



# QUANTITATIVE MEASURES TO EVALUATE PROCESS STABILITY AND ASSESS PROCESS HEALTH

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# OUTLINE

- Motivation
- Overview of Process Stability Metrics
- Applications
  - Stability Metrics to Inform Nelson Violations on Shewhart Charts
  - Combining Process Stability and Process Capability
    - Process Performance Graph in JMP®
- Summary
- References & Acknowledgements

## MOTIVATION

- Develop a more objective and consistent way to determine if a parameter is in a state of statistical control.
- Evaluate the process stability of hundreds of a parameters in an efficient manner.
- Prioritize and track improvement efforts using the two important dimensions of process health: stability and capability.

# PROCESS STABILITY METRICS

- Three metrics were developed:
  - SR Test: short term vs. long term variation
  - ANOVA F-Test: between vs. within variation
  - Instability Ratio ( $I_{NSR}$ ): Western Electric rule violations
- These metrics are used to classify a parameter as:
  - Stable → process is operating with common cause variation
  - Unstable → process is operating with special cause variation
- Ramírez, B and Runger, G. (2006).

## SR TEST: SHORT TERM VS. LONG TERM VARIATION

- Using different estimates for the population std. dev. has been studied, e.g., Podolski (1989), Cruthis and Ridgon (1992), Wheeler (1995).
- In the context of SPC:
  - Long term variation can be estimated using the sample standard deviation,  $s$
  - Short term variation can be estimated using control chart estimates of standard deviation, such as  $\overline{R} \div d_2$  or  $\overline{MR} \div d_2$ .
- When evaluating process variation:
  - Stable process      ► long term variation  $\approx$  short term
  - Unstable process   ► long term variation  $>$  short term

## STABILITY METRIC: SR TEST

- $SR = s^2_{\text{long term}} \div s^2_{\text{short term}} = s^2 \div (\overline{MR} \div d_2)^2$
- Significance Test:
  - $H_0: SR = 1$  (Stable)
  - $H_1: SR > 1$  (Unstable)
  - $SR \sim F_{(N-1), 0.62(N-1)}$
- Aligns with F Max Test (Hartley, 1950), which is used to determine if two variances are equal using the ratio of the larger variance to the smaller variance.

*Cruthis and Ridgon suggest that  $F^*$  (SR) does not follow an F-distribution, but also point out that “the true distribution of  $F^*$  is difficult or impossible to determine analytically”.*

# SR TEST XmR EXAMPLE

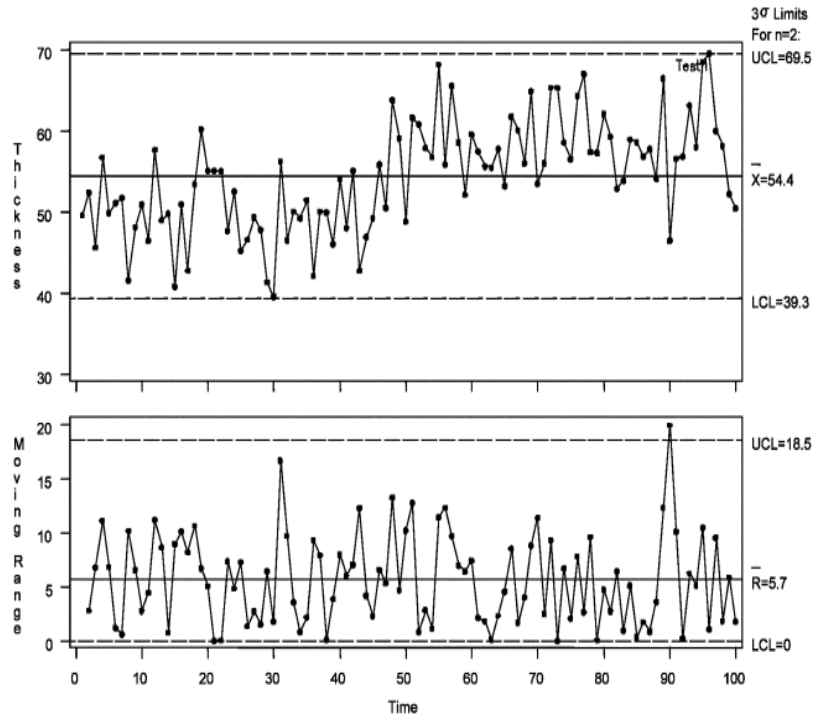


Figure 2. XmR chart of 100 thickness observations example 1.

