

# Application of Neurofuzzy Logic and Parallel Coordinates Techniques in Pan Coating Process Data Analysis

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## OBJECTIVE

To identify cause - effect relationship between process variables and tablet film coat attributes for an aqueous pan coating process using neurofuzzy logic and parallel coordinates techniques.

## METHODS

### Placebo tablets:

- Tool: 8 mm diameter standard concave round tooling
- Press: IMA Comprima 180
- Target tablet weight 200 mg, hardness >90N
- Placebo tablet formulation:

Ingredients	%	mg/tablet	Batch size(kg)
Lactose	92	184	184.0
Microcrystalline cellulose	7	14	14.0
Mg Stearate	1	2	2.0
Total	100	200	200

### Coating solutions:

Ingredients	solid%	mg/tablet	Batch size(g)
Opadry clear (HPMC/PEG400)	11.6	5.8	243.6
Red FD&C 40	0.24	0.12	5.04
Water	N/A	N/A	1848
Total	11.84	5.92	2096.64

- Pan coater: Thomas Compulab 24 pan coater equipped with 24-inch pan
- Coating process parameters: drum speed (DS), spray rate (SR), atomization pressure (AP), and gun to bed distance (GB).

## DESIGN OF EXPERIMENTS

Batch No.	Drum Speed (rpm)	Spray Rate (g/min)	Atomization Pressure (psi)	Gun to Bed (inches)
NB12483-053R1	7	35	29	6.0
NB12483-053B1	7	45	33.35	6.6
NB12483-053C1	7	60	39.15	7.4
NB12483-053D1	7	70	43.5	8.0
NB12483-053E1	9	35	33.35	8.0
NB12483-053F1	9	45	29	7.4
NB12483-053G1	9	60	43.5	6.6
NB12483-053H1	9	70	39.15	6.0
NB12483-053J1	11	35	39.15	6.6
NB12483-053K1	11	45	43.5	6.0
NB12483-053L1	11	60	29	8.0
NB12483-053M1	11	70	33.35	7.4
NB12483-053N1	12	35	43.5	7.4
NB12483-053O1	12	45	39.15	8.0
NB12483-053P1	12	60	33.35	6.0
NB12483-053Q1	12	70	29	6.6

## COATING PROCESS

The placebo core tablets were coated using the Thomas Compulab 24 coater equipped with 24-inch pan (1 gun). The drum speed, spray rate, atomization pressure, and gun to bed distance were altered according to the experimental design. The tablet cores were heated under jog mode prior to the coating and the mean weight of 200 cores was noted prior to the commencement of spraying. The spray gun was positioned 1/3 way down the tablet bed and the line was purged prior to the coating. During the coating run, 25 tablets were sampled every 5 minutes for the first 20 minutes and every 10 minutes thereafter. The details of the batch were recorded when target weight gain was achieved. Batch size: 8.2 kg. Inlet temperature: ~ 60°C Inlet air volume: ~240 CFM Target weight gain: 3% (5.92 mg/tablet)

## EVALUATION OF COATING PROCESS

- Coating uniformity: weight variation, SD
- Surface smoothness (Gloss): Novo-Curve Glossmeter (Elecometer Instruments Ltd.)
- Color gain (Delta E): Colorimeter (UltraScan Hunter Lab)

