Validation of Classification Models

Chemometrics for Spectroscopists

Intensive Course Kraków
2021-11-29 – 12-03

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Topics

1. Introduction
2. Figures of Merit
3. Excursion: Design of Experiments
4. Verification Schemes
5. Resampling Techniques
6. Model Stability
7. Excursion: Model Aggregation
8. Sample Size Planning
9. Validation
10. Data-driven Model Optimization and Hyperparameter Tuning

Validation and Verification

Verification: Making sure/measuring/showing that the model meets the specifications.

Validation: Making sure that the model meets the application needs.

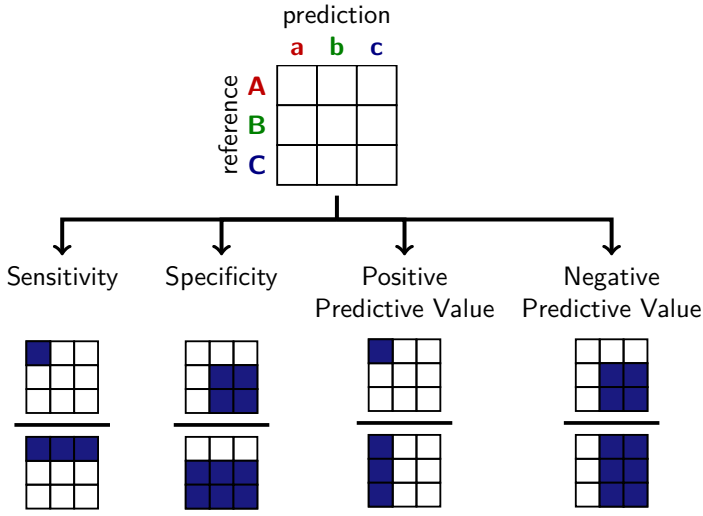
- Chemometric model validation ⇝ typically verification rather than validation is done.
- Characterize model by
- measuring its predictive performance

Model Validation Recipe

Ingredients

- Ready-to-use classifier
  treated as black box: *case* $\mapsto$ *prediction*
- Figures of merit (performance measure)
  Overall Accuracy, Sensitivity, Specificity, Predictive Values, MSE, ...
- Validation *scheme*: *How to get test cases?*
  ~~Autoprediction~~, Resampling, Test Set, Validation study

Figures of Merit: Proportions



Proportion Questions

Sensitivity: of all truly class *A* cases, which fraction is correctly recognized as class *A*?

Specificity: of all cases truly not belonging to class *A*, which fraction is correctly recognized as not belonging to class *A*?

Positive Predictive Value: of all cases predicted to belong to class *A*, which fraction does truly belong to class *A*?

Negative Predictive Value: of all cases predicted not to belong to class *A*, which fraction does truly not belong to class *A*?

accuracy: correct proportion among all predicted cases

error rate: misclassified proportion among all predicted cases

κ: chance-corrected accuracy, inter-observer agreement

Proportions: Characteristics

✔ well-known, widely used

✘ often misunderstood:

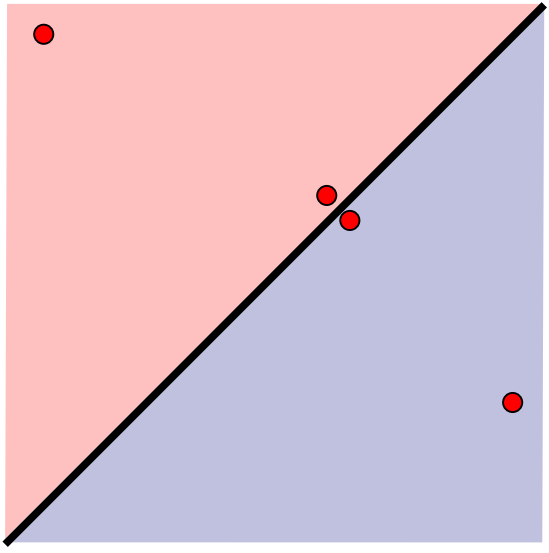
- sensitivity & specificity
  - ✔ easy to measure: test *n* cases of each class, record results
  - ✘ low relevance for application
- predictive values (positive/negative)
  - ✔ high relevance for application
  - ✘ difficult to measure: need to know relative class fequencies under application conditions
    weight rows of confusion matrix accordingly
- “single” figures of merit accuracy, error rate, κ
  - ✘ useless unless corrected for relative class fequencies under application conditions

More figures of merit

- chance-corrected: κ
  - ✔ rescaling possible for other figures of merit
  - ✔ alternative: report chance agreement (or naive model performance) together with figure of merit

- Information gain
  - **positive likelihood ratio:** $LR_A^+ = \frac{Sens_A}{1-Spez_A}$
    How much do the odds to belong to class A increase when a case is predicted to belong to class A?
  - **negative likelihood ratio:** $LR_A^- = \frac{Spez_A}{1-Sens_A}$
    How much do the odds to belong to class A decrease when a case is predicted not to belong to class A?
  - ✔ independent of relative class fequencies under application conditions

Proportions: Behaviour



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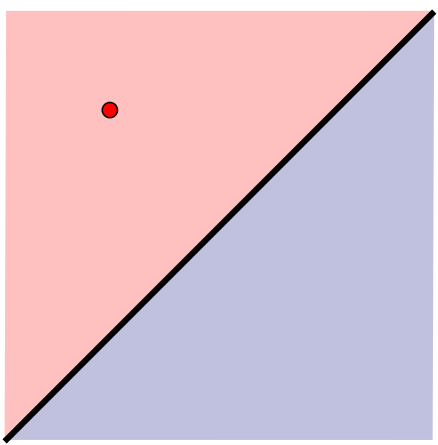

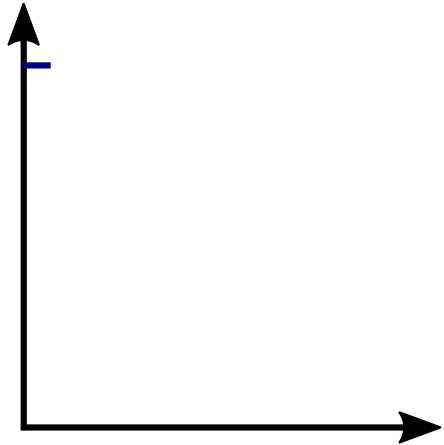

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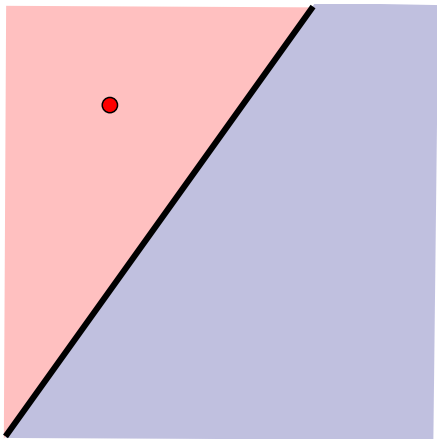

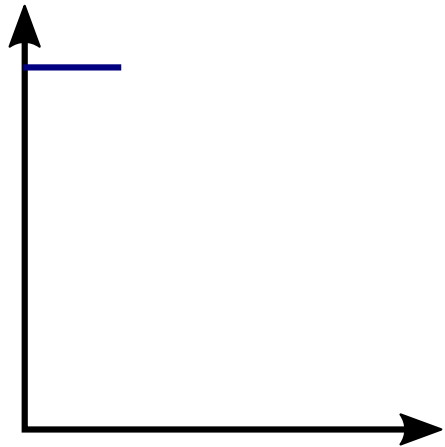

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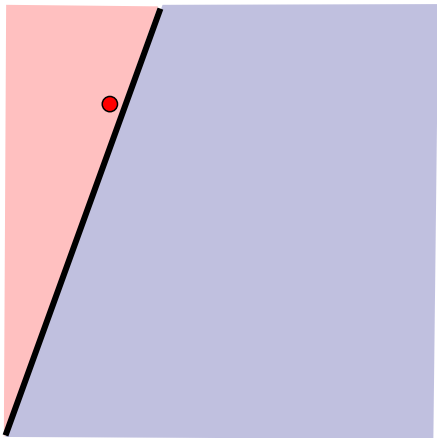

