonable that the HT conformation, on which primary and secondary hydroxyl group are facing each other, are responsible for the imperfection in the cross-linking process, leading to the formation of MT with non-expected number of CD's units as suggested by Boogaard [35]. Furthermore, taking the HT conformations as imperfections, it can be firstly assumed that each HT configuration avoids the cross-linking of adjacent CD's units in the polyrotaxane. Thus, our previous model was adapted, in which the binary sequences are analysed in order to fragment the corresponding polyrotaxane binary

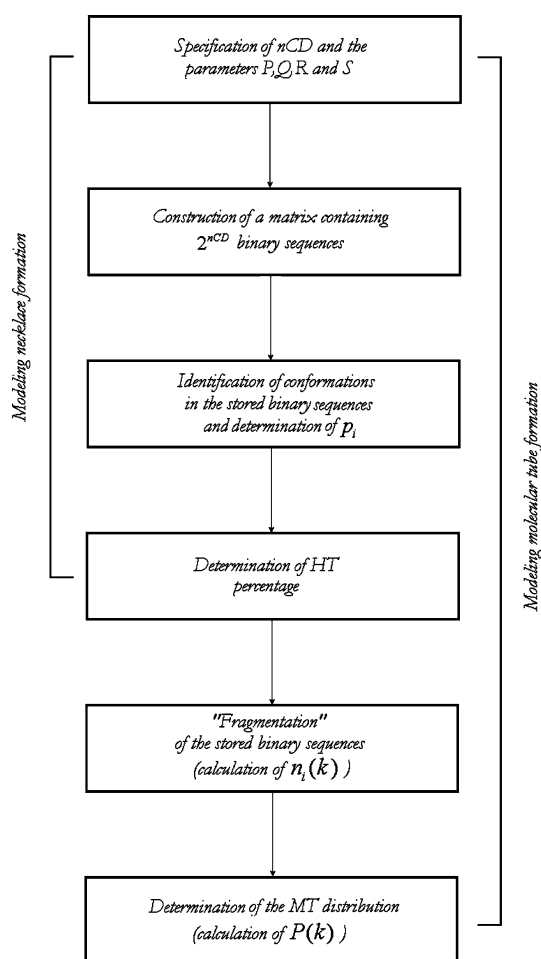
sequences in the positions related to the HT configurations. A new distribution of probabilities was obtained. This distribution is mathematically expressed in our model by the function  $P(k)$ , defined in Eq. 6, standing for the probability of obtaining a MT with a number  $k$  of CD's units. The quantity  $p_i$  corresponds to the probability of finding each necklace (polyrotaxane), defined in (1), and the quantity  $n_i(k)$  corresponds to the number of MT containing  $k$  CD's units, obtained from the polyrotaxane  $i$ . The quantity  $n_i(k)$  is related with the number of CD's units in the polyrotaxanes employed in the synthesis, by the relation (7).

$$P(k) = \frac{\sum_{i=1}^{2^{n_{CD}}} n_i(k)p_i}{\sum_{k=1}^{n_{CD}} \left( \sum_{i=1}^{2^{n_{CD}}} n_i(k)p_i \right)} \quad (6)$$

$$\sum_{i=1}^{n_{CD}} n_i(k)k = n_{CD} \quad (7)$$

According to the Eq. 6, the distribution of necklaces, assuming the HT conformations as responsible for the imperfections in cross-linking process, promotes a corresponding distribution of MT. Therefore, the distribution of lengths of tubes must be built from the distribution of probabilities of necklaces. The distributions of lengths of MTs exhibit a particular characteristic of having a univocal relationship with the parameters employed in our model, once the MTs obtained by the cross-linking process are constituted of associations of HH and TT dimers. Basically, there is no compensation due to the occurrence of a particular entity as a result of the two disputes, what is observed for HT in the model for the formation of necklaces, within a given range, which is coherent with the presence of 20% of the HT dimer. Once the probability distribution is known experimentally for the tubes, the parameters can be safely estimated.

