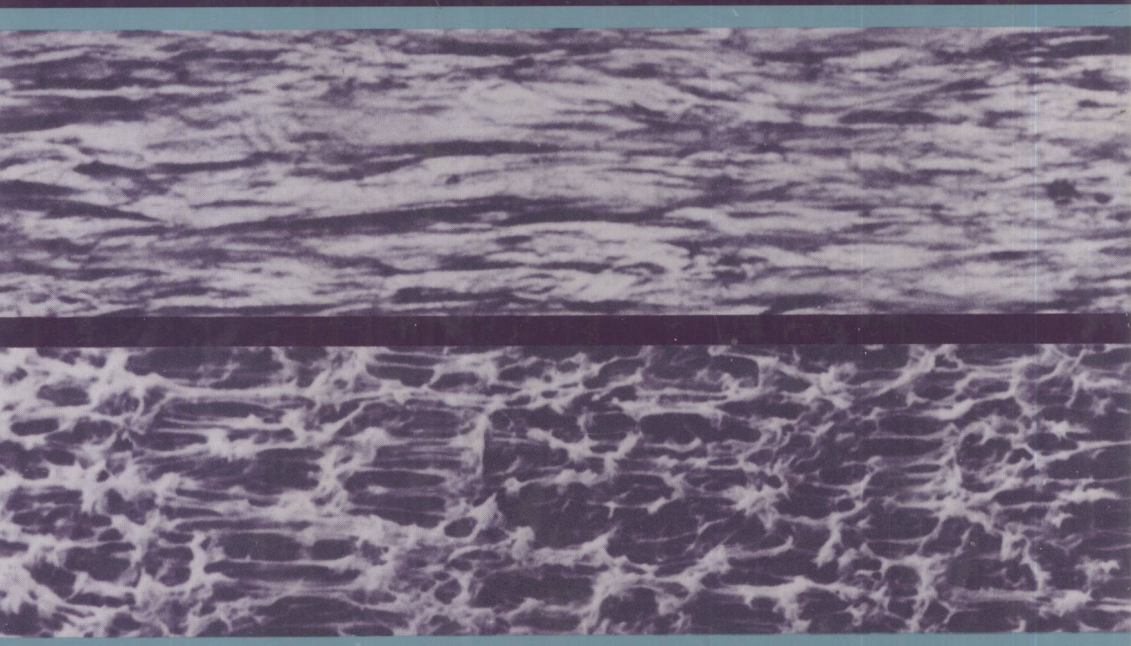
Computer Simulation of Polymers



Editor: E.A. Colbourn

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POLYMER SCIENCE AND TECHNOLOGY SERIES

COMPUTER SIMULATION OF POLYMERS

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CHAPTER 1

Molecular modelling of polymers 9. Description and application of torsion angle unit theory to predict polymer properties

A J HOPFINGER AND M G KOEHLER

1.1 Introduction

1.1.1 History and background of computer-assisted molecular design

The application of computer-assisted molecular design (CAMD) approaches to the development of new polymeric materials is being actively explored.[1] The considerable interest in this 'hi-tech' approach to the development of polymer products arises jointly from the fundamental insight that can be realized, and the enormous gain in design efficiency that is possible from its use. The extension of CAMD approaches in materials science is a natural progression of the significant impact CAMD has had in the pharmaceutical industry. Virtually every major pharmaceutical company, worldwide, has a group of scientists who are doing computer-assisted drug design.[2–4] In terms of macromolecules, computer-assisted drug design has been directed to expand its focus and effort on modelling the interactions of ligands (potential drugs) with biological macromolecules–proteins and polynucleic acids. The conformations of the biological macromolecules have been determined mainly from X-ray crystallography, and, to a lesser extent, from NMR methods. X-ray crystallography and NMR spectroscopy will likely merge with current computer-assisted drug design methods over this decade to yield integrated experimental and computational approaches for the efficient and reliable design of new biopharmaceutical agents.

Unfortunately, the application of CAMD in polymer science is not as direct as it is in the pharmaceutical sciences. In the case of designing a drug, there is usually an isomorphic relationship between a change in the structure of a drug-candidate molecule and the corresponding biological response. Thus, one can deal with discrete molecular entities – the drug candidate, and even better, also its macromolecular receptor – in the molecular design process.