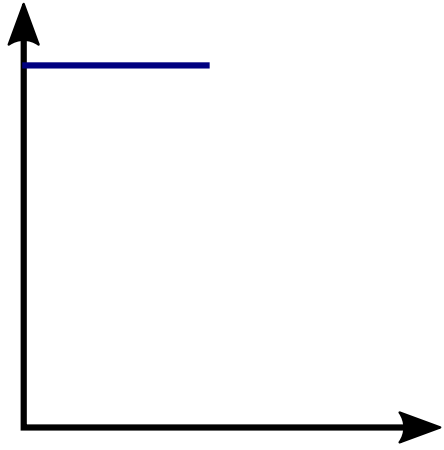

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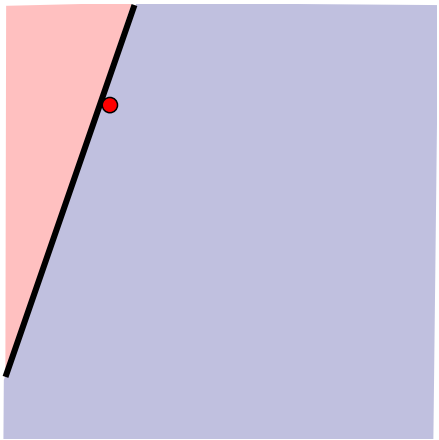

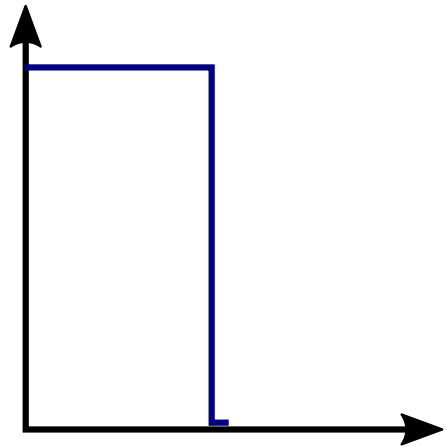

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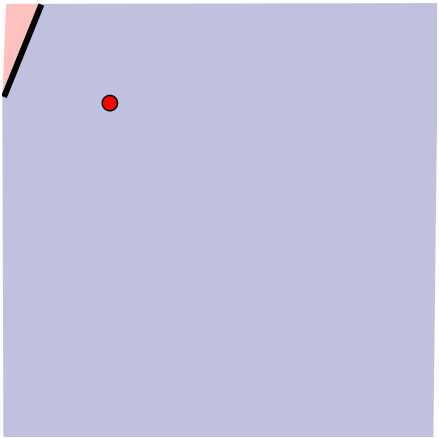
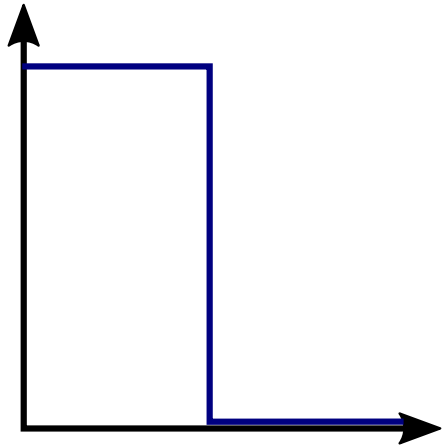
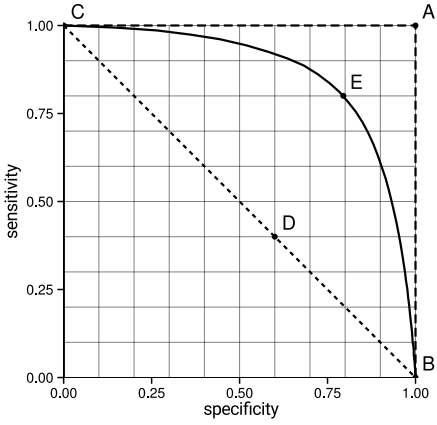
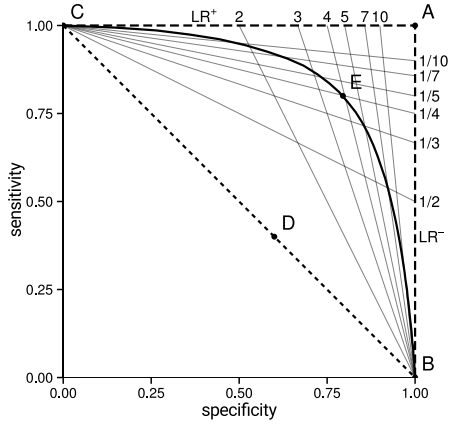




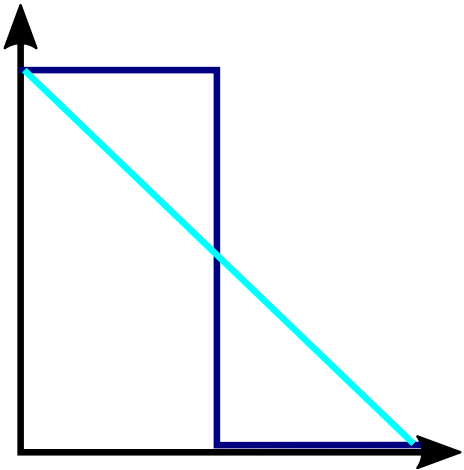
Receiver Operating Charcteristic/Specificity-Sensitivity-Diagram





CHEMO METRIX

(Strictly) Proper Scoring Rules

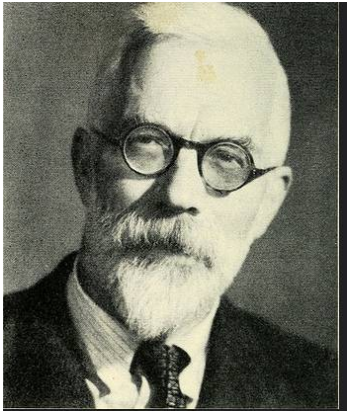


Wanted: Figure of merit that …

- …continuously penalizes closeness to class boundary
- …continuously reacts to changes in the model
- …slight deterioration ⇝ slight drop in measured performance
- …has exactly one optimum
- at the best classifier.

Brier's Score: Mean Squared Error for Classification

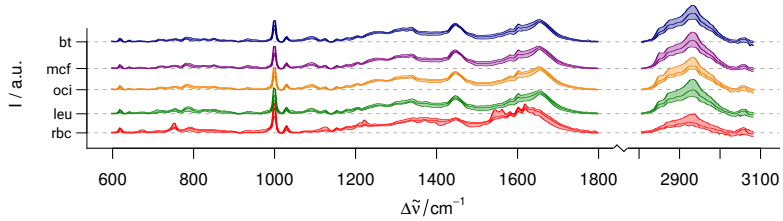
- Classifier that predicts class membership probability rather than labels
- Idea: of all cases where classifier predicts x % class membership, x % should belong to class in question
  a.k.a. *well calibrated prediction*
- Brier's score: $BS = \frac{1}{N}\sum_{i=1}^{N}(\hat{p}_i - p_i)^2$ or
  $BS = \frac{1}{N}\sum_{j=1}^{R}\sum_{i=1}^{N}(\hat{p}_{ij} - p_{ij})^2$ (multiclass version) with
  N . . . number of cases
  i . . . case in question
  R . . . number of classes
  j . . . class in question
  p . . . class membership, usually $\in \{0, 1\}$
  $\hat{p}$ . . . predicted class membership $\in [0, 1]$



To consult the statistician after an experiment is finished is often merely to ask him to conduct a post mortem examination.
He can perhaps say what the experiment died of.

— R. Fisher, 1938

Example: Tumor Cell Identification



rbc	normal red blood cells	5 donors	372 spectra
leu	normal leukocytes	5 donors	569 spectra
oci	acute myelotic leukemia cell line OCI-AML	5 batches	518 spectra
mcf	breast cancer cell line MCF-7	5 batches	558 spectra
bt	breast cancer cell line BT-20	5 batches	532 spectra
total			2549 spectra

Neugebauer2010a
Beleites2013

CHEMO METRIX

Aims

Ensure and/or establish

- validity
- reliability
- repeatability, reproducibility

- statistical power and sensitivity
  - necessary sample size
  - efficiency: get information with lowest possible experimental effort

of the experimental data ⇝ derived model ⇝ interpretation

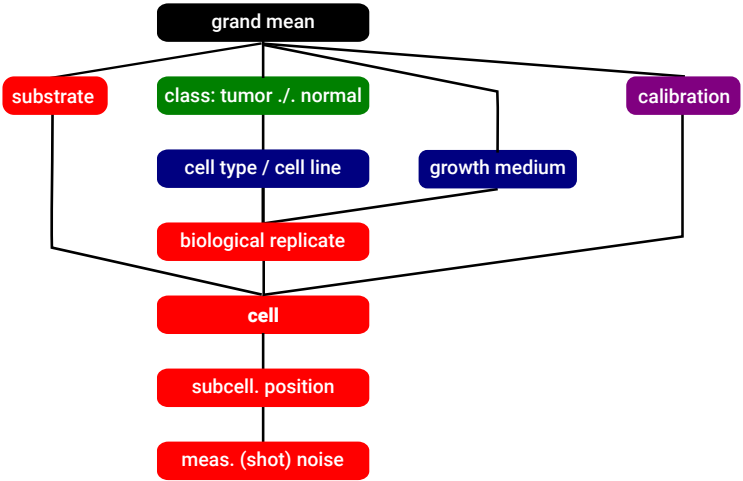
“GLP” for experiment set-up

Vocabulary: factors and effects

- A **factor** influences the system we study (the spectra)
  ⇝ **effect**
- A **confounding factor** is a hidden factor that influences/disturbs our experiment
- The same factor may be of interest or disturbing depending on the study!