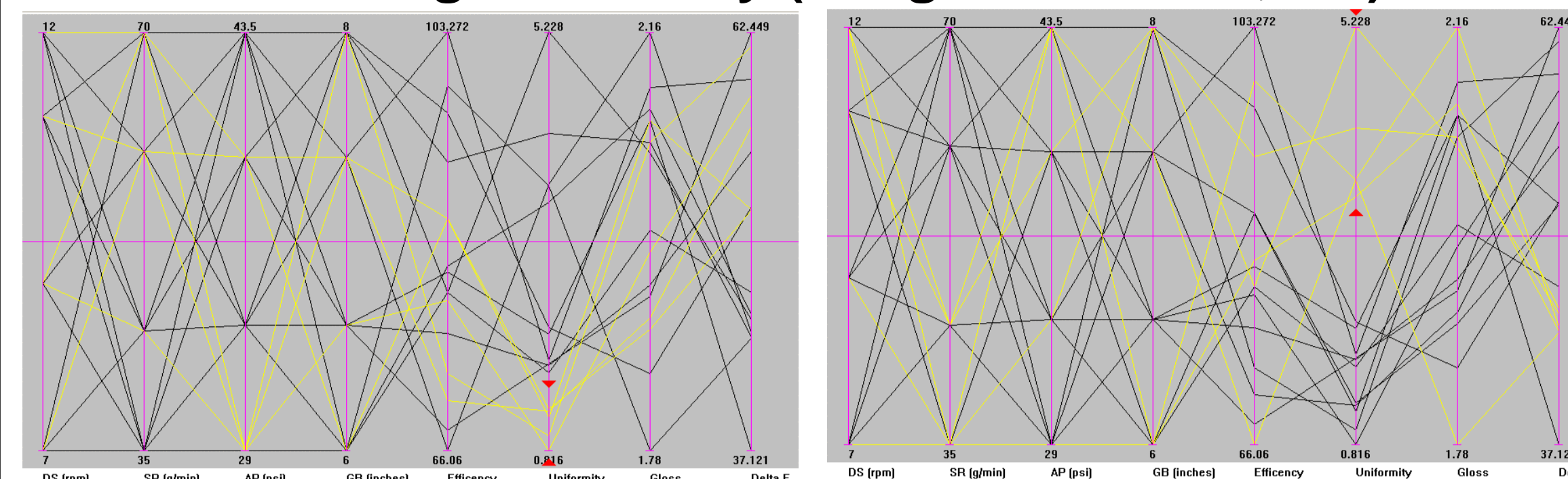


## DATA ANALYSIS

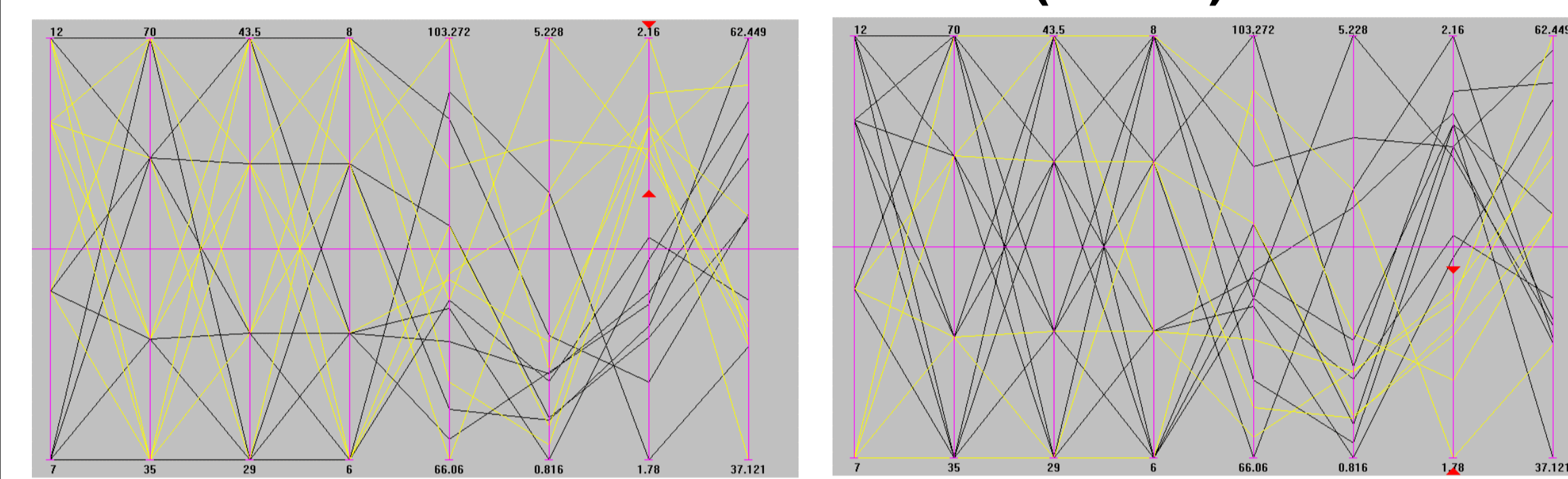
The cause-effect relationship between process variables and coat attributes were analyzed using parallel co-ordinates software: Curvaceous Visual Explore (CVE) (V2.3, Curvaceous Software Limited, UK) and neurofuzzy logic software: FormRules (V3.2, Intelligensys Ltd., UK)