In the case of the design of polymeric materials the problem becomes

more diffuse, less defined. What must be evaluated (modelled) is a volume element of the polymeric material that is of sufficient size so as to allow the estimation of key molecular properties that, at the least, correlate to, or are indicative of, the bulk properties of the material. Moreover, the polymer is not a distinct molecular entity unto itself. Issues of molecular weight, chemical defects and structural defects must be considered in even the most simple linear, synthetic polymers. In other words, there is not necessarily an isomorphic relationship between the physicochemical properties of a single polymer molecule and the bulk properties of a material derived from the polymer. Overall, the lack of an isomorphic molecule–property relationship makes polymer design more difficult than drug design.

1.1.2 Approaches to computer-assisted polymer design

The most comprehensive approach to the modelling of structural features of polymeric materials is computer simulation–molecular dynamics and/or Monte Carlo techniques.[5,6] Computer simulation of polymer structure permits estimation of average properties of polymer systems containing multiple polymer chains and other types of molecular entities such as solvent, plasticizer and/or crosslinking agents. At this time in the evolution of CAMD there are two significant drawbacks to the use of computer simulation of polymers in a practical design mode.

1. The time, effort and computer resources to do a polymer simulation are often so large as to negate the impact of the calculation on a design programme. It may simply be easier to make and test a targeted polymer system than to do the corresponding simulation.
2. It is often difficult to abstract the relevant information/molecular properties from a simulation that are indicative of the bulk property of interest. For example, what motions in molecular dynamics simulations correspond to the onset of the glass transition, T_g?

Molecular simulations on meaningful models of polymer materials have only been possible for a short time. Hence other approaches to predicting bulk properties, obviously of much less computational intensity, have been considered over the past years. The most straightforward of these approaches are models which are based upon the group additive property (GAP) concept.[7–9] The GAP concept assumes that some intrinsic contribution to any bulk property, $P_B(i)$, is associated with the ith structural group of the polymer. Most of the GAP models deal with homopolymers so that consideration of the structural groups composing the monomer unit is sufficient to define all contributions to the bulk property, P_B. P_B is

simply taken to be the sum of the $P_B(i)$ composing the monomer,

$$P_B = \sum_{i=1}^{m} P_B(i) \qquad [1]$$

In Eqn [1] the index m corresponds to the number of structural groups in the monomer unit. Clearly, group additivity is often far from a reasonable assumption, and most GAP models include non-additive correction factors, $f_B(i)$, so that Eqn [1] becomes

$$P_B = \sum_{i=1}^{m} (P_B(i) + f_B(i)) \qquad [2]$$

The majority of polymer GAP models have been developed to predict one particular bulk property with a strong bias favouring the estimation of T_g.[7,10–13] However, VanKrevelen has undertaken the monumental task, with considerable success, of devising a family of homologous GAP models to estimate a wide variety of bulk properties of homopolymers for both the solution and solid-states (amorphous, semi-crystalline and crystalline).[7] While the mathematical formats of the VanKrevelen GAP models vary somewhat, they can be characterized by

$$P_B = \sum_{i=1}^{m} \frac{P_B(i) + f_B(i-1, i, i+1)}{M_W} \qquad [3]$$

where $P_B(i)$ is the weighing factor for the ith group for bulk property P_B, $f_B(i-1, i, i+1)$ is a non-additive correction factor for the ith group, and M_W is the monomer molecular weight. The introduction of M_W in the VanKrevelen GAP models means that the bulk polymer properties are estimated from a parameter set that scales to monomer molecular weight. The individual $P_B(i)$ and $f_B(i-1, i, i+1)$ are determined by fitting procedures using a training set of polymers for which the bulk property of interest has been measured.

The VanKrevelen GAP formalism, overall, has been quite successful. In particular, it has been reliable in predicting relative differences in bulk properties of polymers having structural homology. Moreover, GAP methods are quite easy to employ and interpret. The calculations are simple and fast, and the end-point bulk property well defined.

However, GAP methods have three serious limitations:

1. If the group parameters are not available for the polymer of interest, then a bulk property estimation is not possible. Moreover, there do not appear to be any overall guidelines to estimate group parameters for any of the more popular/general GAP formalisms.
2. The real world is not group-additive, and even the introduction of non-additive correction factors still leaves, ultimately, a chemical topological (graph) model, as opposed to a three-dimensional molecular

model. Consequently, those bulk properties that are highly dependent upon spatial behaviour on the molecular level may not be estimated accurately.