Table 2  
Calculations for SR test for example 1

Component	Value
$S_{\text{method1}}^2 = \sum_i (X_i - \bar{X})^2 / (100 - 1), i = 1 \text{ to } 100$	45.212
$S_{\text{method2}}^2 = (\bar{MR} / d_2)^2$	$(5.7 \div 1.128)^2 = 25.24$
$SR = S_{\text{method1}}^2 + S_{\text{method2}}^2$	$45.212 \div 25.24 = 1.79$
$df_{\text{method1}} = (100 - 1)$	99
$df_{\text{method2}} = 0.62 \times (100 - 1)$	62
$p\text{-value for } 1.79, 99, 62 \text{ using } F\text{-distribution}$	0.0072

## STABILITY METRIC: ANOVA F-TEST

- Compare “within” subgroup variation to “between” subgroup variation to detect differences in subgroup means.
- Natural extension of how control limits for  $\bar{X}R$  and  $\bar{X}S$  charts are created.
- Significance Test:
  - $H_0: \mu_1 = \mu_2 = \dots \mu_k$  (Stable)
  - $H_1: \text{at least two means are not equal}$  (Unstable)
  - $F \sim F_{(k-1), k(n-1)}$
- ANOVA F-test:
  - Well defined and documented
  - We can control the type I error rate



# ANOVA F-TEST XMR EXAMPLE

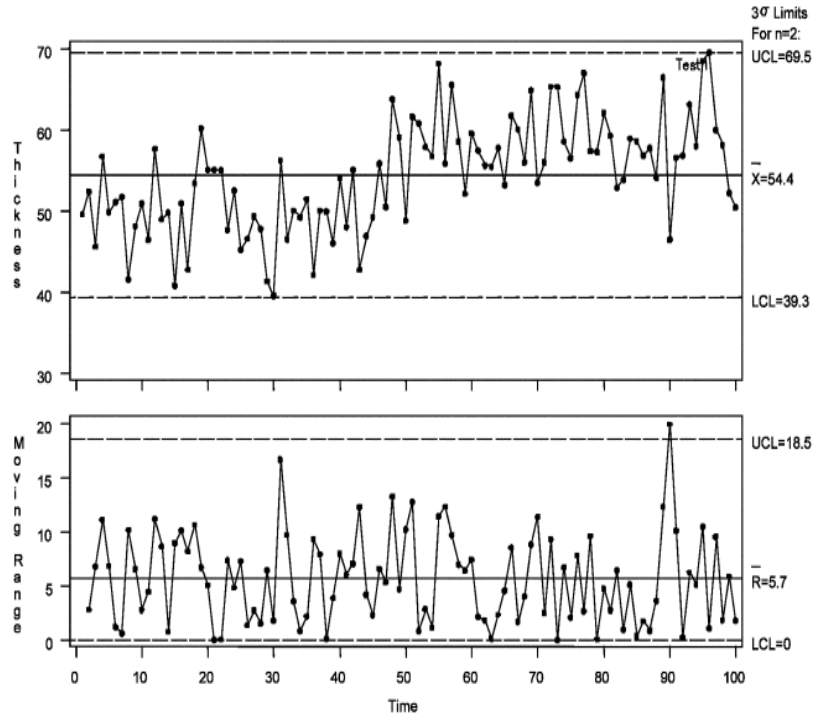


Figure 2. XmR chart of 100 thickness observations example 1.

- For XmR charts, an artificial subgroup is created, where consecutive groups of size  $n$  are formed.