- Distinguish: *fixed* vs. *random* factors
- Relations between factors: *crossed* vs. *nested* factors
- Design: *orthogonal* and *balanced* designs/data

Hasse Diagrams



Crossed Factors

. . . occur independent of each other:

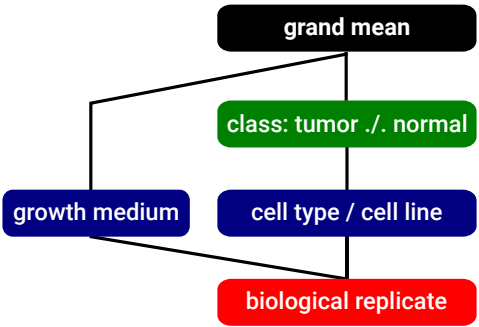
- **Fully Crossed:** measurements available for all combinations

	cell line		
medium	bt	mcf	oci
RPMI	46	51	57
DMEM	49	56	78

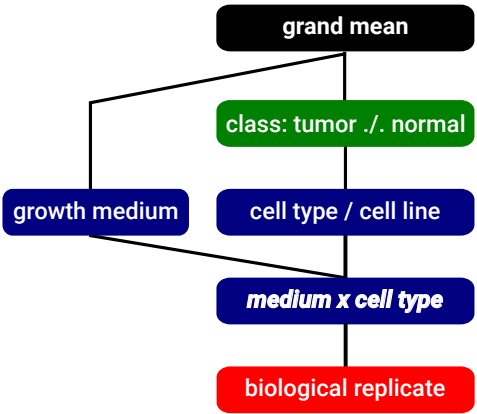
- **Partially Crossed:** measurements only of some combinations

	cell line		
medium	bt	mcf	oci
RPMI	·	51	57
DMEM	49	56	·

Excursion: Interactions



Excursion: Interactions



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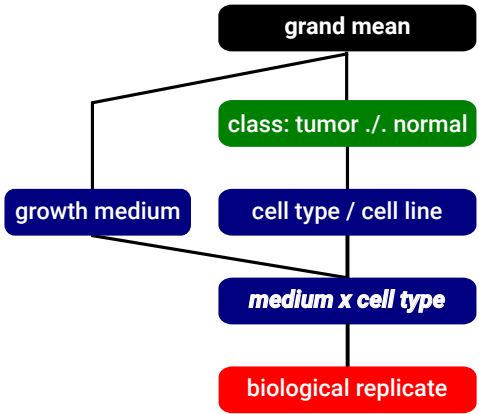

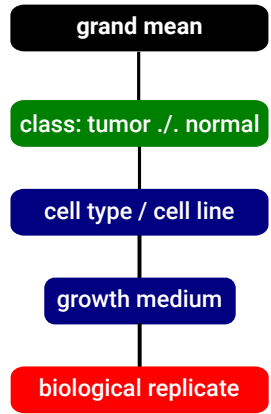

CHEMO METRIX

Nested Factors

Levels of inner factor occur only within *one* level of outer factor

e.g. ***cell within sample****: another sample never contains the same cell*

✔ Explicit Coding:

	cell									
sample	1	2	3	4	5	6	7	8	9	10
A	10	10	·	·	·	·	·	·	·	10
B	·	·	·	·	10	10	10	10	·	·
C	·	·	10	10	·	·	·	·	10	·

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A	10	10	·	·	·	·	·	·	·	10
B	·	·	·	·	10	10	10	10	·	·
C	·	·	10	10	·	·	·	·	10	·

✘ Implicit Coding:

	cell			
sample	1	2	3	4
A	10	10	10	·
B	10	10	10	10
C	10	10	10	·

Nested Factors

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e.g. ***cell within sample****: another sample never contains the same cell*

✔ Explicit Coding:

	cell									
sample	1	2	3	4	5	6	7	8	9	10
A	10	10	·	·	·	·	·	·	·	10
B	·	·	·	·	10	10	10	10	·	·
C	·	·	10	10	·	·	·	·	10	·

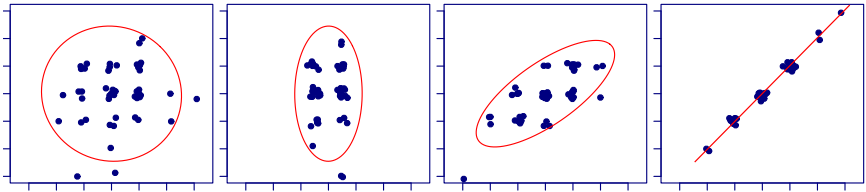
✘ Implicit Coding:

	cell			
sample	1	2	3	4
A	10	10	10	·
B	10	10	10	10
C	10	10	10	·

✔ Make sure crossed factors do not appear nested in your DoE!
Crossed factor with interaction ≠ nested factor!

Design: Orthogonality and Balance

- *Orthogonality:* no correlation between factors

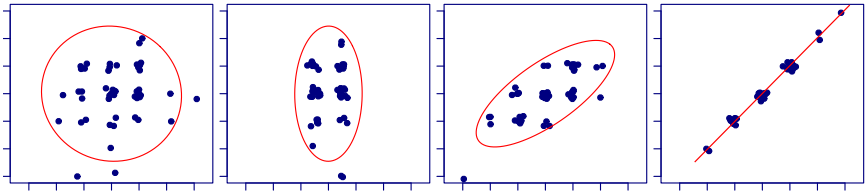


- *Balance:* for each factor, all other factor levels occur with the same frequency

	day								
cell line	a	b	c	d	e	f	g	h	i
bt	50	50	50	50	50	50	50	50	50
mcf	50	50	50	50	50	50	50	50	50
oci	50	50	50	50	50	50	50	50	50

Design: Orthogonality and Balance

- *Orthogonality:* no correlation between factors



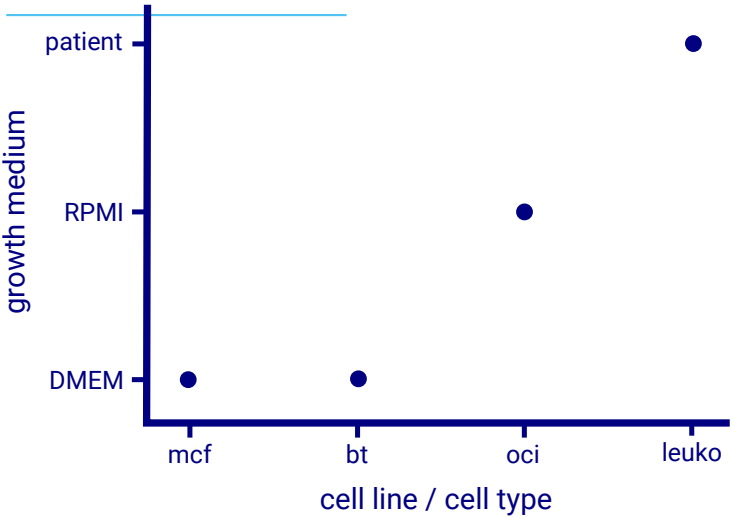
✔ Orthogonal design (data): effects of factors can be completely separated

- *Balance:* for each factor, all other factor levels occur with the same frequency

	day								
cell line	a	b	c	d	e	f	g	h	i
bt	50	50	50	50	50	50	50	50	50
mcf	50	50	50	50	50	50	50	50	50
oci	50	50	50	50	50	50	50	50	50

✔ Balanced data easier to analyze

Your turn! Crossed? Partially crossed? Nested? Orthogonal design? Balanced?