## CURVACEOUS VISUAL EXPLORE RESULTS

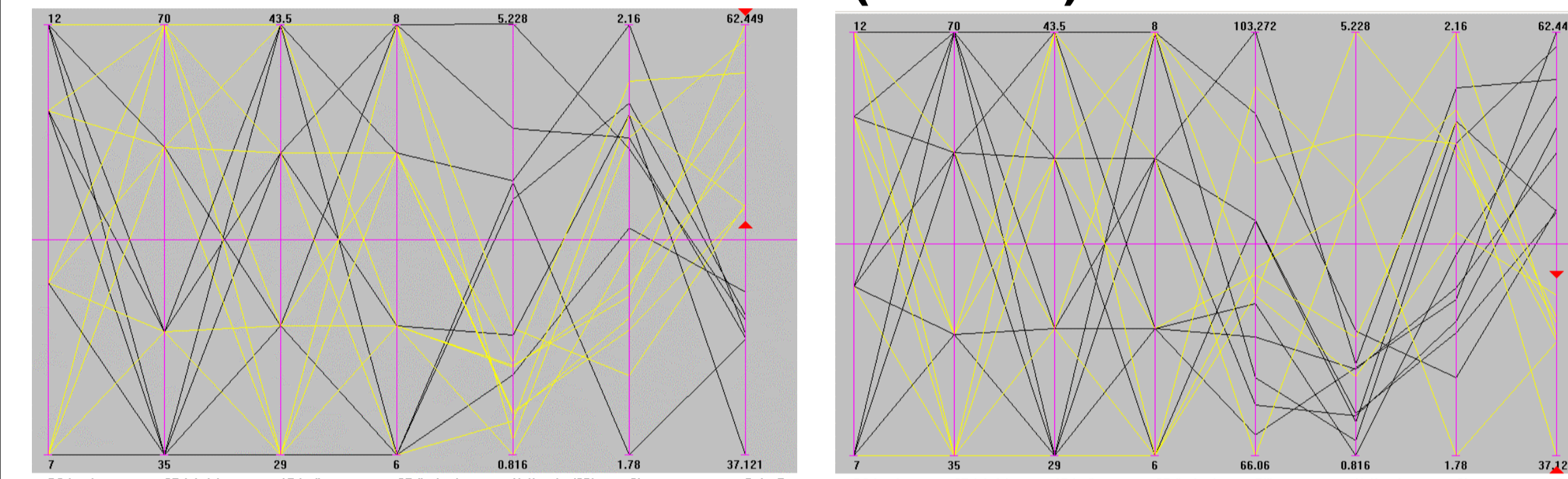
### Coating Uniformity (Weight Variation, SD)



### Surface Smoothness (Gloss)



### Color Gain (Delta E)



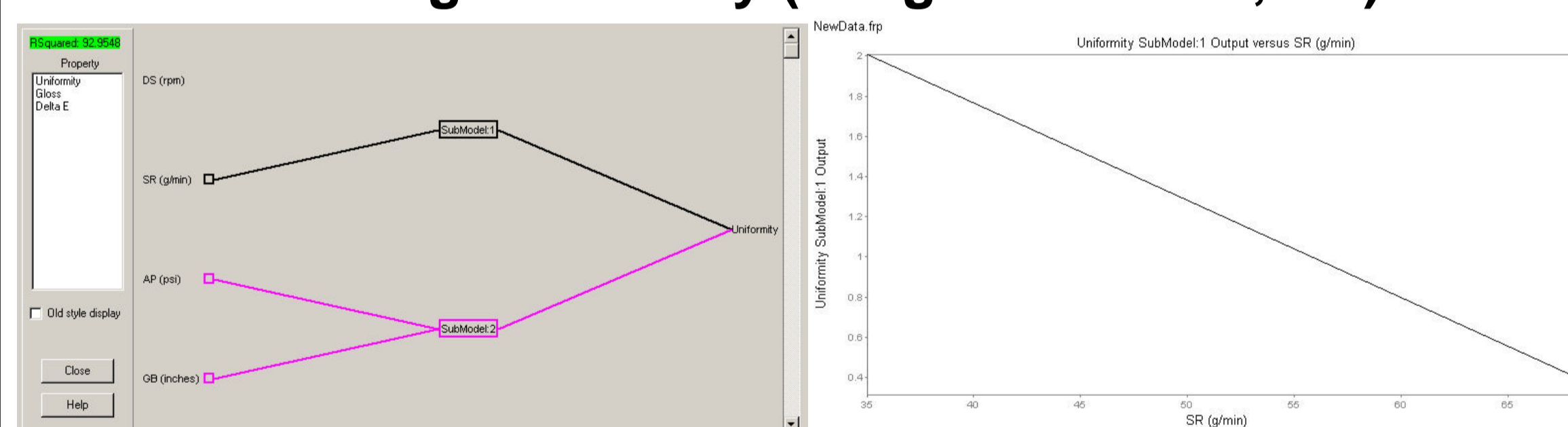
CVE quickly discovered major pattern and cause-effect relationship between processing variables and coating attributes. The results also demonstrated that parallel coordinates (CVE) is a good tool for analysing multi-variate data based on visual clues.