3. GAP models do not provide mechanistic information that can be used to provide an understanding of why a particular polymer exhibits a particular bulk property measure. This information can only come from higher level modelling.

There is a level of polymer modelling intermediate to GAP formalisms on the one hand, and molecular simulation on the other. This level (class) of molecular modelling can be described as three-dimensional static (3DS) modelling and encompasses conformational analyses of polymer chains,[14] polymer crystal packing calculations,[15] and statistical mechanics formalisms of which Flory's Rotational Isomeric State (RIS) theory[16] is most prominent. 3DS modelling studies actually represent the majority of polymer structure calculations over the past thirty years. However, 3DS studies have not often been used to predict bulk polymer properties with the exception of crystal structures. 3DS calculations have been used, in the main, to provide 'pictures' of polymer chain conformations under different conditions, usually ranging from the amorphous to crystalline solid-state, and/or dilute to dense solution states.

1.1.3 Overview of torsion angle unit theory

Given the current situation regarding approaches to the molecular modelling of polymers, with the goal of predicting properties, we asked ourselves if some hybrid technique could be devised which maximizes the advantages of each of the current techniques, but minimizes their respective drawbacks. One additional constraint was considered in formulating our answer – that computational power will increasingly grow so that the applications of large molecular simulations will become increasingly practical.

The remainder of this chapter describes our answer to the question posed above. We have developed a polymer modelling formalism we call torsion angle unit, TAU theory.[17,18] The essential features of TAU theory, which are expanded upon in the balance of this chapter, are:

1. The theory, in its current state of development, only treats homopolymers, and uses the structural repeat unit (SRU), which is the monomer in most cases, of a polymer, as the fundamental building block.
2. The SRU of the homopolymer is decomposed into its corresponding set of TAUs, and the molecular physicochemical properties of each TAU are taken from an existing table, or computed directly using

3DS modelling and/or molecular simulations. The net physicochemical property of the polymer is then taken as the sum of TAU contributions, that is, group additivity is assumed.

3. Step 2 is repeated for each member of a set of homopolymers for which the target bulk property (T_g, T_m, modulus, etc.) has been measured.
4. Step 3 leads to the generation of a structure–property relationship (SPR) table for the 'training set' of homopolymers. The data in the SPR table are used to formulate a quantitative structure–property relationship (QSPR). The measured bulk polymer properties are considered as dependent variables to the set of calculated physicochemical properties of the SPR table which, in turn, are derived from the TAU of the SRU.
5. The QSPR is generated by performing multi-dimensional linear regression analyses of the molecular physicochemical properties against the bulk polymer property measures. The preferred QSPR is that which maximizes the statistical significance of fit between a specific set of molecular physicochemical properties and the measured bulk polymer property.

1.2 Torsion angle unit (TAU) theory

1.2.1 The torsion angle unit

The key to being able to efficiently estimate physicochemical properties of polymers is the representation of the polymer in terms of torsion angle units, TAUs. A TAU is schematically defined as

$$G_i \xrightarrow{\theta_i} G_{i+1}$$

where G_i and G_{i+1} are structural groups connected by a bond about which the torsion angle θ_i occurs. The polymer is built up by connecting TAUs together such that the 'right' structural group of the ith torsion angle becomes the 'left' structural group of the $i + 1$ TAU. Figure 1.1 illustrates the structure of a linear polymer in terms of TAUs.

TAUs permit a global molecular property of a polymer system to be computed as a scalar sum of the individual molecular properties of the constituent TAUs. That is, we have formulated the estimation of global molecular properties in terms of a GAP model. The global molecular properties can be correlated to macroscopic properties of the system to hopefully yield a QSPR.

A major limitation of GAP models is that the requisite GAP parameters needed to make an estimation of a bulk property are not always available.

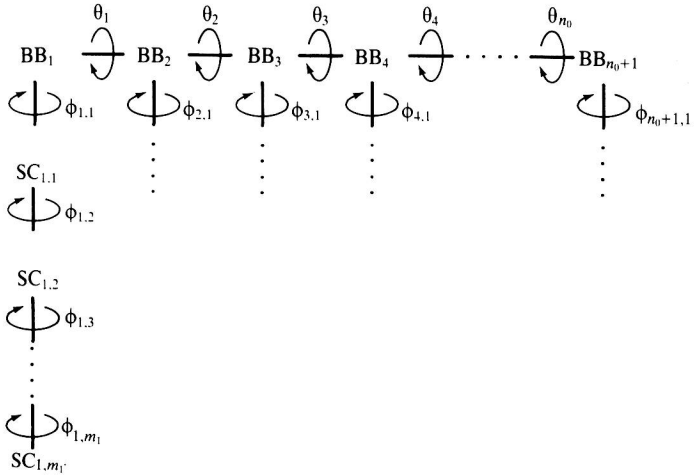


Figure 1.1 Structure of a linear polymer as formulated to define torsion angle units. BB refers to backbone TAUs and SC to sidechain TAUs.

