Package ‘PPQplan’

September 3, 2019

Type Package

Title Process Performance Qualification (PPQ) Plans in Chemistry, Manufacturing and Controls (CMC) Statistical Analysis

Version 1.0.0

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Depends R (>= 3.2.0)

Imports tolerance, ggplot2, plotly

Description Assessment for statistically-based PPQ sampling plan, including calculating the passing probability, optimizing the baseline and high performance cutoff points, visualizing the PPQ plan and power dynamically. The analytical idea is based on the simulation methods from the textbook ``Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Methods for CMC Applications. In Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry (pp. 227-250). Springer, Cham."

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Suggests knitr, rmarkdown

VignetteBuilder knitr

NeedsCompilation no

RoxygenNote 6.1.1

Encoding UTF-8

URL https://allenzhuaz.github.io/PPQplan/,
https://github.com/allenzhuaz/PPQplan

BugReports https://github.com/allenzhuaz/PPQplan/issues

LazyData true

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Repository CRAN

Date/Publication 2019-09-03 16:20:04 UTC

R topics documented:

`heatmap_ly` *A General Heatmap for Dynamically Assessing Power of the Sampling Plan Using a General Specification Limit.*

Description

The function for dynamically plotting (ggplot) the heatmap to evaluate the sampling plan based on a general lower and/or upper specification limits.

Usage

```
heatmap_ly(attr.name, attr.unit, Llim, Ulim, mu, sigma, n, test.point, dynamic)
```

Arguments

`attr.name`	(optional) user-defined attribute name for sampling plan assessment
`attr.unit`	(optional) user-defined attribute unit
`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`test.point`	(optional) actual process data points for testing whether the processes pass PPQ
`dynamic`	logical; if `TRUE`, then convert the plain heatmap to dynamic graph using plotly.

Value

A Plain or Dynamic Heatmap for Sampling Plan Assessment.

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`pp` and `PPQ.occurve`.

Examples

```
## Not run:
heatmap_ly(attr.name = "Thickness", attr.unit = "%",Llim = -0.2, Ulim = 0.2,
mu = seq(-0.2, 0.2, 0.001), sigma = seq(0,0.2, 0.001),
test.point=data.frame(c(0.1,-0.05),c(0.15,0.05)), n=2, dynamic = T)

## End(Not run)
```

`pi.ctplot` *Heatmap/Contour Plot for Assessing Power of the CQA PPQ Plan Using Prediction Interval.*

Description

The function for plotting the heatmap to evaluate the PPQ plan based on the specification test, given lower and upper specification limits.

Usage

```
pi.ctplot(attr.name, attr.unit, Llim, Ulim, mu, sigma, n, n.batch, alpha, test.point)
```

Arguments

`attr.name`	user-defined attribute name for PPQ assessment
`attr.unit`	user-defined attribute unit
`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`alpha`	significant level for constructing the prediction interval.
`test.point`	(optional) actual process data points for testing whether the processes pass PPQ

Value

Heatmap (or Countour Plot) for PPQ Assessment.

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`pi.pp` and `pi.occurve`.

Examples

```
## Not run:
## Example verifying simulation resutls in the textbook page 249
mu <- seq(95, 105, 0.1)
sigma <- seq(0.2, 3.5, 0.1)
pi.ctplot(attr.name = "Composite Assay", attr.unit = "%LC",
mu = mu, sigma = sigma, Llim=95, Ulim=105)
mu <- seq(90, 110, 0.5)
pi.ctplot(attr.name = "Composite Assay", attr.unit = "%LC",
mu = mu, sigma = sigma, Llim=90, Ulim=110)

mu <- seq(95,105,0.1)
sigma <- seq(0.1,2.5,0.1)
pi.ctplot(attr.name = "Sterile Concentration Assay", attr.unit = "%",
mu = mu, sigma = sigma, Llim=95, Ulim=105)
test <- data.frame(mean=c(97,98.3,102.5), sd=c(0.55, 1.5, 1.2))
pi.ctplot(attr.name = "Sterile Concentration Assay", attr.unit = "%", Llim=95, Ulim=105,
mu = mu, sigma = sigma, test.point=test)

## End(Not run)
```

`pi.occurve` *Operating Characteristic (OC) Curves for the CQA PPQ Plan using Prediction Interval.*

Description

The function for plotting the OC curves and optimizing the baseline and high performance PPQ plans, given lower and upper specification limits.