## NEUROFUZZY LOGIC MODELS AND RULES

Coating Attributes	Uniformity (SD)	Gloss	Delta E
Fitness Function	SRM	SRM	LOOCV
Model Parameters	C1= 0.76	C1= 0.70	N/A
Train Set R-squared	92.9548	98.3569	82.6975
Computed f ratio	6.5973	14.9649	5.4629

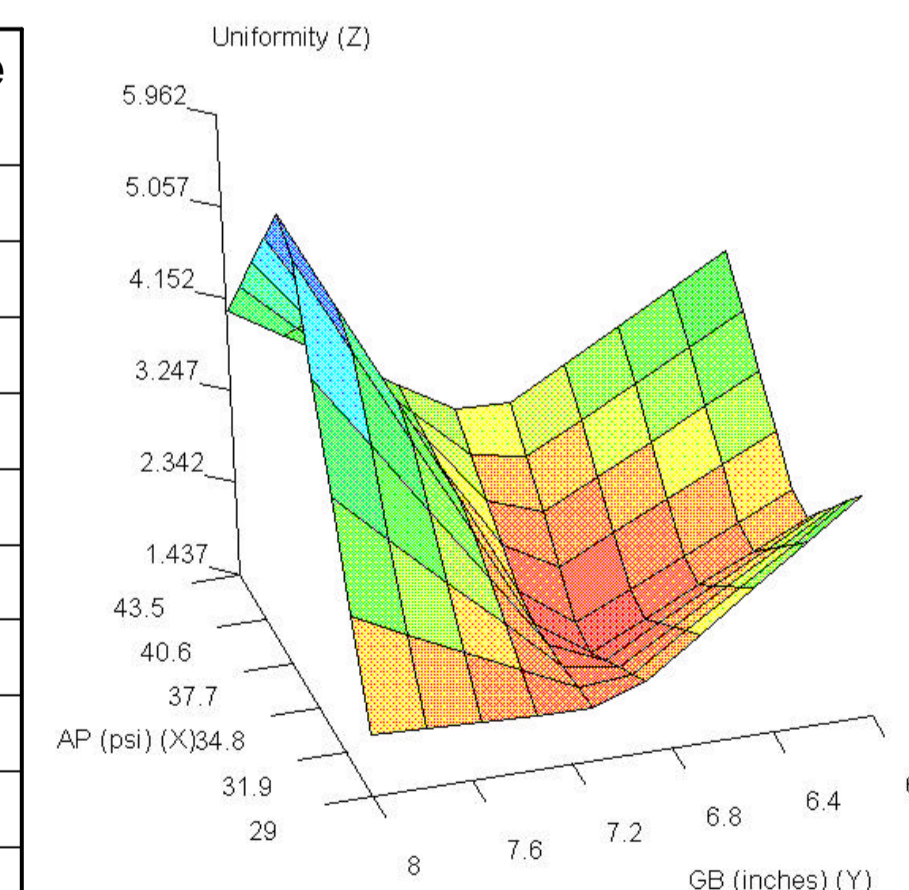
Assessment of trained FormRules models  
Structural Risk Minimization (SRM)  
Leave one out cross validation (LOOCV)