Thus, while the calculation of the global molecular property is straightforward, it cannot be done because of the missing data. However, the formulation of a GAP model using TAUs permits the application of molecular modelling methods to estimate the GAP parameters associated with any TAU. Thus, one only needs to know, or develop, a scheme to compute the requisite group additive properties using molecular modelling to ensure being able to parameterize any TAU. Moreover, once the GAP properties are computed for a TAU they can be stored in a database and used whenever the TAU turns up in a study. Overall, the marriage of molecular modelling and GAP approaches, and their joint application to estimate TAU molecular properties, provides an open-ended, general approach to estimate bulk polymer properties.

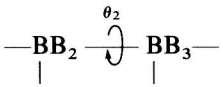
It should be pointed out that the TAU described and used in this chapter is one-dimensional (one degree of conformational freedom) in torsion angle, θ_i, when bond lengths and angles are held constant. This representation of the TAU is not a restriction. Higher dimensional TAUs can be defined if needed. For example,

$$SG_{i-1} \xrightarrow{\theta_i} SG_i \xrightarrow{\theta_{i+1}} SG_{i+1}$$

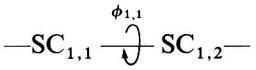
defines a two-dimensional TAU. Obviously, the computational effort needed to compute the molecular properties increases with increasing torsion angle dimensionality. However, the coupling of structural units composing the polymer chain also increases which should enhance the

quality of the estimation of molecular properties. The polymer chain can also be decomposed into arbitrary sequences of TAUs of different torsion angle dimensions.

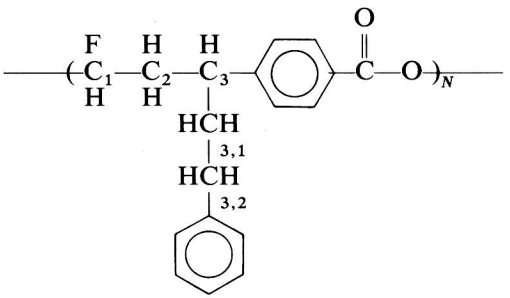
In Figure 1.1 the G_is are abbreviated as BB_k or $SC_{k,j}$, which indicates whether the structural group is part of the backbone or a sidechain, respectively. That is, within the notation of Fig. 1.1



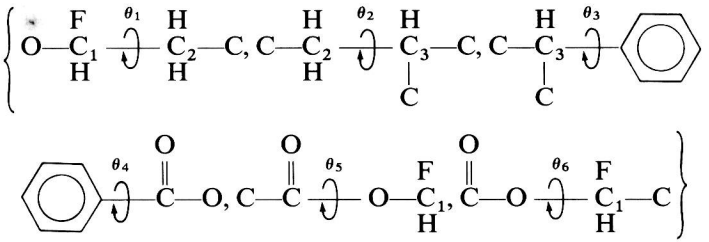
is a representative backbone torsion angle unit, and



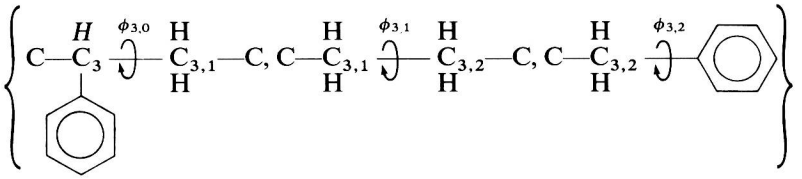
is a typical sidechain torsion angle unit. It is perhaps more informative to give an example of how the torsion angle units are derived from a monomer unit. Suppose



is the monomer used in the example. Then the set of backbone torsion angle units is



The only set of sidechain torsion angle units is



In the example above, a nine-dimensional problem, in terms of torsion angles, is reduced to nine one-dimensional problems by application of TAU theory. Of course this spatial decoupling process, which is what TAU theory achieves, is paid for at the expense of the accuracy and reliability of predicting the corresponding physicochemical properties of the polymer system. It is reiterated that loss in accuracy and reliability in estimating physicochemical properties can be 'controlled' by selection of TAUs of a higher torsion angle dimension than one.