Table 9  
ANOVA for XmR example 1

Source of variation	Sums of squares	Degrees of freedom	Mean squares	Computed F	P-value
"Between" subgroups	3181.49	49	64.93	2.51	0.0008
"Within" subgroups	1294.52	50	25.89		
Total	4476.01	99			

# STABILITY METRIC: INSTABILITY RATIO

- Patterns of variation:
  - Stable: common cause variation, random about a mean, no unusual patterns or trends
  - Unstable: special cause variation, unusual patterns and trends
- Based upon runs tests violations, such as, Western Electric rules or Nelson rules:
  - 1 point outside of  $3\sigma$  limits
  - 8 points in a row on one side of the center line
  - 2 of 3 points  $2\sigma$  and beyond
  - 4 of 5 points  $1\sigma$  and beyond
- $I_{NSR}$ : Ratio of the number of subgroups with  $\geq 1$  violations to the total number of subgroups

# INSTABILITY RATIO XmR EXAMPLE

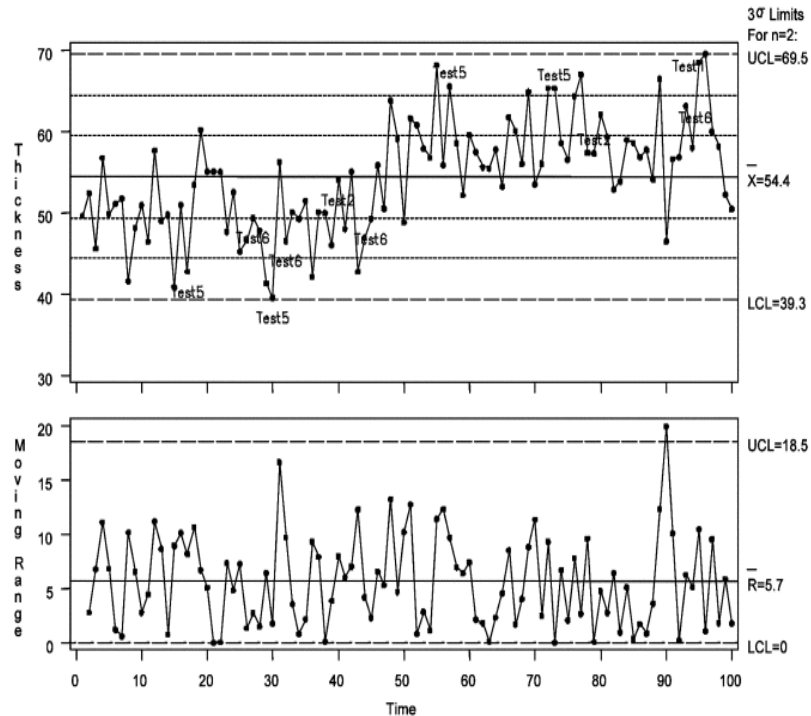


Figure 8. XmR chart with rules turned on example 1.

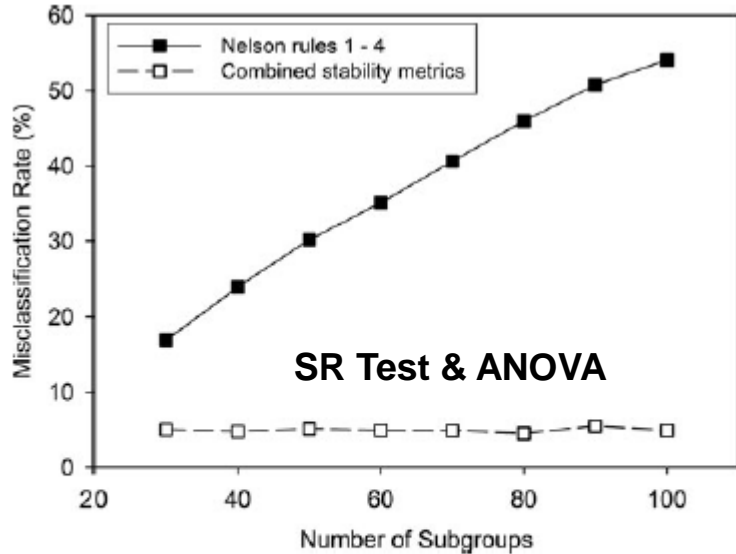
An informal test was proposed:  
Unstable process if INSR > 4.5%

- 11 subgroups with one or more violations
- $INSR = 100 \times (11/100) = 11\%$
- Since  $11\% > 4.5\%$ , the process is unstable