### Coating Uniformity (Weight Variation, SD)



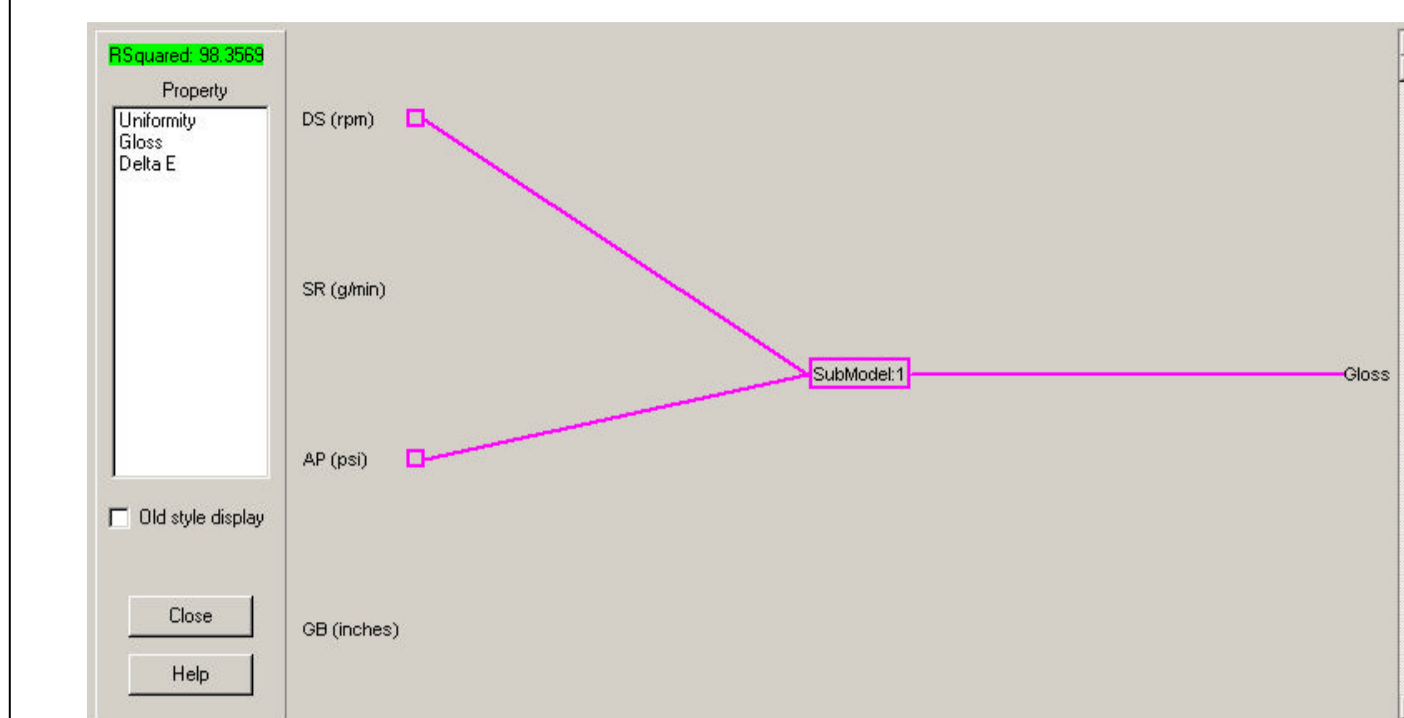
Rules for coating uniformity (tablet weight SD, mg) generated by the neurofuzzy logic model

Spray rate	Gun to bed	Atomization Pressure	Uniformity (SD)	Confidence Level
1 Low			HIGH	0.91
2 High			LOW	0.86
3	Low	Low	LOW	0.64
4	Low	Medium	LOW	1.00
5	Low	High	LOW	0.54
6	Medium	Low	LOW	1.00
7	Medium	Medium	LOW	1.00
8	Medium	High	LOW	1.00
9	High	Low	LOW	1.00
10	High	Medium	HIGH	1.00
11	High	High	HIGH	0.55



The model showed that gun to bed distance and atomization pressure were the major process variables that affected film coat uniformity and showed interaction. Spray rate also affects coat uniformity but to a lesser extent.