1.2.2 Advantages of TAU theory in predictive polymer modelling

The one-dimensional TAU units, which will be the only TAUs discussed hereafter, represent relatively simple structures to use in both 3DS modelling and/or molecular simulation studies. In being able to make this statement TAU theory intrinsically overcomes two major drawbacks of GAP models, and one limitation of full-scale molecular simulation, to polymer property predictions. First, physicochemical molecular properties can be determined by prescribed molecular modelling schemes, described below, for any TAU. Thus, there is no parameterization limitation in TAU theory as is the case in GAP models. TAU theory provides an open-ended means to compute requisite physicochemical properties (the parameters).

Since TAU theory involves explicit three-dimensional geometries, that can be as complex as the user selects in terms of numbers of torsion angles, many of the non-additive properties inherent to polymer systems can be taken into account. Thus, TAU theory can overcome some of the shortcomings of GAP formalisms implicit to the additivity assumption.

The overall structural simplicity of TAUs makes the calculation of associated physicochemical properties quite rapid and straightforward. Thus, there are not the computational limitations inherent to molecular simulations of samples of polymer systems.

TAU theory does provide structure–property models that have more insight than GAP formalisms in terms of understanding mechanisms of bulk property behaviour. These TAU structure–property models are generally expressed as QSPRs. The QSPRs are derived from performing multi-dimensional regression analysis on a training set of polymers in which a bulk polymer property of interest is correlated against one, or more, TAU physicochemical properties. This is discussed in the next section. It is not clear at this time in the evaluation of polymer modelling to what extent the mechanistic information of a QSPR has as much insight or meaning compared to that possible from molecular simulations.

1.3 Estimation of intramolecular TAU physicochemical properties

1.3.1 Scaling intramolecular TAU calculations

All TAU calculations must be scaled with respect to the structure of the polymer. Only treatment of homopolymers has been developed to date. The SRU of the polymer, which is normally the monomer unit, serves to define the set of TAU units associated with a polymer chain. The TAUs are divided, as noted earlier, into backbone and sidechain TAUs. Backbone torsion angles of the ith BB–TAU are denoted by θ_i, while sidechain torsion angles of the SC–TAU are given as $\phi_{i,j}$, where j stands for the jth torsion angle of the sidechain attached to the ith backbone TAU. Using this notation the scaled backbone physicochemical TAU property for the entire SRU, F_{BB}, is given by

$$F_{BB} = \frac{\sum_{i=1}^{N_{BB}} f_{BB}(\theta_i)}{N_{BB}} \qquad [4]$$

where $f_{BB}(\theta_i)$ is the physicochemical property for the ith backbone TAU and N_{BB} is the number of BB–TAU in the SRU.

In like fashion to Eqn [4] the physicochemical property of the ith sidechain for the monomer $F_{SC}(i)$ is given by

$$F_{SC}(i) = \frac{\sum_{i=1}^{N_{SC}(i)} f_{SC}(\phi_{i,j})}{N_{SC}(i)} \qquad [5]$$

where $f_{SC}(\phi_{i,j})$ is analogous to $f_{BB}(\theta_i)$ and $N_{SC}(i)$ corresponds to N_{BB} in Eqn [4]. The total sidechain contribution for the monomer, F_{SC}, can be directly computed as

$$F_{SC} = \frac{\sum_{i=1}^{N_{BB}} F_{SC}(i)}{N_{BB}} \qquad [6]$$

Three important components of TAU theory, expressed by Eqns [4]–[6], are (a) the set of TAU is defined by the SRU; (b) each physicochemical property is normalized/scaled against the number of backbone and/or sidechain torsion angles; and (c) physicochemical properties can be partitioned between backbone and sidechain structures as well as between individual sidechains of an SRU. TAU theory does not normalize/scale against SRU molecular weight, as does the VanKrevelen formalism.[7] Molecular weight within TAU theory, is, as discussed below, treated as a physicochemical property.

1.3.2 Conformational entropy, $s_{BB}(\theta_i)$ and $s_{SC}(\phi_{ij})$

The principal property used to quantitatively estimate intramolecular flexibility is the conformational entropy associated with TAUs. The