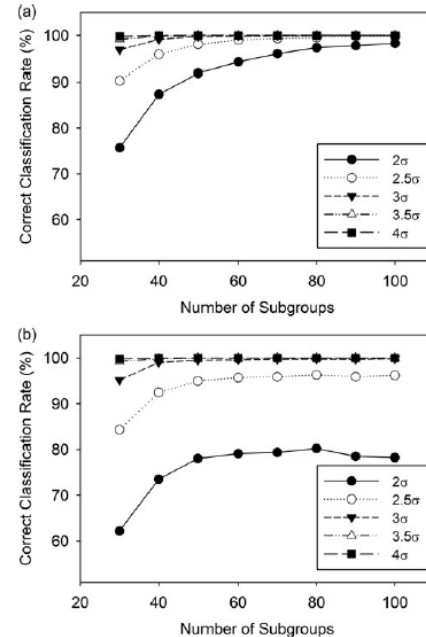
## STABILITY METRIC PERFORMANCE

- Statistical performance has been documented, e.g., Cruthis and Ridgon (1992), Ramirez and Runger (2006), Greene (2007), Britt, Ramirez and Mistretta (2016)
- Conditions studied:
  - Random noise, different sample sizes
  - Special cause variation, different sample sizes and shifts

# STATISTICAL PERFORMANCE OF SELECTED METRICS



**Figure 3.** Misclassification rate (i.e., false positives; y-axis) calculated from 10,000 simulations as a function of the number of subgroups (x-axis). The results of simulations using XmR charts with Nelson rules 1–4 and stability metrics are compared.



**Figure 4.** Correct classification rate (i.e., power; y-axis) calculated from 10,000 simulations using (A) Nelson rules 1–4 and (B) combined stability metrics is plotted as a function of the number of subgroups (x-axis) for datasets where a mean shift was introduced in the last 15 observations using an XmR chart. Results of simulations for mean shifts of increasing magnitude are overlaid.

Nelson Rules  
1- 4

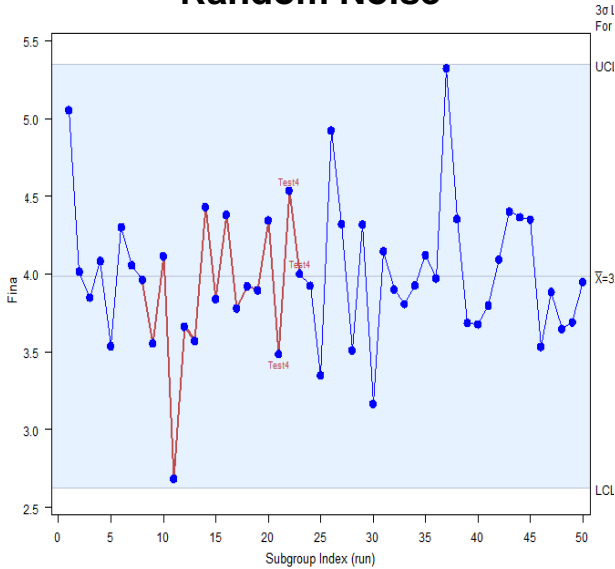
SR Test &  
ANOVA

# OUTLINE

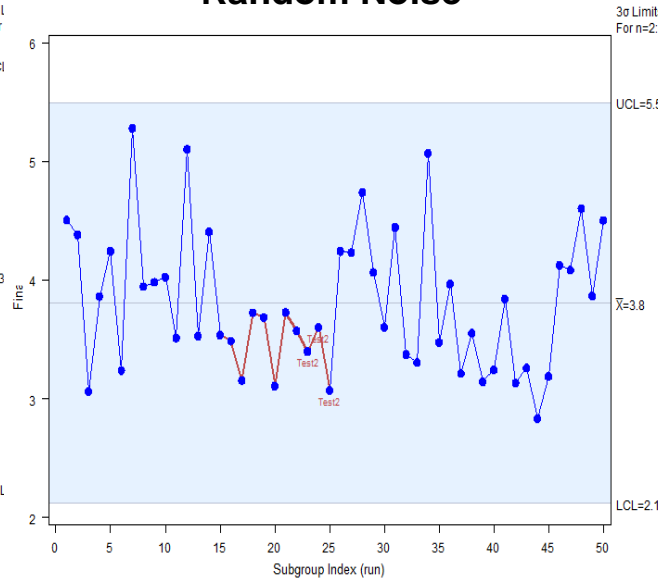
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# CHALLENGES USING SHEWHART CHARTS & NELSON RULES