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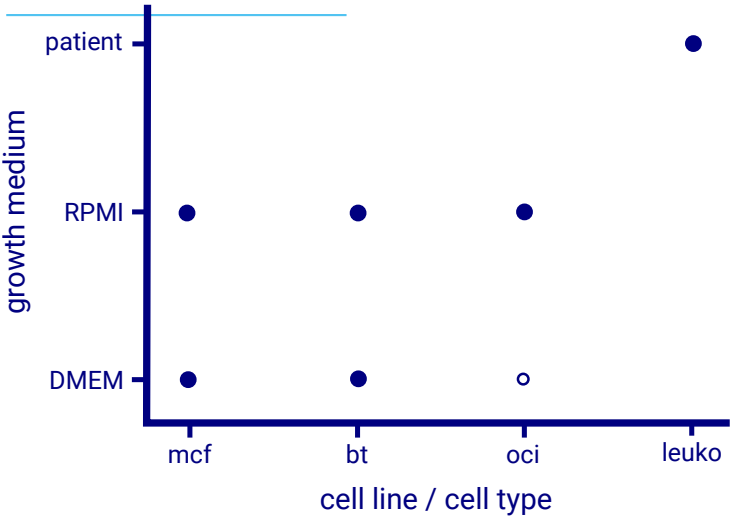

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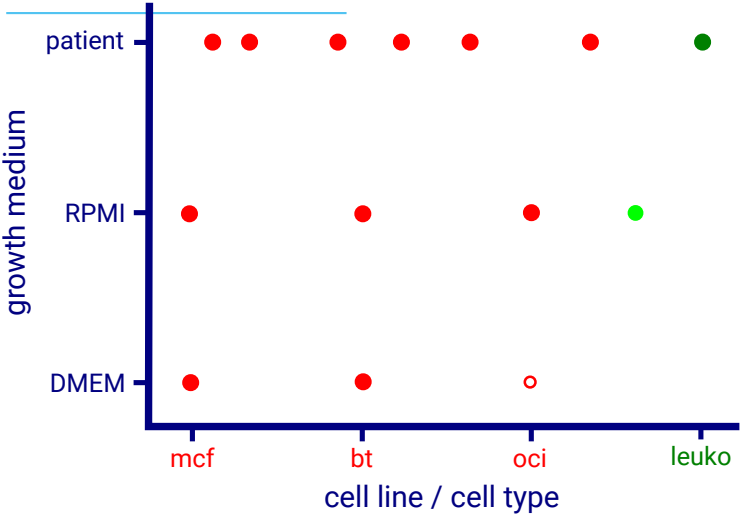


Random and Fixed Factors

Fixed Factor

- occurs at levels which
  - ✔ We can either *know* and *reproduce*, or even
  - ✔ *set* (*fix*).

Random Factor

- occurs at levels which
  - – We can *know*, but
  - ✘ will never meet again (*reproduce*)

⚠ The same factor may be fixed in one study/application and random in another!

Random and Fixed Factors

Fixed Factor

- occurs at levels which
  - ✔ We can either *know* and *reproduce*, or even
  - ✔ *set* (*fix*).

✔ Recognize/predict the level/value for new unknown data

Random Factor

- occurs at levels which
  - – We can *know*, but
  - ✘ will never meet again (*reproduce*)

✘ New unknown data always corresponds to new level of a random factor

⚠ The same factor may be fixed in one study/application and random in another!

Random and Fixed Factors

Fixed Factor

- occurs at levels which
  - ✔ We can either *know* and *reproduce*, or even
  - ✔ *set* (*fix*).

✔ Recognize/predict the level/value for new unknown data

✔ Account for *known* level/value for new unknown data

Random Factor

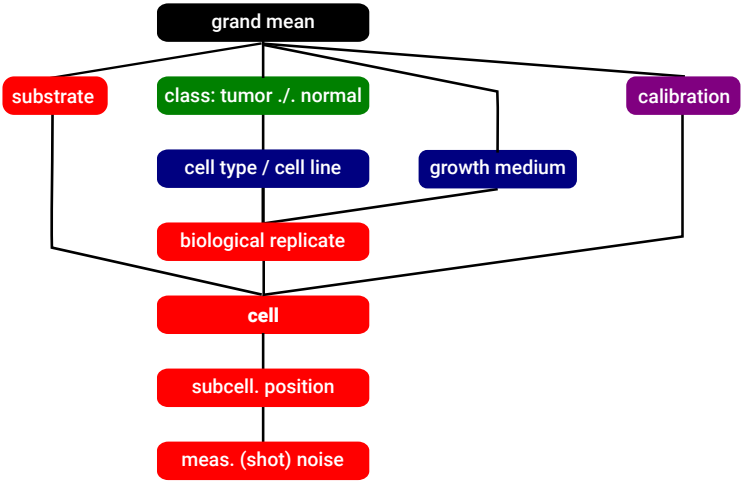
- occurs at levels which
  - – We can *know*, but
  - ✘ will never meet again (*reproduce*)

✘ New unknown data always corresponds to new level of a random factor

✘ Account for random factors only by general (population) behaviour.

⚠ The same factor may be fixed in one study/application and random in another!

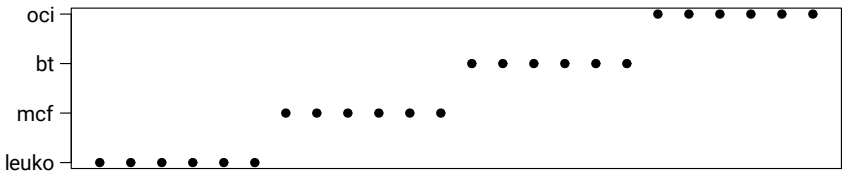
Hasse Diagrams



Dealing with Factors Disturbing our Experiment

- ✔ Include fixed factors in model
- ✔ Reduce variance as much as possible:
  - measure and reduce systematic influence: e.g. instrument calibration
  - standard operating procedures
  - automation
  - quality control, e.g. positive and negative controls
- ✔ *Representative sampling* ⇝ train model with *reduced influence*.
- ✔ Randomization
- ✔ Blocking/Stratification
- *Disregard* confounders which are *known* to be unimportant
- Possibly: reproducible (= fixed factor) subgroups
  - use *local* models

Randomization and Blocking/Stratification



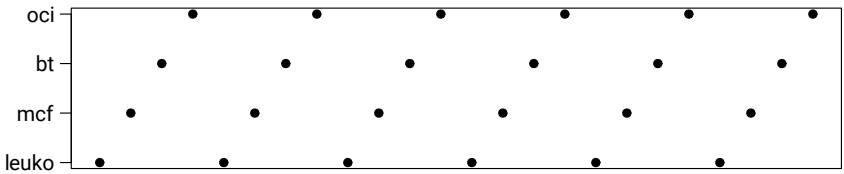
- **Blocking:** Factor causing groups ⇝ repeat smaller (sub)experiment for each group

✔ **Randomize** assignment of samples/cases to fixed factors

✔ **Randomize** measurement order for random factors

CHEMO METRIX

Randomization and Blocking/Stratification

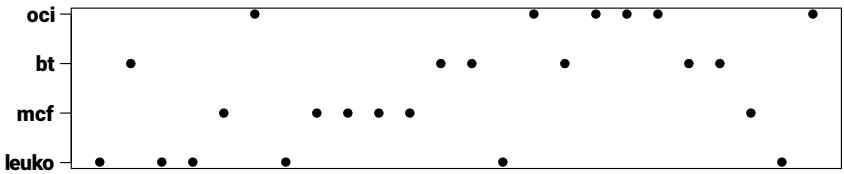


- **Blocking:** Factor causing groups ⇝ repeat smaller (sub)experiment for each group

✔ **Randomize** assignment of samples/cases to fixed factors

✔ **Randomize** measurement order for random factors

Randomization and Blocking/Stratification



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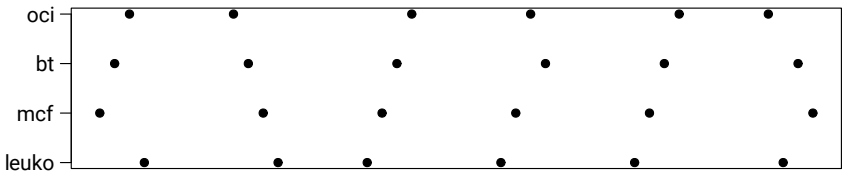
Randomization and Blocking/Stratification



- **Blocking:** Factor causing groups ⇝ repeat smaller (sub)experiment for each group

✔ **Randomize** assignment of samples/cases to fixed factors

✔ **Randomize** measurement order for random factors

Model Testing: Measure the Model's Performance

Different kinds of test samples
⇝ different performance measures

Goodness of fit: *training samples*
⇝ residuals

Generalization error: statistically independent samples
resampling,
test set measured at same time as training set

Future performance: samples measured *after* training samples
dedicated test set for detection of drift

Resampling for Classifier Validation

✘ We don't have enough samples

- Training:
  - Model quality depends on ratio $n_{train} : d.f.$
  - Linear classifier: 5 samples/(variate · class)