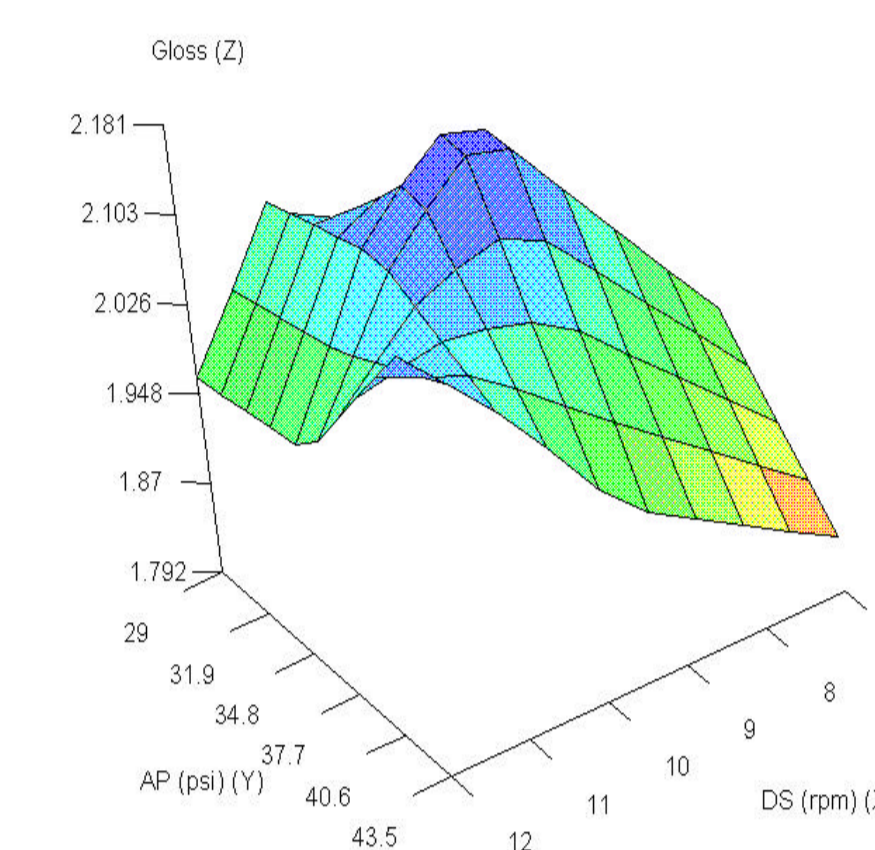
### Surface Smoothness (Gloss)