Usage

```
pi.occurve(attr.name, attr.unit, Llim, Ulim, mu, sigma, n, n.batch, alpha, add.reference)
```

Arguments

`attr.name`	user-defined attribute name
`attr.unit`	user-defined attribute unit
`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`alpha`	significant level for constructing the prediction interval.
`add.reference`	logical; if `TRUE`, then add reference OC curves (Baseline and High Performance) in the plot.

Value

OC curves for specification test and PPQ plan.

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`pi.pp` and `rl.pp`.

Examples

```
## Not run:
pi.occurve(attr.name = "Total Protein", attr.unit = "mg/mL",
sigma = seq(0.01,1,0.01))
pi.occurve(attr.name = "Total Protein", attr.unit = "mg/mL",
sigma = seq(0.01,1,0.01), n.batch=3)
# Baseline curve
pi.occurve(attr.name = "Total Protein", attr.unit = "mg/mL",
sigma = seq(0.01,1,0.01), alpha = 0.1135434)
# High performance curve
pi.occurve(attr.name = "Total Protein", attr.unit = "mg/mL",
```

```
sigma = seq(0.01,1,0.01), alpha = 0.0225518)

# 95% with reference curves
pi.occurve(attr.name = "Total Protein", attr.unit = "mg/mL",
sigma = seq(0.01,1,0.01), add.reference=TRUE)
pi.occurve(attr.name = "Composite Assay", attr.unit = "%",
mu = 100, sigma = seq(0.1,6,0.1), Llim=95, Ulim=105, n.batch=1, add.reference=TRUE)

pi.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%",
mu=97, sigma=seq(0.1, 10, 0.1), Llim=95, Ulim=105, n=10, add.reference=TRUE)

pi.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%",
mu=100, sigma=seq(0.1, 10, 0.1), Llim=95, Ulim=105, n=10, add.reference=TRUE)

pi.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%",
mu=seq(95,105,0.1), sigma=1, Llim=95, Ulim=105, n=10, add.reference=TRUE)

pi.occurve(attr.name = "Protein Concentration", attr.unit="%",
mu=seq(90, 110, 0.1), sigma=1.25, Llim=90, Ulim=110, add.reference=TRUE)

## End(Not run)
```

`pi.pp` *Probability of Passing PPQ Test using Prediction Interval*

Description

The function for calculating the probability of passing critical quality attributes (CQA) PPQ test .

Usage

```
pi.pp(Llim, Ulim, mu, sigma, n, n.batch, alpha)
```

Arguments

`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`alpha`	significant level for constructing the prediction interval.

Value

A numeric value of the passing/acceptance probability

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`rl.pp`.

Examples

```
## Not run:
pi.pp(sigma=0.5, mu=2.5, n=10, n.batch=1, Llim=1.5, Ulim=3.5, alpha=0.05)

sapply(X=c(0.1,0.5, 1,2,3,4,5,10), FUN = pi.pp, mu=97, n=10, Llim=95, Ulim=105,
n.batch=1, alpha=0.05)
sapply(X=c(0.1,0.5, 1,2,3,4,5,10), FUN = pi.pp, mu=100, n=10, Llim=95, Ulim=105,
n.batch=1, alpha=0.05)

## End(Not run)
```

---

pp — *Probability of Passing General Upper and/or Lower Specification Limit*

Description

The function for calculating the probability of passing a general upper and/or lower boundary.

Usage

```
pp(Llim, Ulim, mu, sigma, n)
```

Arguments

`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations)

Value

A numeric value of the passing/acceptance probability

Author(s)

Yalin Zhu

See Also

`rl.pp` and `PPQ.pp`.