✔ We want to use all samples for training

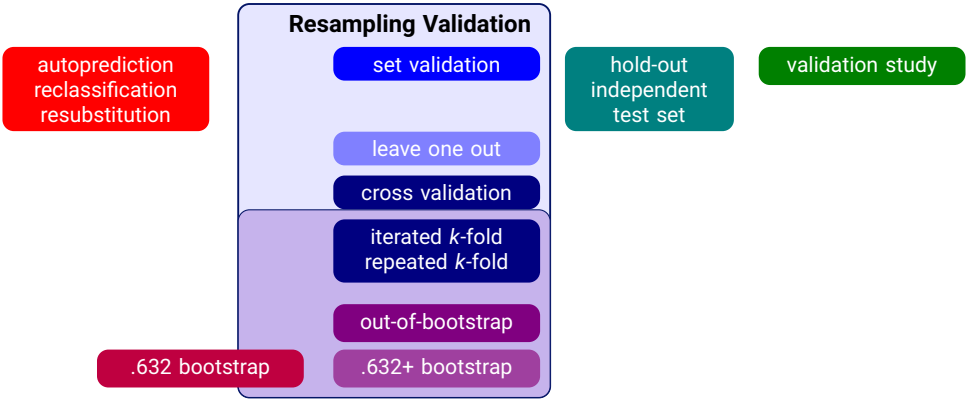
Resampling for Classifier Validation

✘ We don't have enough samples

- Training:
  - Model quality depends on ratio $n_{train} : d.f.$
  - Linear classifier: 5 samples/(variate · class)
  - ✔ We want to use all samples for training

- Testing:
  - ✔ We want to know whether the model is stable
  - Quality of the performance measure depends on n_{test}
  - Width of 95 % confidence interval $\overset{!}{\leq}$ 10 % for $p = 90\,\%$: $n_{test} \geq 140$
  - ✔ We want to use all samples for testing

Validation Schemes: Overview

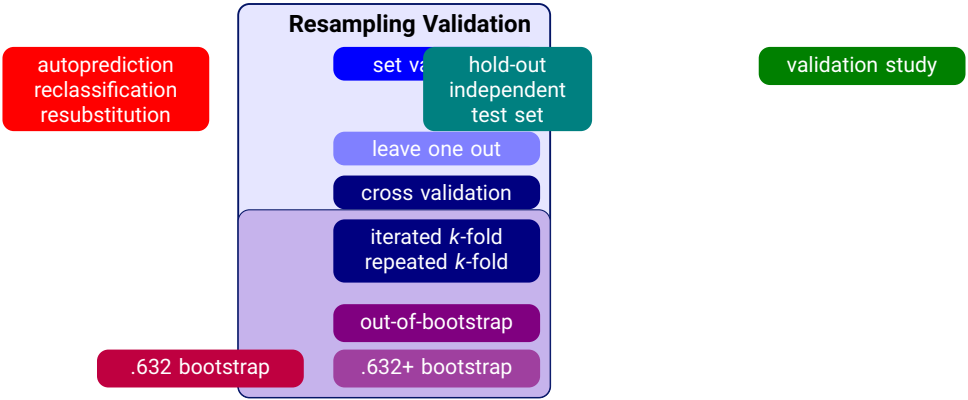


R Kohavi: **A Study of Cross-Validation and Bootstrap for Accuracy Estimation and Model Selection**. In: *Proc. 14th International Joint Conference on Artificial Intelligence*, 1995, Morgan Kaufmann, USA, 1995, 1137–1145.

Beleites2005

CHEMO METRIX

Validation Schemes: Overview



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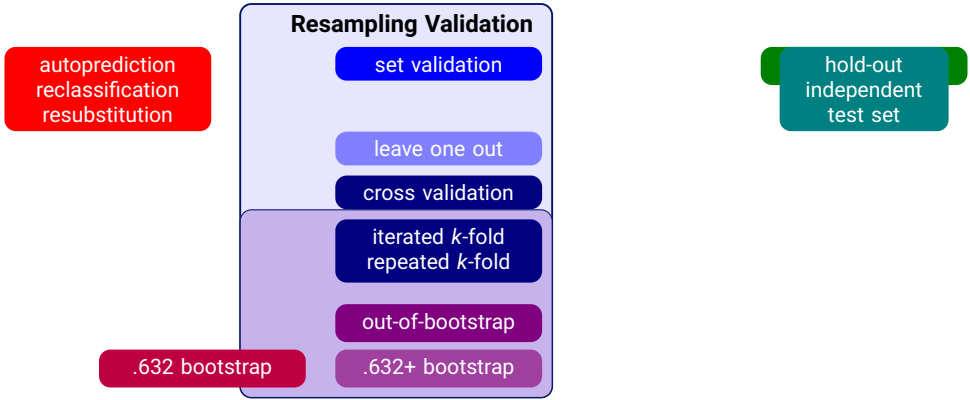

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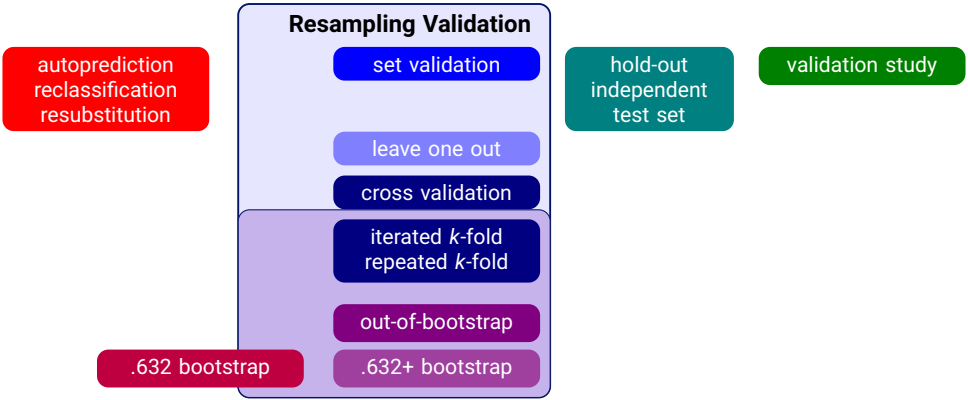

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Beleites2005

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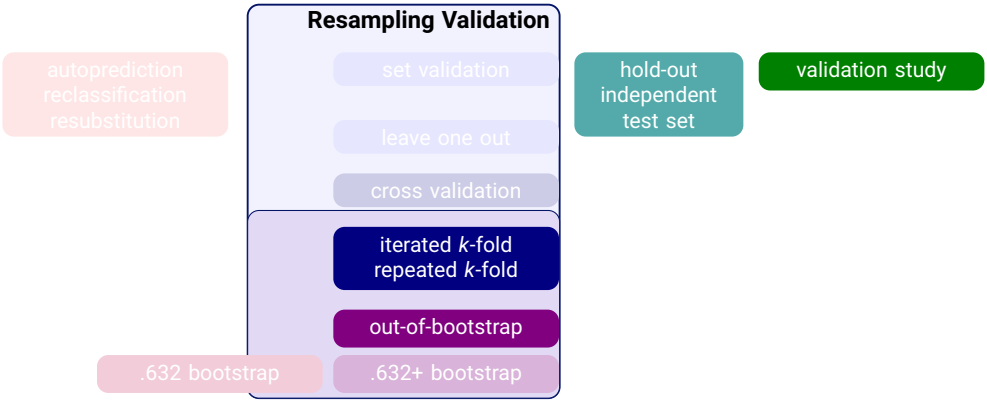
Validation Schemes: Recommendations



Kohavi1995

Beleites2005

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Resampling vs. Validation Study

	Resampling	Validation Study
statistical properties		
bias	✔ pessimistic (low)	✔ unbiased
variance	$f(n)$	$f(n_{test})$
efficient use of cases	✔	✔
measure model stability	✔ iterated	✔/✘
measure drift	✘	✔ DoE
future case performance	✘	✔ DoE
out-of-spec cases	✘	✔ DoE
practical properties		
independence	⚠ splitting error prone	✔
effort	✔ computational	✘ experimental

Beleites2008
Esbensen2010

CHEMO METRIX

Resampling vs. Hold Out

	Resampling	Hold Out (Set) Validation
statistical properties		
bias	✔ pessimistic (low)	✔ unbiased
variance	✔ $f(n)$ lower	✘ $f(n_{test})$ HUGE
efficient use of cases	✔	✘
measure model stability	✔ iterated	✘
measure drift	✘	✘
future case performance	✘	✘
out-of-spec cases	✘	✘(✔)
practical properties		
independence	⚠ splitting error prone	⚠ same as resampling
effort	✔ computational	✔ low