The calculation steps required in order to modelling the necklace and the MT formations, implemented in *FORTRAN* computational language, are outlined in the Fig. 4. As discussed previously, the MT distribution is derived from the necklace binary representation and both distributions are indicated in the diagram. After the specification of the number of CD's units and the set of parameters of our approach, binary sequences are generated and stored in a matrix containing  $2^{n_{CD}}$  polyrotaxane representations. Then, the sequences stored are analysed. The three possible associations of adjacent CDs are identified and individual probabilities ( $p_i$ ) are calculated. The HT percentage is determined, concluding the steps related with necklace formation. In order to obtain the MT distribution, the



**Fig. 4** Calculation steps required in order to modelling the necklace and the MT formations, implemented in *FORTTRAN* computational language, according to our approach

binary sequences stored are “fragmented”, what is equivalent in our approach to the determination of HT positions for the calculation of  $n_i(k)$ . Finally, the MT distribution, the function  $P(k)$ , is calculated, allowing the construction of histograms.

Based on the number of CD’s units of the polyrotaxanes synthesized in the reference used for comparison [32], we handled binary sequences corresponding to  $n_{CD} = 18$ . Histograms were constructed showing the probability of obtaining a number  $k$  of CD’s in the MT derived from such polyrotaxanes, as depicted in Fig. 5. The histograms indicates that the probability of obtain a long MT is very small and, according to our model, the MT will be synthesized as a mixture comprising a wide range of molecular weight, in qualitative accordance with the results reported by Ikeda e co-workers [32–34]. But, in order to validate de initial hypothesis, concerning the HT influence in the distributions, a numerical comparison between experimental and binary data, is indispensable.

As mentioned previously, Ikeda and co-workers synthesized MT according to the Harada’s procedure and obtained a mixture of MT in a wide molecular weight range. The prepared MT was separated into seven fractions by GPC (Gel Permeation Chromatography) in order to obtain MT with narrow molecular weight distribution. The authors reported, in the paper used as ref. [32], the numbering-average molecular weight ( $M_n$ ) of non-fractioned MT. In addition, it was also reported that the broad peak obtained by GPC, of non-fractioned MT, covered molecular weight from 2,000 to 20,000  $g\ mol^{-1}$ . This indicates that the free CD’s units are not present in the non-fractioned MT.