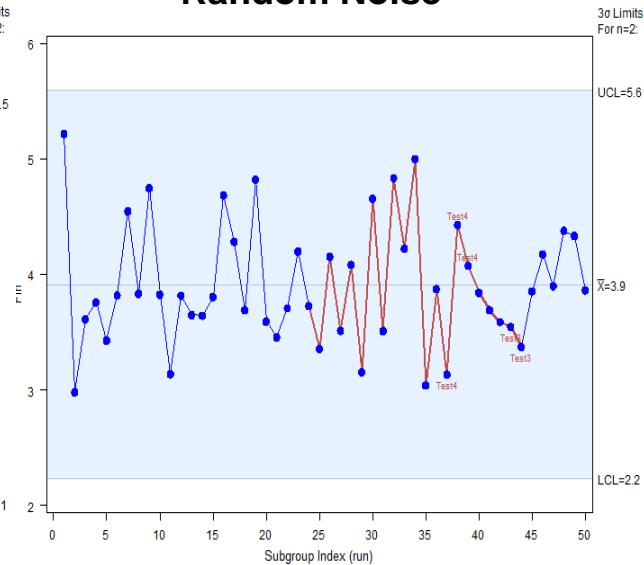
## Random Noise



## Random Noise



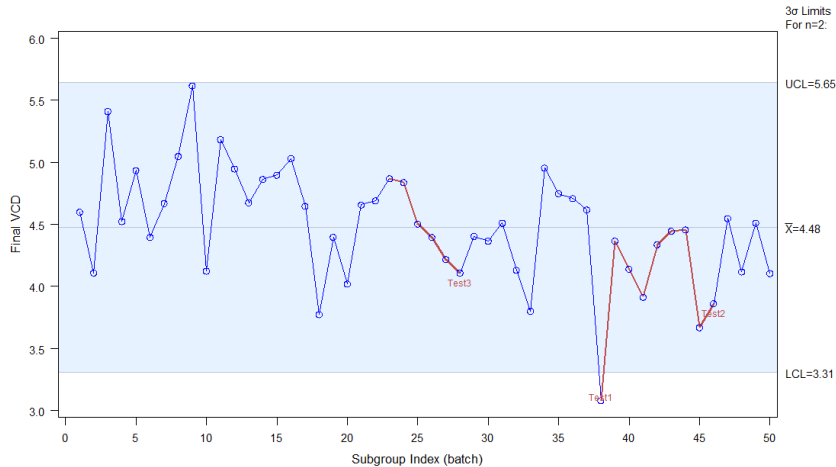
## Random Noise



What is causing these patterns: *common* or *special cause* variation?