Beleites2008
Esbensen2010

CHEMO METRIX

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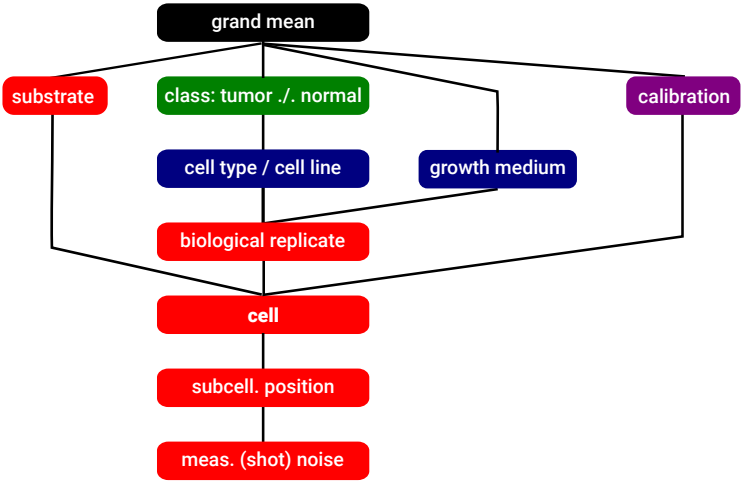
Beleites2008
Esbensen2010

CHEMO METRIX

Hasse-Diagram revisited



CHEMO METRIX

Validation Check List

- Randomize order of measurements
- Split at highest level in sample hierarchy and independently for known confounders use Hasse diagram to determine
- Split before 1st step that involves multiple cases
- Additional independent validation for data-driven optimization/tuning/model selection
- Test cases: reference labels must be independent of cases (measurements, spectra, chromatograms, . . .)
- Ensure correctness of code

CHEMO METRIX

Validation Check List

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- Split at highest level in sample hierarchy and independently for known confounders
  use Hasse diagram to determine patients, strains, cell lines,
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Validation Check List

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  use Hasse diagram to determine patients, strains, cell lines,
  day of measurement, before/after new calibration, . . .
- Split before 1st step that involves multiple cases
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  use Hasse diagram to determine patients, strains, cell lines,
  day of measurement, before/after new calibration, . . .
- Split before 1st step that involves multiple cases
  centering, PCA preprocessing, . . .
- Additional independent validation for data-driven optimization/tuning/model selection
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- Split before 1st step that involves multiple cases
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- Additional independent validation for data-driven optimization/tuning/model selection
  nested/double cross validation or train-validate-test ⇝ necessary patient numbers
  HUGE
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- Randomize order of measurements
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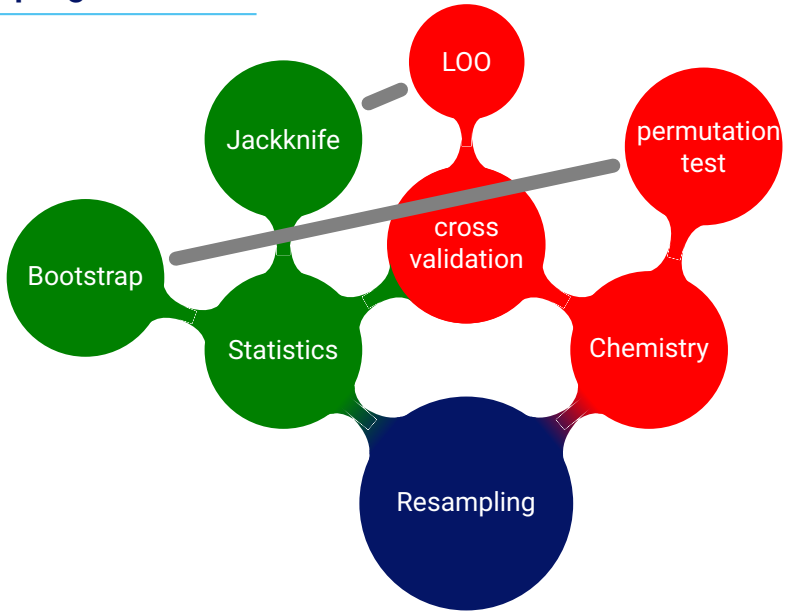
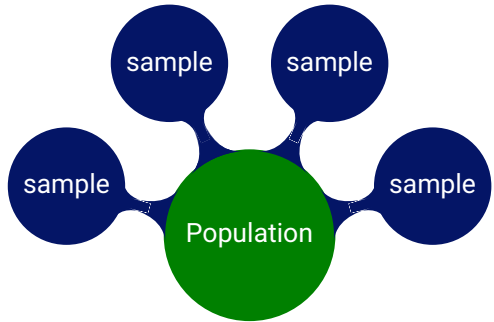
  HUGE
- Test cases: reference labels must be independent of cases (measurements, spectra, chromatograms, . . .)
  cluster analysis to assign labels → OK for training cases
- Ensure correctness of code

Resampling: Fields of Use



CHEMO METRIX

The Concept behind Resampling



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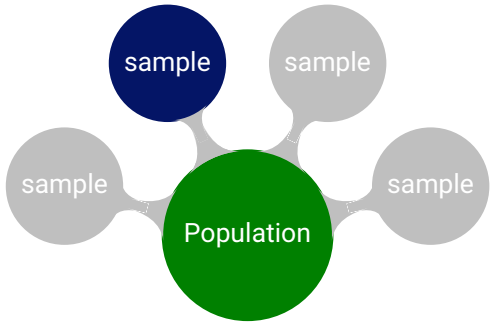

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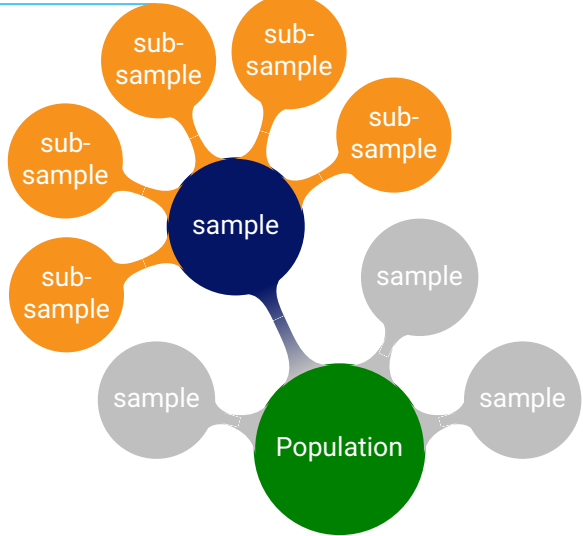


- Subsamples are approximations of (more) real samples
- Subsample is perturbed version of the real sample

CHEMO METRIX

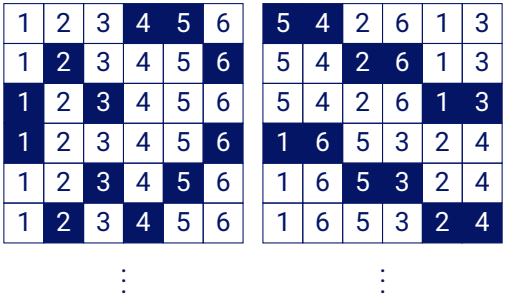
Cross Validation: Drawing without Replacement

1	2	3	4	5	6
1	2	3	4	5	6
1	2	3	4	5	6

5	4	2	6	1	3
5	4	2	6	1	3
5	4	2	6	1	3

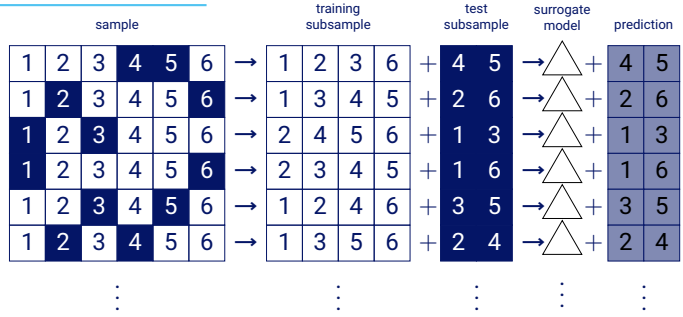
- ✔ Each sample is left out exactly once
- ✔ No copies

Cross Validation: Drawing without Replacement



- ✔ Each sample is left out exactly once per iteration
- ✔ No copies
- • Iterations possible also with *k*-fold or leave-*n*-out cross validation
- ✘ Leave-one-out cannot be iterated

Resampling for Model Validation: Assumptions



- Surrogate model equals model of real sample
- Surrogate models equal to each other
- All samples are equal (come from the same distribution)

