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Modelling properties of powders using artificial neural networks and regression: the case of limited data

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Introduction

It is desirable to develop quantitative relationships between properties of interest for any given system as a function of the independent variables. This knowledge of the relationships can enhance our understanding and enable optimisation of the properties of interest. In developing a model one needs experimental data. For confidence in the model the number of data should be considerably more than the fitted parameters. Typically, however, particularly for optimisation, one is confronted with many variables but practically one can collect only limited data.

Artificial neural networks (ANN) and regression are commonly used for modelling relationships. This study examines the ability of both ANN and regression to model properties of powders when only limited amount of data is available. The data used here have been taken from a previously published article that dealt with hard-gelatin capsule formulations (Hogan et al. 1996). This data is very limited (in terms of characterising phase space) as the study involved only 33 experiments although there were 9 independent variables that were manipulated. For comparison, a full factorial design conducted at 3 levels would mean 19683 (3^9) experiments and this is clearly not feasible.

Experimental Data

In the capsule formulation study a total of 33 formulations of hard gelatin capsules were manufactured. The independent variables that were manipulated were particle size, solubility, filler type, filler level, disintegrant type, disintegrant level, lubricant level, glidant level, and drug concentration. The response variables were minimum bulk density, maximum bulk density, Hausner's ratio, Carr's compressibility index, coefficient of fill weight variation, area under the dissolution curve, mean dissolution time, variance of the dissolution time, and disintegration time. Overall, 9 independent variables and 9 response variables were examined.

Development of ANN and Regression Models

The ANN models employed perceptrons and were developed by examining different topologies, and different learning methods including backpropagation and radial basis function. There were 9 input units and 9 output neurons in all the topologies. The effect of number of epochs (iterations) was also explored. The regression equations were derived only from a simple linear model of the form $a_1*x_1 + a_2*x_2 + \ldots + a_9*x_9 = y$. Hence the maximum coefficients in the model could only be 9. Four different methods of variable selection were employed: no selection (simple linear model), stepwise regression, backward elimination and forward selection.

The generalisation ability of both the ANN and regression models was determined using the 'leave-one-observation-out-at-a-time' method (Hussain et al. 1994).

Results and Discussion

Both the ANN and regression succeeded in predicting 5 out of the 9 response variables. The responses that were modelled successfully were the same for both ANN and regression, namely, minimum bulk density (Vmin), maximum bulk density (Vmax), Hausner's ratio (H), Carr's compressibility index (Carr) and disintegration time (DT). The mean relative error (average percentage deviation between predicted and observed values) for these 5 response variables, for both the regression and the ANN models, are given in Table 1. The best ANN models used backpropagation with momentom and adaptive learning rate. One-tailed paired t-test at 95% confidence level was conducted on the mean relative error values to examine if ANN models are statistically significant better than regression models in their predictive ability. The result was negative. In summary, for the case of limited data, both ANN and regression can model some of the responses and ANN have not been found to be any better.

Table 1. Mean relative error for the best regression/ANN models.

	Vmin	*Vmax*	*H*	*Carr*	*DT*
Regression	4.17	4.16	2.86	5.49	13.04
ANN	3.69	3.55	2.86	5.86	12.14
ANN topology	9:4:9	9:4:9	9:1:9	9:3:9	9:4:9
ANN epochs	2560	2000	1280	1000	640

Hogan, J. et al. (1996) Pharm. Res. 13:944-949
Hussain et al. (1994) Drug. Dev. Ind. Pharm. 20:1739-1752.