`PPQ.ctplot` *Heatmap/Contour Plot for Assessing Power of the CQA PPQ Plan Using General Multiplier.*

Description

The function for plotting the heatmap to evaluate the PPQ plan based on the specification test, given lower and upper specification limits.

Usage

```
PPQ.ctplot(attr.name, attr.unit, Llim, Ulim, mu, sigma, n, n.batch, k, test.point)
```

Arguments

`attr.name`	(optional) user-defined attribute name for PPQ assessment
`attr.unit`	(optional) user-defined attribute unit
`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`k`	general mulipler for constructing the specific interval
`test.point`	(optional) actual process data points for testing whether the processes pass PPQ

Value

Heatmap (or Countour Plot) for PPQ Assessment.

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

PPQ.pp and PPQ.occurve.

Examples

```
## Not run:
mu <- seq(1.6,3.4,0.05)
sigma <- seq(0.05,0.8,0.01)
PPQ.ctplot(attr.name = "Total Protein", attr.unit = "mg/mL", Llim=1.5, Ulim=3.5,
mu = mu, sigma = sigma, k=2.373)

## Example verifying simulation resutls in the textbook page 249
mu <- seq(95, 105, 0.1)
sigma <- seq(0.2, 5, 0.1)
PPQ.ctplot(attr.name = "Composite Assay", attr.unit = "%LC", Llim=95, Ulim=105,
mu = mu, sigma = sigma, k=2.373)
mu <- seq(90, 110, 0.5)
PPQ.ctplot(attr.name = "Composite Assay", attr.unit = "%LC", Llim=90, Ulim=110,
mu = mu, sigma = sigma, k=2.373)

mu <- seq(95,105,0.1)
sigma <- seq(0.1,2.5,0.1)
PPQ.ctplot(attr.name = "Sterile Concentration Assay", attr.unit = "%", Llim=95, Ulim=105,
mu = mu, sigma = sigma, k=2.373)
test <- data.frame(mean=c(97,98.3,102.5), sd=c(0.55, 1.5, 1.2))
PPQ.ctplot(attr.name = "Sterile Concentration Assay", attr.unit = "%", Llim=95, Ulim=105,
mu = mu, sigma = sigma, k=2.373, test.point=test)

## End(Not run)
```

PPQ.ggplot — *Heatmap/Contour GGPlot for Dynamically Assessing Power of the CQA PPQ Plan Using General Multiplier.*

Description

The function for dynamically plotting (ggplot) the heatmap to evaluate the PPQ plan based on the specification test, given lower and upper specification limits.

Usage

```
PPQ.ggplot(attr.name, attr.unit, Llim, Ulim, mu, sigma, n, n.batch, k,
test.point, dynamic)
```

Arguments

attr.name	(optional) user-defined attribute name for PPQ assessment
attr.unit	(optional) user-defined attribute unit

Llim	lower specification limit
Ulim	upper specification limit
mu	hypothetical mean of the attribute
sigma	hypothetical standard deviation of the attribute
n	sample size (number of locations) per batch
n.batch	number of batches for passing PPQ during validation
k	general mulipler for constructing the specific interval
test.point	(optional) actual process data points for testing whether the processes pass PPQ
dynamic	logical; if TRUE, then convert the heatmap ggplot to dynamic graph using plotly.

Value

Dynamic Heatmap (or Countour Plot) for PPQ Assessment.

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

PPQ.pp and PPQ.occurve.

Examples

```
## Not run:
mu <- seq(95, 105, 0.1)
sigma <- seq(0.1,1.7,0.1)
PPQ.ggplot(attr.name = "Sterile Concentration Assay", attr.unit = "%", Llim=95, Ulim=105,
mu = mu, sigma = sigma, k=2.373, dynamic = FALSE)
test <- data.frame(mu=c(97,98.3,102.5), sd=c(0.55, 1.5, 0.2))
PPQ.ggplot(attr.name = "Sterile Concentration Assay", attr.unit = "%", Llim=95, Ulim=105,
mu = mu, sigma = sigma, k=2.373, test.point = test)

## End(Not run)
```

PPQ.occurve — *Operating Characteristic (OC) Curves for the CQA PPQ Plan Using General Multiplier.*

Description

The function for plotting the OC curve to show the PPQ plan, given lower and upper specification limits.