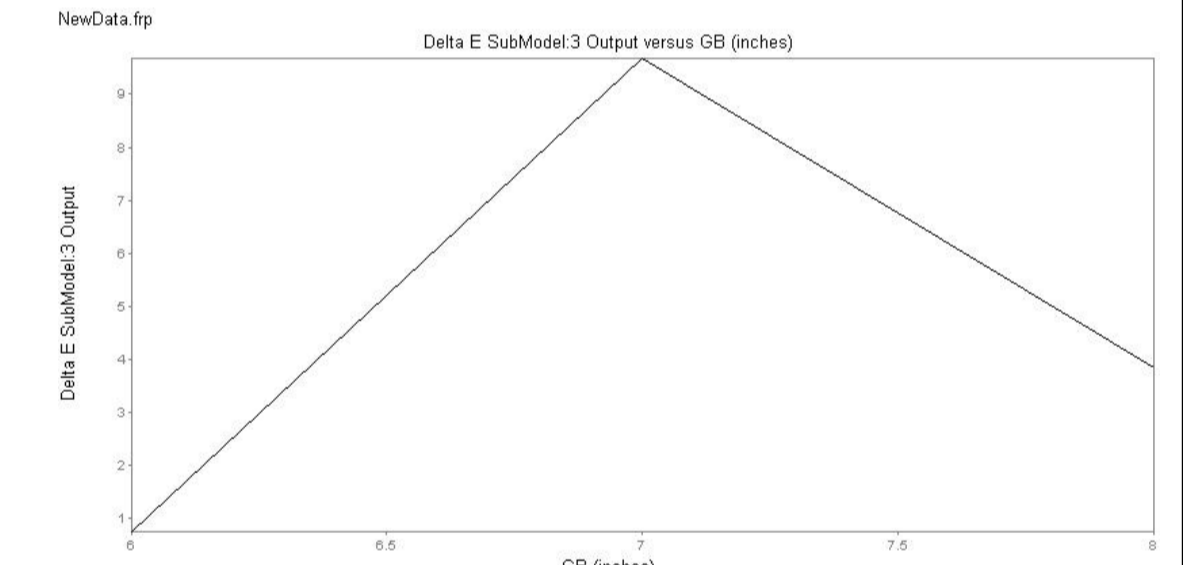
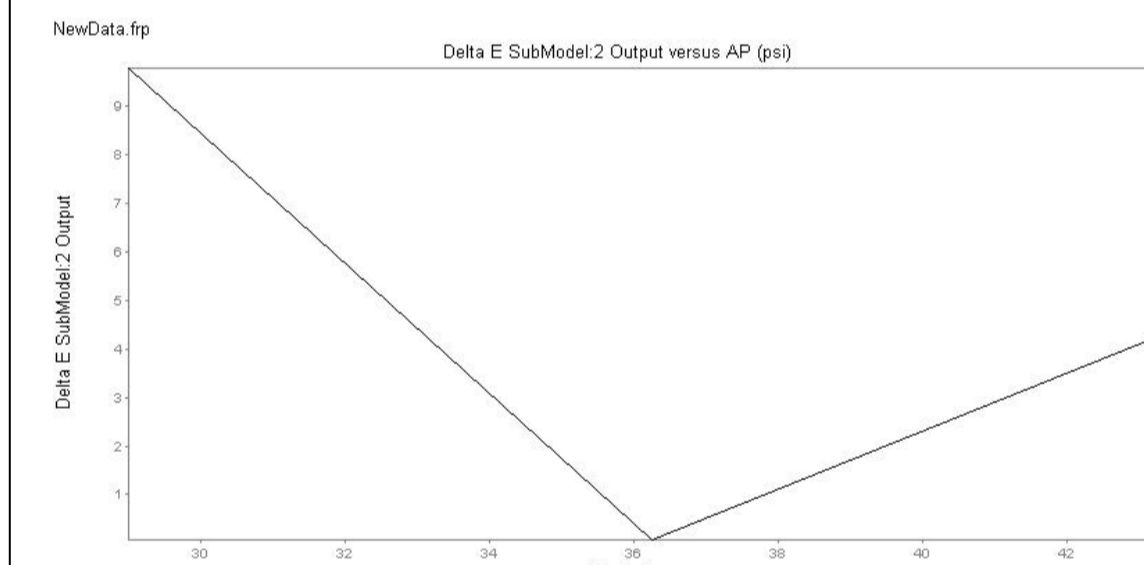
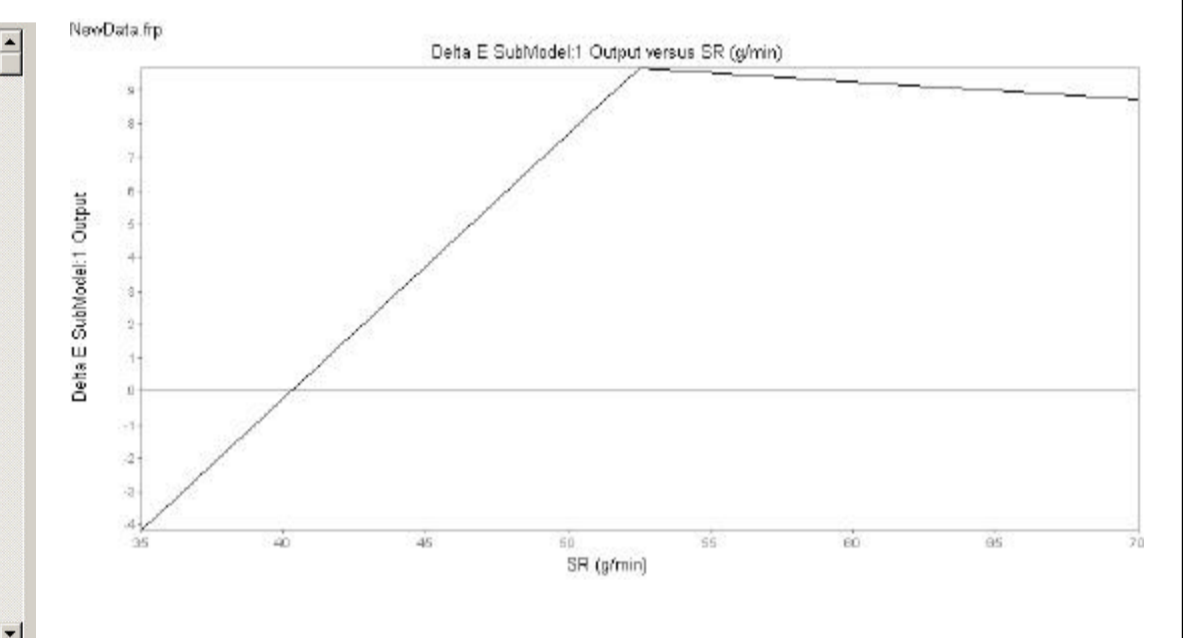
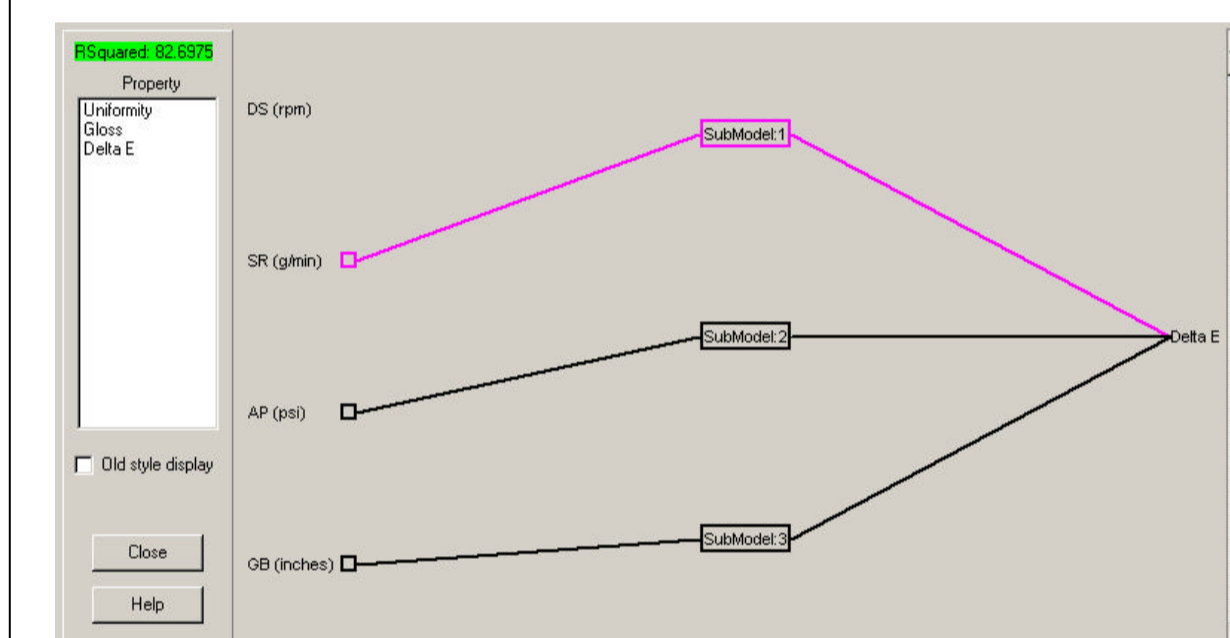
The model showed that surface smoothness of the coated tablets was mainly affected by drum speed and atomization pressure and these two process variables showed strong interaction.