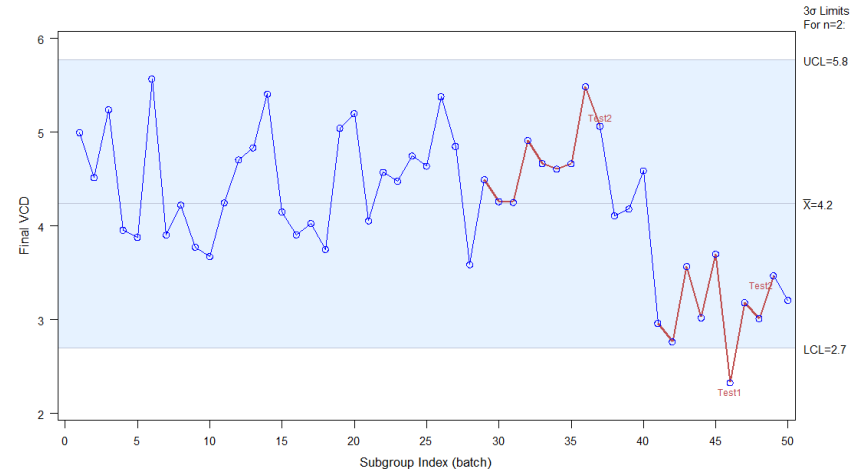
# STABILITY METRICS TO INFORMING NELSON VIOLATIONS

## Random Noise Common Cause Variation



SR = 1.40, p-value = 0.1629  
F = 1.32, p-value = 0.2475

## Deliberate Mean Shift Special Cause Variation



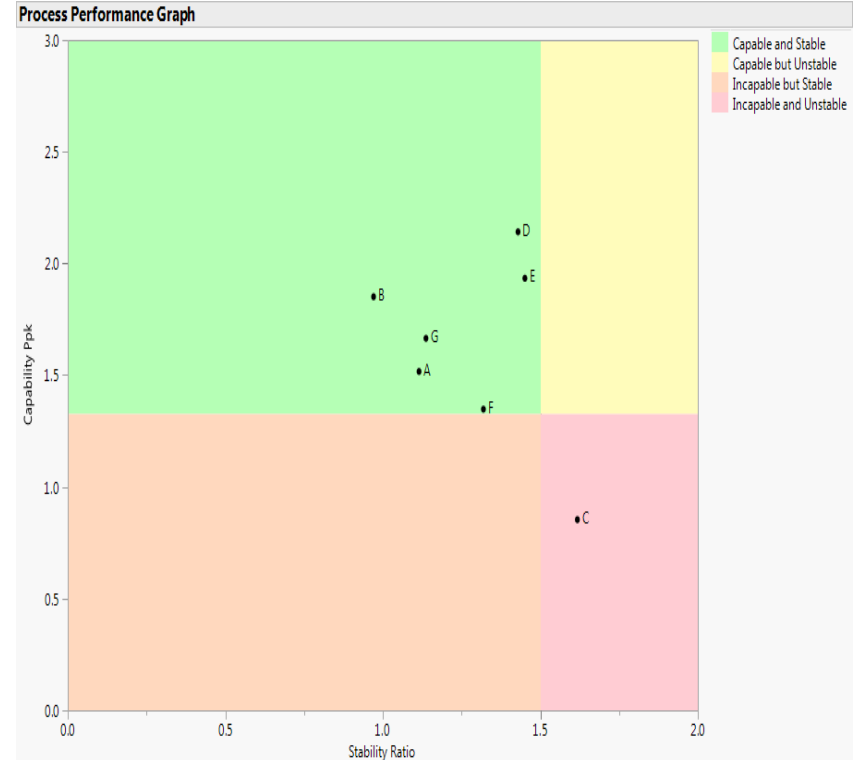
SR = 2.19, p-value = 0.0118  
F = 3.63, p-value = 0.0011



# COMBINING PROCESS STABILITY & PROCESS CAPABILITY

JMP® V13

	Stable YES	Stable NO
Capable YES	<p><b>Ideal State</b></p> <p>Process in control and 100% conformance.</p>	<p><b>Predictability Issue</b></p> <p>All may seem OK, but . . .</p>
Capable NO	<p><b>Yield Issue</b></p> <p>Must change process or readjust specifications.</p>	<p><b>Double Trouble</b></p> <p>First eliminate special causes from process. Then re-engineer.</p>



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## SUMMARY

- Three measures and test criteria were developed for classifying process output as 'stable' or 'unstable'
  - SR Test
  - ANOVA F-test
  - $I_{NSR}$
- Quantitative measures of process stability can be used to inform Nelson violations during Phase I monitoring
- Stability and capability assessments can be combined to provide an overall assessment of Process Health using the Process Performance Graph in JMP.

## REFERENCES

- Garry Poldoski (1989), Standard deviation: root mean square versus range conversion, *Quality Engineering*, 2:2, 155-161
- Emma N. Cruthis & Steven E. Rigdon (1992), Comparing two estimates of the variance to determine the stability of a process, *Quality Engineering*, 5:1, 67-74.
- Brenda Ramírez & George Runger (2006), Quantitative techniques to evaluate process stability, *Quality Engineering*, 18: 53 – 68.
- Al Greene (2007), Process Stability: A Method to Quantify the Stability of Your Process Using the Stability Ratio (SR), A Presentation to the American Society for Quality, Louisville, KY, April 12, 2007.
- Keith A. Britt, Brenda Ramirez & Tom Mistretta (2016) Process monitoring using statistical stability metrics: Applications to biopharmaceutical processes, *Quality Engineering*, 28:2, 193-211

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