Usage

```
PPQ.occurve(attr.name, attr.unit, Llim, Ulim, mu, sigma, n, n.batch, k, add.reference)
```

Arguments

`attr.name`	(optional) user-defined attribute name
`attr.unit`	(optional) user-defined attribute unit
`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`k`	general mulipler for constructing the specific interval
`add.reference`	logical; if `TRUE`, then add reference OC curves (Baseline and High Performance) in the plot.

Value

OC curves for specification test and PPQ plan.

Author(s)

Yalin Zhu

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`PPQ.pp` and `rl.pp`.

Examples

```
## Not run:
PPQ.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%", Llim=95, Ulim=105,
mu=97, sigma=seq(0.1, 10, 0.1), n=10, k=2.373, add.reference=TRUE)
PPQ.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%", Llim=95, Ulim=105,
mu=100, sigma=seq(0.1, 10, 0.1), n=10, k=2.373, add.reference=TRUE)
PPQ.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%", Llim=95, Ulim=105,
mu=seq(95,105,0.1), sigma=1, n=10, k=2.373)
PPQ.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%", Llim=95, Ulim=105,
mu=seq(95,105,0.1), sigma=1, n=10, k=2.373, add.reference=TRUE)

PPQ.occurve(attr.name = "Protein Concentration", attr.unit="%", Llim=90, Ulim=110,
mu=seq(90, 110, 0.1), sigma=1.25, k=2.373)

## Only display referece curves, leave k as NULL by default
PPQ.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%LC", Llim=95, Ulim=105,
mu=98, sigma=seq(0.1, 10, 0.1), n=10, add.reference=TRUE)

## End(Not run)
```

PPQ.pp *Probability of Passing PPQ Test Using General Multiplier*

Description

The function for calculating the probability of passing critical quality attributes (CQA) PPQ test .

Usage

```
PPQ.pp(Llim, Ulim, mu, sigma, n, n.batch, k)
```

Arguments

`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`k`	general mulipler for constructing the specific interval

Value

A numeric value of the passing/acceptance probability

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`rl.pp`.