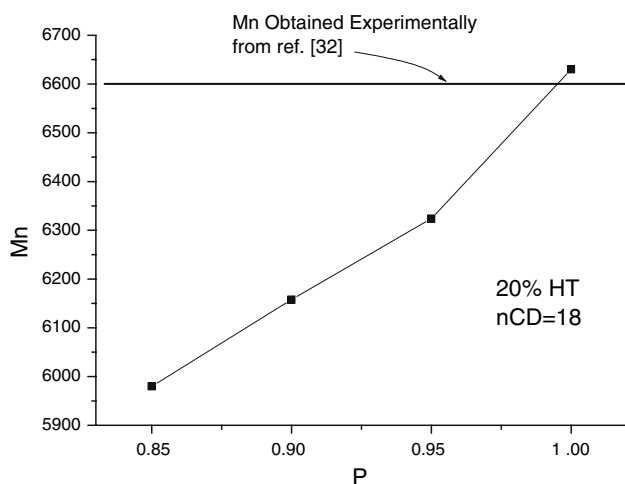
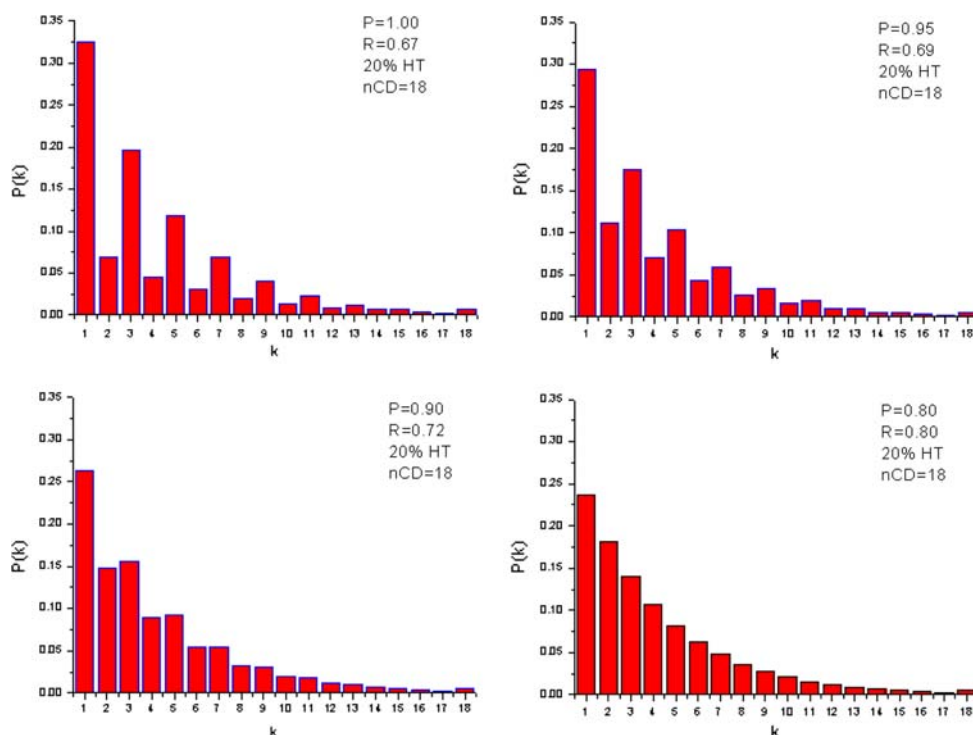
The Numbering-average molecular weight ( $M_n$ ) can be readily calculated from the histograms depicted in Fig. 5, employing in the calculation an expression for the determination of the molecular weight of specific MT with  $k$  CD’s units, according to the average number of cross-linking bridges present in the MT synthesized. The mentioned expression was determined from MALDI-TOF mass spectroscopy by Ikeda and co-workers [32] and is reproduced in Eq. 8, where  $k$  stands for the number of  $\alpha$ -CD’s units in a particular MT  $i$ , with molecular weight  $M_i$ , and  $m$  stands for the average number of cross-linking bridges between adjacent CD’s units, a number approximately equals to 3. In Eq. 8, the number 58 corresponds to the increment to the molecular weight due to the existence of each cross-linking bridge. Thus, the numbering-average molecular weight ( $M_n$ ) can be promptly calculated by the expression 9 [38].

$$M_i = 973 \times k + 58 \times m \times (k + 1) \quad (8)$$

$$M_n = \frac{\sum_i n_i M_i}{\sum_i n_i} = \sum_i p_i M_i \quad (9)$$

The  $M_n$  value reported for non-fractioned MT by Ikeda and co-workers is 6,600  $g\ mol^{-1}$  and the values obtained by our model, considering some allowed  $P$  values, are depicted in Fig. 6. We found, as best result, a  $M_n$  value equals to 6,630  $g\ mol^{-1}$ . For the calculus we excluded the probability of obtained single  $\alpha$ -CD, according to the molecular weight range mentioned previously. The results obtained by our approach are very interesting given an error relative to the actual value of only 0.5%. These results, strongly indicates that the hypothesis made initially [35] that insufficient cross-linking is due to the existence of HT conformations, may be the major factor controlling the MT size. The agreement elucidates, for the first time, the role played by the HT conformations in the MT molecular weight distribution on quantitative basis. In addition, according to Fig. 6, the correct value of the  $P$  constant is close to the imposed by Harada’s group in order to explain

**Fig. 5** Histograms showing the probabilities of obtaining a MT containing  $k$  CD's units, for four allowed  $P$  and corresponding  $R$  values, in accordance with experimental data [30], where 20% HT was found to exist. The histograms were constructed considering  $n_{CD} = 18$ , according to the polyrotaxanes employed in the synthesis of MT, in ref. [32]



**Fig. 6** Numbering-average molecular weight ( $M_n$ ) obtained theoretically, for some  $P$  values, assuming that the HT conformation is responsible for the insufficient cross-linking between adjacent  $\alpha$ -CD's units in polyrotaxanes employed in synthesis of MT, for  $n_{CD} = 18$ , and in accordance with the existence of 20% of HT conformations

the observed 20% of HT conformations ( $P = 1$ ), reported in ref. [30].

