Molecular Modeling the Water Uptake of Biomaterials

V.Kholodovych[1], W J Welsh[1], Rashmi Thakur[2] ,B.Michniak[2], J Kohn[2]
[1]University of Medicine & Dentistry of NJ, Piscataway, NJ, USA
[2]Rutgers, The State University of NJ, New Brunswick, NJ, USA

Introduction

Absorption of water by biodegradable materials and swellable polymers affects their properties significantly and impacts their potential utility. Their applications span a broad range, from biomedical (controlled drug release, ocular devices, and biomimetics) and personal care to agricultural and industrial [1].

Experimental measurements of water uptake are a time-consuming and labor-intensive process, often ranging from several days to weeks. Here we present a computational model for prediction of water adsorption of biodegradable polymers that have been designed for tissue engineering applications. The Polynomial Neural Network (PNN) [2], a new computational technique co-developed at UMDNJ, has been applied due to its many advantages over traditional regression-based QSPR methods. The PNN embodies many of the attractive features of Partial Least Squares (PLS) and Artificial Neural Networks (ANNs) within a single entity [2]. First, it can generate both linear and nonlinear regression equations of any order and any number of terms up to a user-specified value. Second, it automatically produces any user-specified number of QSPR equations that best correlate the inputs (molecular descriptors) and outputs (target properties) and sorts them in order of their predictive ability. Furthermore, the PNN is specifically designed to process both very small data sets and very large (> 5000 compounds) data sets, even when the data are "noisy" or contain irrelevant values (outliers). The predictions of the PNN model, when compared with experimental water-uptake measurements, showed excellent self-consistency and predictive ability.

Materials and Methods

Test polymers were selected at random from a library of polyarylates prepared previously by Kohn and coworkers [2]. The polymers were compression molded using a Carver Press. The resulting thin films were cut into samples 1.5 cm in diameter and approximately 0.2mm thickness to maintain consistency across the polymer library. Each sample has been immersed in ^{3}H-labelled radioactive water (Sigma-Aldrich) of 0.2µci/ml concentration. At specific time points (1, 2, 3, 4, 8, 9, 10, 11 days), films were removed, wiped and dissolved in scintillation cocktails. "Hot" water with the scintillation cocktail and THF as background were used as the control.

Model compounds were constructed for each polymer using the Molecular Operating Environment (MOE) molecular modelling software [3]. 750 empirical descriptors for each polymer were generated using the Dragon Software [4] and 104 molecular topological descriptors were calculated using MOE. Thus, a total of 854 molecular properties were calculated for each polymer entry and used in the PNN analysis.

Results and Discussion

The PNN model was developed based on the experimental data for the set of 14 polyarylates selected at random. The final PNN model was statistically self-consistent (r^2=0.87) and internally predictive (r_{CV}^2=0.67). Corresponding values of the PNN-predicted versus experimental data are plotted in Fig 1. Residuals between predicted and experimental values, reflecting an absolute accuracy of prediction for each individual polymer were shown in the inset of Fig.1. Notably, the majority of the absolute values of residuals is less than 0.5% demonstrating a very good agreement between a theoretical model and an experiment.

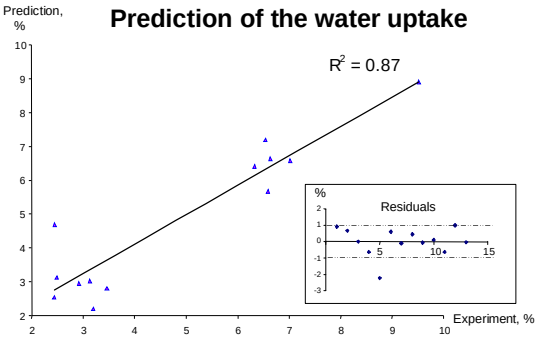

Figure 1 PNN model: Predicted vs Experimental Values. Inset: Residuals between predicted and experimental values for water uptake experiments.

Summary/Conclusions

Our data indicate that the PNN model is reasonably accurate in predicting water uptake across a wide range of polymers chosen at random from a combinatorially designed library of polyarylates. Water uptake is a key polymer property that affects many aspects of the polymer's performance, both *in vitro* and *in vivo*. Since the experimental determination of water uptake in polymeric biomaterials is laborious and time consuming, the development of a computational model of water uptake is a significant advance that can reduce the cost and time required to discover new biomaterials compositions.

References

1. Tetko IV, Aksenova TI et al., *SAR and QSAR in Environmental Research*, 2000, 11, 263-280.
2. Brocchini S, James K, V. Tangpasuthadol and J. Kohn, *J. Amer. Chem. Soc*., 1997, 119, 4553-4554.
3. http://www.chemcomp.com
4. http://www.disat.unimib.it/chm

Acknowledgment

This work was supported in part by "RESBIO - The National Resource for Polymeric Biomaterials" funded under NIH grant P41 EB001046.