Examples

```
## Not run:
PPQ.pp(Llim = 90, Ulim = 110, mu=105, sigma=1.5, n=10, k=3.1034)

# One-sided tolerance interval with k=0.753 (95/67.5 one-sided tolerance interval LTL)
PPQ.pp(sigma=0.03, mu=1.025, n=40, Llim=1, Ulim=Inf, k=0.753)

sapply(X=c(0.1,0.5, 1,2,3,4,5,10), FUN = PPQ.pp, mu=97, n=10, Llim=95, Ulim=105, k=2.373)
sapply(X=seq(0.1,10,0.1), FUN = PPQ.pp, mu=97, n=10, Llim=95, Ulim=105, k=2.373)

sapply(X=c(0.1,0.5, 1,2,3,4,5,10), FUN = PPQ.pp, mu=100, n=10, Llim=95, Ulim=105, k=2.373)

sigma <- seq(0.1, 4, 0.1)
pp1 <- sapply(X=sigma, FUN =  PPQ.pp, mu=97, n=10, Llim=95, Ulim=105, k=2.373)
pp2 <- sapply(X=sigma, FUN =  PPQ.pp, mu=98, n=10, Llim=95, Ulim=105, k=2.373)
pp3 <- sapply(X=sigma, FUN =  PPQ.pp, mu=99, n=10, Llim=95, Ulim=105, k=2.373)
pp4 <- sapply(X=sigma, FUN =  PPQ.pp, mu=100, n=10, Llim=95, Ulim=105, k=2.373)
plot(sigma, pp1, xlab="Standard Deviation", main="LSL=95, USL=105, k=2.373, n=10",
ylab="Probability of Passing", type="o", pch=1, col=1, lwd=1, ylim=c(0,1))
lines(sigma, pp2, type="o", pch=2, col=2)
lines(sigma, pp3, type="o", pch=3, col=3)
lines(sigma, pp4, type="o", pch=4, col=4)
legend("topright", legend=paste0(rep("mu=",4),c(97,98,99,100)), bg="white",
col=c(1,2,3,4), pch=c(1,2,3,4), lty=1, cex=0.8)

mu <- seq(95, 105, 0.1)
pp5 <- sapply(X=mu, FUN =  PPQ.pp, sigma=0.5, n=10, Llim=95, Ulim=105, k=2.373)
pp6 <- sapply(X=mu, FUN =  PPQ.pp, sigma=1, n=10, Llim=95, Ulim=105, k=2.373)
pp7 <- sapply(X=mu, FUN =  PPQ.pp, sigma=1.5, n=10, Llim=95, Ulim=105, k=2.373)
pp8 <- sapply(X=mu, FUN =  PPQ.pp, sigma=2, n=10, Llim=95, Ulim=105, k=2.373)
pp9 <- sapply(X=mu, FUN =  PPQ.pp, sigma=2.5, n=10, Llim=95, Ulim=105, k=2.373)
plot(mu, pp5, xlab="Mean Value", main="LSL=95, USL=105, k=2.373, n=10",
ylab="Probability of Passing", type="o", pch=1, col=1, lwd=1, ylim=c(0,1))
lines(mu, pp6, type="o", pch=2, col=2)
lines(mu, pp7, type="o", pch=3, col=3)
lines(mu, pp8, type="o", pch=4, col=4)
lines(mu, pp9, type="o", pch=5, col=5)
legend("topright", legend=paste0(rep("sigma=",5),seq(0.5,2.5,0.5)), bg="white",
col=c(1,2,3,4,5), pch=c(1,2,3,4,5), lty=1, cex=0.8)

## End(Not run)
```

rl.pp *Probability of Passing Specification Test for a Release Batch*

Description

The function for calculating the probability of passing critical quality attributes (CQA) specification test .

Usage

```
rl.pp(Llim, Ulim, mu, sigma, NV)
```

Arguments

`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`NV`	nominal volume for the specification test.

Value

A numeric value of the passing/acceptance probability

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`PPQ.pp`, `pi.pp` and `ti.pp`.

Examples

```
rl.pp(Llim=1.5, Ulim=3.5, mu=2.5, sigma=0.8)
```

ti.ctplot *Heatmap/Contour Plot for Assessing Power of the PPQ Plan using Tolerance Interval.*

Description

The function for plotting the heatmap to evaluate the PPQ plan based on the specification test, given lower and upper specification limits.

Usage

```
ti.ctplot(attr.name, attr.unit, Llim, Ulim, mu, sigma, n, n.batch,
alpha, coverprob, side, test.point)
```

Arguments

`attr.name`	user-defined attribute name for PPQ assessment
`attr.unit`	user-defined attribute unit
`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`alpha`	significant level for constructing the tolerance interval.
`coverprob`	converage probability for constructing the tolerance interval
`side`	whether a 1-sided or 2-sided tolerance interval is required (determined by side = 1 or side = 2, respectively).
`test.point`	(optional) actual process data points for testing whether the processes pass PPQ

Value

Heatmap (or Countour Plot) for PPQ Assessment.

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`ti.pp` and `ti.occurve`.