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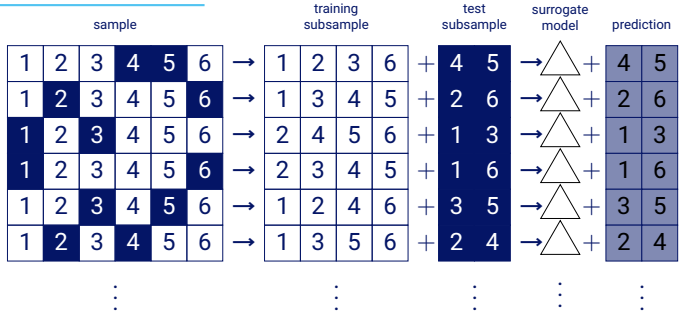
Resampling for Model Validation: Assumptions



- Surrogate model equals model of real sample
- ✘ Violation ⇝ pessimistic bias
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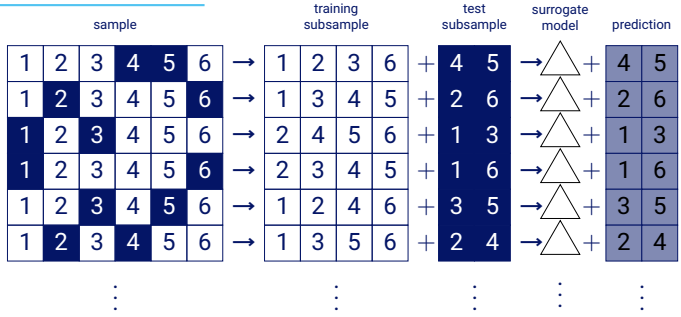
Resampling for Model Validation: Assumptions



- Surrogate model equals model of real sample
- ✘ Violation ⇝ pessimistic bias
- Surrogate models equal to each other
- ✘ Violation (instability) ⇝ higher variance
- All samples are equal (come from the same distribution)

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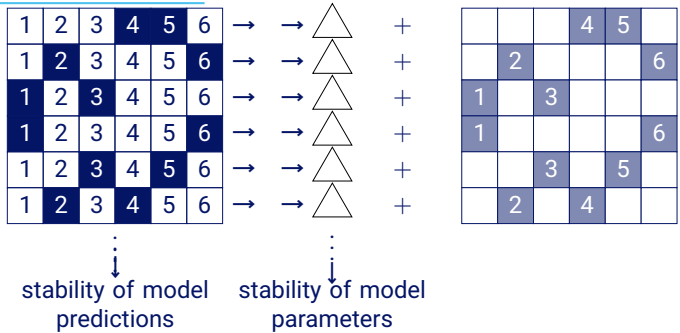
Model Stability

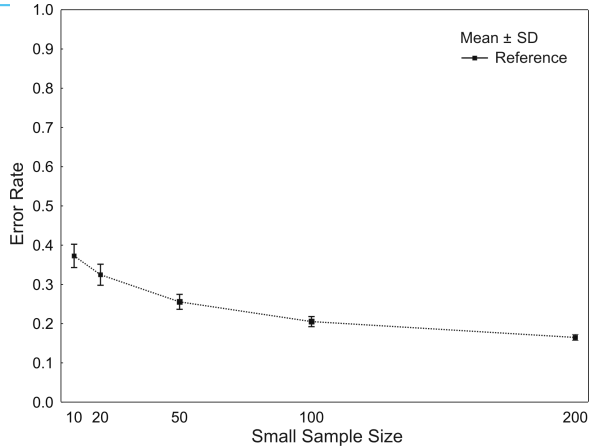


- Subsamples are perturbed versions of real sample
- ✔ Measure stability of model
  - Stability of model parameters
  - Stability of predictions

- Iterated cross validation reduces variance due to instability of surrogate models.

CHEMO METRIX

Bias and Variance of Classifier Performance



- PLS-DA with 2 latent variables
- simulated data: 200 variate normal distribution
- overlap of classes ca. 10 %

CHEMO METRIX

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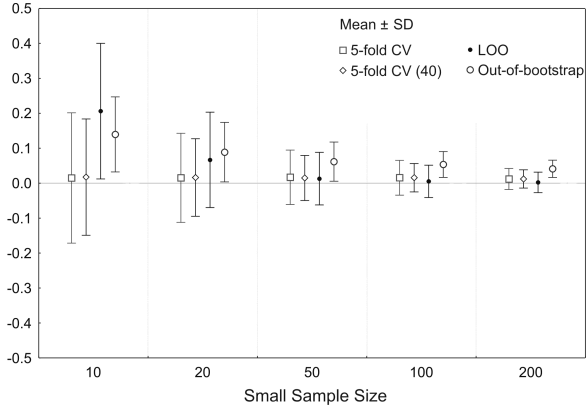

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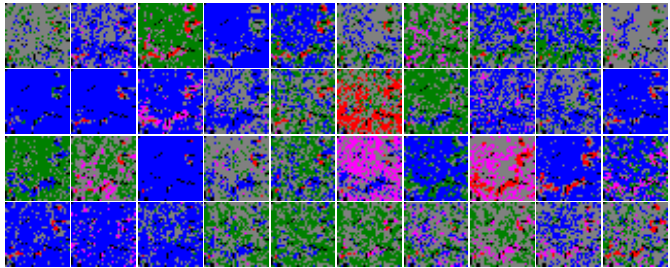
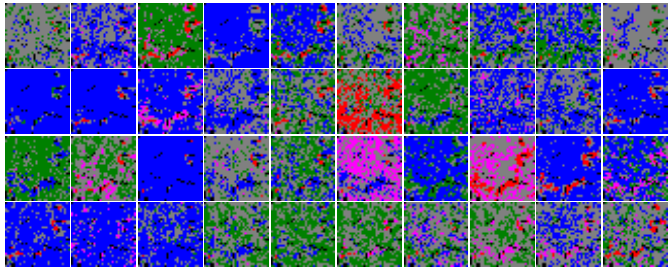
CHEMO METRIX

Model Stability: 40× 8-fold cross validation



- FTIR images of tumour sections (normal, °II, °III, °IV)
- total: 150 images of 58 patients: 133 000 spectra
  smallest class: °II, 4 800 spectra (3 patients, 5 images)
- LDA after automatic selection of 8 spectral regions
- reject spectra with posterior probability <0.85

Model Stability: 40× 8-fold cross validation



✘ Classification: unstable = bad

- Deviation is always in direction “wrong”

CHEMO METRIX

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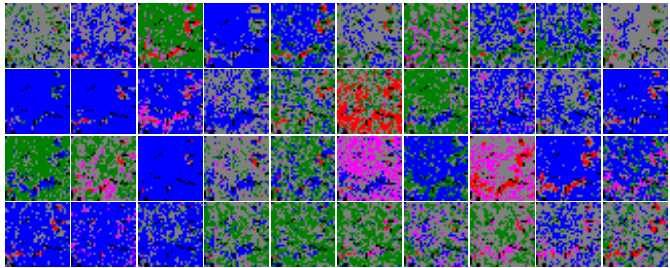
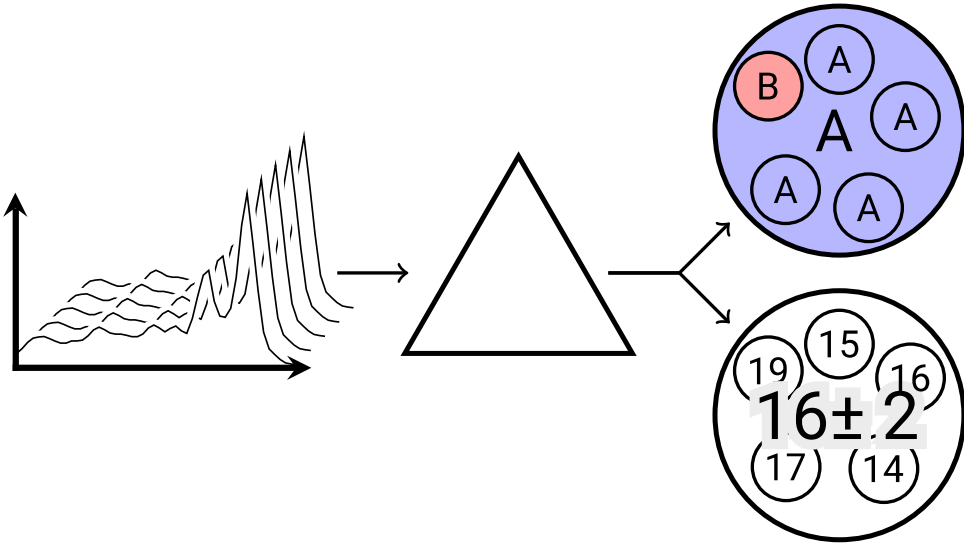