Besides the numbering-average molecular weight ( $M_n$ ), which is an arithmetic mean of the weight of molecules, the weight-average molecular weight ( $M_w$ , Eq. 10) is also a valuable property, used to define the polydispersity index ( $d = M_w/M_n$ ). This index is a measurement of the range of molecular weight in the MT mixture. The values of  $M_w$  and  $d$  were reported by Ikeda and co-workers taking the non-fractionated MT ( $M_w = 14,454 \text{ g mol}^{-1}$  and  $d = 2.19$ ) [32].

$$M_w = \frac{\sum_i n_i M_i^2}{\sum_i n_i M_i} = \sum_i p_i M_i \left( \frac{M_i}{M_n} \right) \quad (10)$$

The predicted values by our model were  $M_w = 9,017 \text{ g mol}^{-1}$  and  $d = 1.36$  that are 38% underestimated relative to the observed data, indicating that the mixture found theoretically has lower polydispersity. The disagreement pointed out before can be partially understood by the analysis of Eqs. 9 and 10. These functions differ by the ratio  $(M_i/M_n)$  in the summation of Eq. 10, which varies linearly with the increase in the degree of polymerisation ( $k$  in Eq. 8). According to Eq. 8, we found the ratio  $(M_i/M_n) > 1$  for  $k \geq 6$ , using  $M_n = 6,630 \text{ g mol}^{-1}$ . Therefore, the presence of slightly longer MT's than the average hexamer, contributes significantly to enlarge  $M_w$ . This mathematical aspect indicates that small differences between predicted and actual probabilities may change the  $M_w$  value, significantly. Due to the number of terms in the summations used and the complexity of the probability distribution function, that seems to be of exponential decay nature, the numerical reason for the low predicted value of  $M_w$  can not be completely determined.

It is now prudent to recognize the limitations of our model, which is purely based on statistical grounds and thus, in principle, is physically not meaningful. Nevertheless the perfect agreement found for  $M_n$  can not be discarded, once most of thermodynamic measurements are based on the number of molecules present and hence depend on  $M_n$ . We are now engaged in a more challenging

task, which is find intrinsic molecular properties that may control the distribution of species.

## Conclusion

In this paper, we proposed the use of binary numbers to examine the  $\alpha$ -CD necklace formation process in detail. We pointed out that by using our theoretical model, predictions of the number of HH, TT and HT conformations of a given necklace can be made. But the correct values of the ratio of the formation of the dimers involved in the polyrotaxane synthesis cannot be satisfactory determined without additional information. Thus we modified our model in order to study the MT molecular weight distribution according to characterization data addressed in the literature, concerning the synthesis of MT by the Harada's procedure. An excellent agreement with experimental characterization of MT was obtained, for the first time, assuming that the insufficient cross-linking between adjacent CD's units in polyrotaxanes, is due to the existence of 20% of the HT conformations. We also pointed out that the correct value of the ratio of the formation of the dimers mentioned are close to the reported by Miyake and co-workers in order to explain the observed 20% of HT conformations. In addition, we conclude that the HT conformation promotes the molecular weight distributions of MT synthesized by the procedure develop by Harada and co-workers.

Finally, one cannot ignore that our approach, based on simple statistics considerations, implies in a considerable computational task that strongly indicates that the results obtained are not fortuitous. The simple statistic assumptions may promptly provide an adequate theoretical model to the formation of the supramolecular structures studied. Supported by the results obtained, in light of the approximations of our model, the existence of HT conformations in the polyrotaxanes can explain the molecular distribution of MT.

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