Rules for surface smoothness (Gloss) generated by the neurofuzzy logic model

Drum Speed	Atomization Pressure	Gloss	Confidence Level
1 Low	Low	LOW	0.97
2 Low	Medium	HIGH	0.51
3 Low	High	LOW	0.85
4 Medium-1	Low	LOW	0.62
5 Medium-1	Medium	HIGH	1.00
6 Medium-1	High	LOW	0.57
7 Medium-2	Low	HIGH	0.83
8 Medium-2	Medium	HIGH	0.95
9 Medium-2	High	HIGH	0.75
10 High	Low	LOW	0.52
11 High	Medium	HIGH	0.54
12 High	High	HIGH	1.00



### Color Gain (Delta E)



Rules for coating color gain (Delta E) generated by the neurofuzzy logic model

Spray rate	Atomization Pressure	Gun to bed	Delta E	Confidence Level
1 Low			LOW	1.00
2 Medium			HIGH	1.00
3 High			HIGH	1.00
4	Low		HIGH	1.00
5	Medium		LOW	0.99
6	High		HIGH	0.52
7		Low	LOW	0.91
8		Medium	HIGH	1.00
9		High	LOW	0.55

The model showed that spray rate was the major process variables on color gain. Atomization pressure and gun to bed distance also affected color gain but to a lesser extent. No interaction was observed between all three process variables on coating color gain.

## CONCLUSIONS

- CVE was a useful tool to discover patterns and relationships between variables based on visual clues.
- FormRules models successfully predicted target coating attributes and it also generated simple and understandable rules.