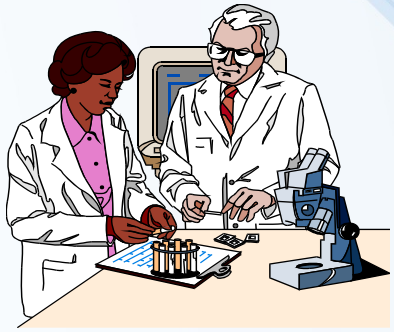
Ruggedness, robustness, stability



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Ruggedness Testing

- the degree of reproducibility of results obtained under a variety of conditions, such as different laboratories, analysts, instruments, environmental conditions, operators and materials
- a measure of reproducibility of test results under normal, expected operational conditions from laboratory to laboratory and from analyst to analyst
- determined by the analysis of aliquots from homogeneous lots in different laboratories

Ruggedness testing

- by considering each effect separately, by repeating measurements after varying a particular parameter by a small amount (say 10%) and controlling the other conditions appropriately
- this can be labour-intensive as a large number of effects may need to be considered
- for a well-developed method, most of the effects can be expected to be small, it is possible to vary several parameters at the same time
- any stable and homogeneous sample within the scope of the method can be used for ruggedness-testing

Plackett–Burman design of ruggedness testing

- **7** parameters, each tested at two levels (**low-high**) e.g.
  - 1. volume of sample
  - 2. time of extraction
  - 3. flow rate
  - 4. temperature
  - 5. pH
  - 6. salt concentration
  - 7. modifier addition

128 possible combinations!

low	high	Combinations
0	7	**1**
1	6	**7**
2	5	**21**
3	4	**35**
4	3	**35**
5	2	**21**
6	1	**7**
7	0	**1**
SUM		**128**

Plackett–Burman design of ruggedness testing

- The design described allows information to be gathered from only **eight** experiments
- **A, B, C, D, E, F** and **G** – nominal level
- **a, b, c, d, e, f** and **g** - alternative level
- The chosen levels may be the **extreme values** of the parameter, e.g. the two extremes of temperature likely to be encountered during use of the method

Plackett–Burman design of ruggedness testing

To find if changing factor ‘A’ to ‘a’ has an effect, A is calculated

Experiment number	Method parameter						Observed result
1		B	C	D	E	F	G	
2		B	c	D	e	f	g	
3		b	C	d	E	f	g	
4		b	c	d	e	F	G	
5	a	B	C	d	e	F	g	v
6	a	B	c	d	E	f	G	x
7	a	b	C	D	e	f	G	y
8	a	b	c	D	E	F	g	z

$$\Delta_A = \text{[redacted]} - \frac{v + x + y + z}{4}$$

Plackett–Burman design of ruggedness testing

With this combination the effect of the other factors cancels out!

Experiment number		Method parameter						Observed result
1	A							
2	A							
3	A							
4	A							
5	a	B	C	d	e	F	g	v
6	a	B	c	d	E	f	G	x
7	a	b	C	D	e	f	G	y
8	a	b	c	D	E	F	g	z

$$\Delta_A = \frac{l + m + p + w}{4} - \frac{v + x + y + z}{4}$$

Plackett–Burman design of ruggedness testing

Changing factor ‘B’ to ‘b’ is examined by calculating B, as follows:

Experiment number	Method parameter							Observed result
1	A		C	D	E	F	G	
2	A		c	D	e	f	g	
3	A	b	C	d	E	f	g	p
4	A	b	c	d	e	F	G	w
5	a		C	d	e	F	g	
6	a		c	d	E	f	G	
7	a	b	C	D	e	f	G	y
8	a	b	c	D	E	F	g	z

$$\Delta_B = \qquad - \frac{p + w + y + z}{4}$$

Plackett–Burman design of ruggedness testing

- The next step is to arrange the seven differences, A to G, in numerical order (ignoring the sign).
- To calculate if any of the differences are statistically significant, a statistical test (*t -test) is applied.*
- Equation below is used to compare the difference $|\Delta_i|$ *with the expected precision of the method,* ***s*** and the level of confidence used (t-test).

$$|\Delta_i| > \frac{ts}{\sqrt{2}}$$

- For cases where equation is true, the change from the nominal to the alternative level is significant.

Plackett–Burman design of ruggedness testing

- NOTE! the results of the test will be misleading if the factors investigated are not independent
- Such a study may be used to set the level of control that should be applied at particular stages of the method, e.g. adjust the pH to 6.5 ± 0.2
- It is also possible to study the effect of potential interferences by using this approach