Examples

```
mu <- seq(95,105,0.1)
sigma <- seq(0.1,2.5,0.1)
ti.ctplot(attr.name = "Sterile Concentration Assay", attr.unit = "%",
mu = mu, sigma = sigma, Llim=95, Ulim=105)

ti.ctplot(attr.name = "Extractable Volume", attr.unit = "% of NV=1mL",
Llim = 100, Ulim = Inf, mu=seq(100, 110, 0.5), sigma=seq(0.2, 15 ,0.5), n=40,
alpha = 0.05, coverprob = 0.675, side=1)
```

---

ti.occurve — *Operating Characteristic (OC) Curves for the PPQ Plan using Tolerance Interval.*

Description

The function for plotting the OC curve to show the PPQ plan based on the specification test, given lower and upper specification limits.

Usage

```
ti.occurve(attr.name, attr.unit, Llim, Ulim, mu, sigma, n, n.batch, alpha,
coverprob, side, add.reference, NV)
```

Arguments

`attr.name`	user-defined attribute name
`attr.unit`	user-defined attribute unit
`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`alpha`	significant level for constructing the tolerance interval.
`coverprob`	converage probability for constructing the tolerance interval
`side`	whether a 1-sided or 2-sided tolerance interval is required (determined by side = 1 or side = 2, respectively).
`add.reference`	logical; if `TRUE`, then add reference OC curves (Baseline and High Performance) in the plot.
`NV`	nominal volume for the specification test.

Value

OC curves for specification test and PPQ plan.

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`ti.pp` and `rl.pp`.

Examples

```
ti.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%",
mu=97, sigma=seq(0.1, 10, 0.1), Llim=95, Ulim=105, n=10, add.reference=TRUE)

ti.occurve(attr.name = "Sterile Concentration Assay", attr.unit="%",
mu=100, sigma=seq(0.1, 10, 0.1), Llim=95, Ulim=105, n=10, add.reference=TRUE)

ti.occurve(attr.name = "Extractable Volume", attr.unit = "% of NV=3mL",
Llim = 100, Ulim = Inf, mu=102.5, sigma=seq(0.2, 6 ,0.05), n=40,
alpha = 0.05, coverprob = 0.97, side=1, NV=3)

ti.occurve(attr.name = "Extractable Volume", attr.unit = "% of NV=3mL",
Llim = 100, Ulim = Inf, mu=102.5, sigma=seq(0.2, 6 ,0.05), n=40,
alpha = 0.05, coverprob = 0.992, side=1, NV=3)
```

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ti.pp — *Probability of Passing PPQ Test using Tolerance Interval*

Description

The function for calculating the probability of passing critical quality attributes (CQA) PPQ test .

Usage

```
ti.pp(Llim, Ulim, mu, sigma, n, n.batch, alpha, coverprob, side)
```

Arguments

`Llim`	lower specification limit
`Ulim`	upper specification limit
`mu`	hypothetical mean of the attribute
`sigma`	hypothetical standard deviation of the attribute
`n`	sample size (number of locations) per batch
`n.batch`	number of batches for passing PPQ during validation
`alpha`	significant level for constructing the tolerance interval
`coverprob`	coverage probability for constructing the tolerance interval
`side`	whether a 1-sided or 2-sided tolerance interval is required (determined by side = 1 or side = 2, respectively).

Value

A numeric value of the passing/acceptance probability

Author(s)

Yalin Zhu

References

Burdick, R. K., LeBlond, D. J., Pfahler, L. B., Quiroz, J., Sidor, L., Vukovinsky, K., & Zhang, L. (2017). Statistical Applications for Chemistry, Manufacturing and Controls (CMC) in the Pharmaceutical Industry. *Springer*.

See Also

`rl.pp`.

Examples

```
ti.pp(sigma=0.5, mu=2.5, n=10, n.batch=1, Llim=1.5, Ulim=3.5, alpha=0.05)

sapply(X=c(0.1,0.5, 1,2,3,4,5,10), FUN = ti.pp, mu=97, n=10, Llim=95, Ulim=105,
n.batch=1, alpha=0.05)
sapply(X=c(0.1,0.5, 1,2,3,4,5,10), FUN = ti.pp, mu=100, n=10, Llim=95, Ulim=105,
n.batch=1, alpha=0.05)
```

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