✘ Classification: unstable = bad

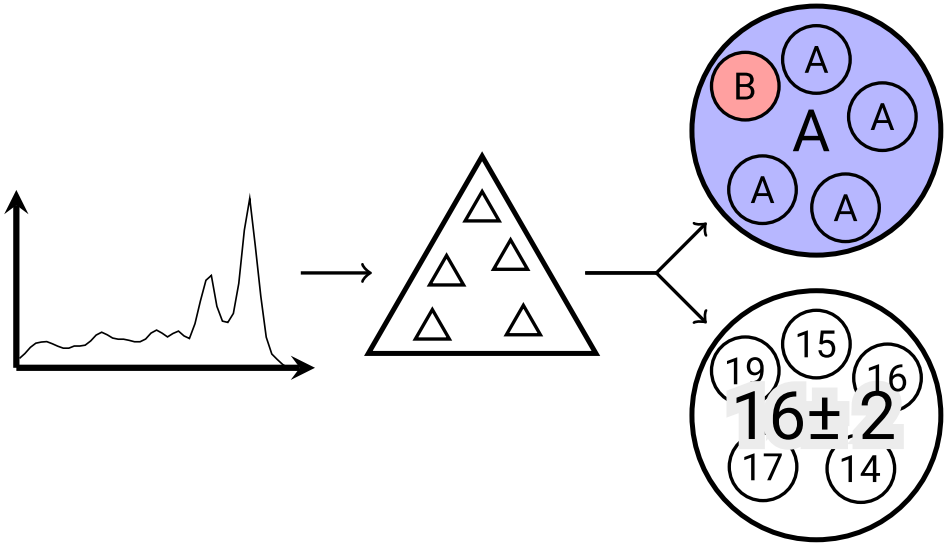
- Deviation is always in direction “wrong”
- Stabilization of the model ⇝ improved performance

CHEMO METRIX

Model Aggregation



Model Aggregation



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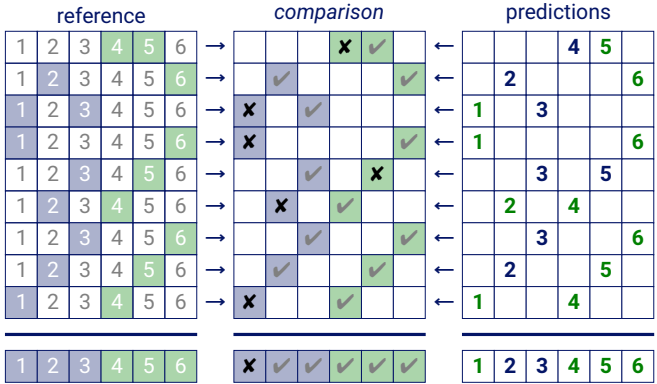
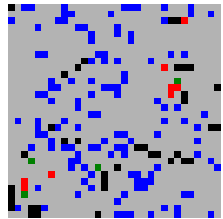
Model Aggregation: Testing

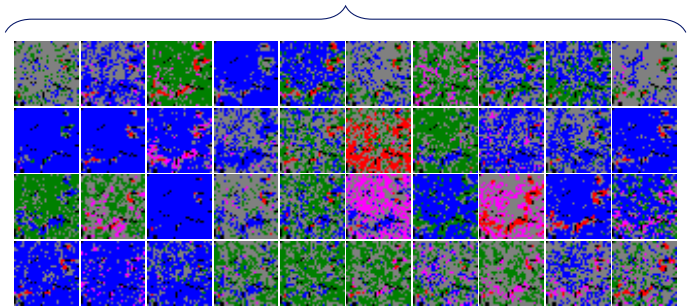


- 3× 3-fold cross validation: $\frac{6}{18} = 33\,\%$ errors
- aggregated model (majority vote): $\frac{1}{6} = 17\,\%$ errors

CHEMO METRIX

Again the Tumour Sample





CHEMO METRIX

How many cases do we need?

... **to train a good classifier?**

- rules of thumb
  linear classifier: $\frac{n}{p} \geq 3 - 5$ in each class

... **to measure the classifier's performance?**

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$\Rightarrow$ learning curve

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⇒ learning curve

. . . to measure the classifier's performance?

⇝ confidence intervals for test results

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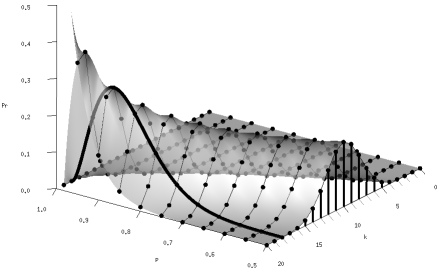
⇒ learning curve

... **to measure the classifier's performance?**

⇝ confidence intervals for test results

- rules of thumb
  100 test cases to estimate a proportion

Confidence Intervals for Proportions



- Statistical description: Bernoulli trial
- Uncertainty on proportion: $var(\hat{p}) = \frac{p(1-p)}{n_{test}}$

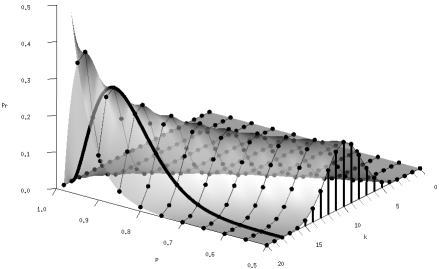
✘ normal approximation appropriate only with $np \geq 5$ and $n(1-p) \geq 5$

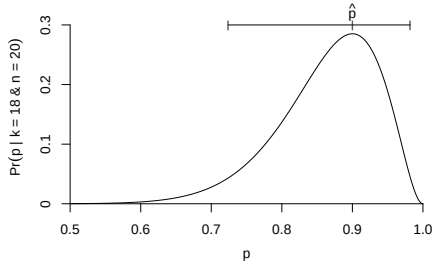
✔ ⇝ use binomial distribution

⇝ Estimate necessary n_{test}

CHEMO METRIX

Confidence Intervals for Proportions





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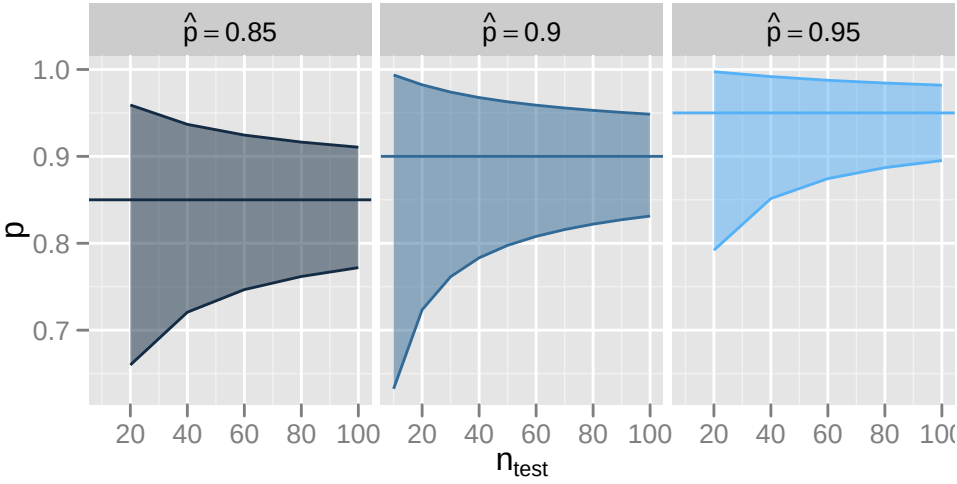
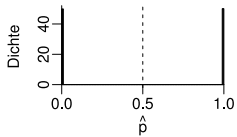
CHEMO METRIX

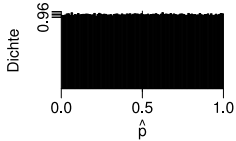
Sample size from Confidence Interval

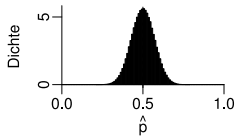


CHEMO METRIX

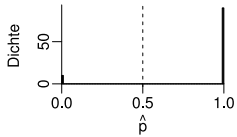
Variance Uncertainty: Brier's Score

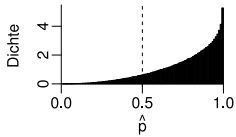


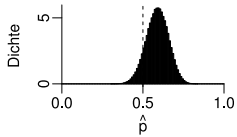




	$\bar{x} \pm s(x)$	$\frac{s^2(x)}{s^2(x^{hart})}$	$\bar{x} \pm s(x)$	$\frac{s^2(x)}{s^2(x^{hart})}$	$\bar{x} \pm s(x)$	$\frac{s^2(x)}{s^2(x^{hart})}$
$Sens^{(hart)}$	0,50 ± 0,050		0,50 ± 0,050		0,50 ± 0,050	
$Sens^{MSE}$	0,50 ± 0,050	1,00	0,67 ± 0,030	0,36	0,75 ± 0,007	0,02



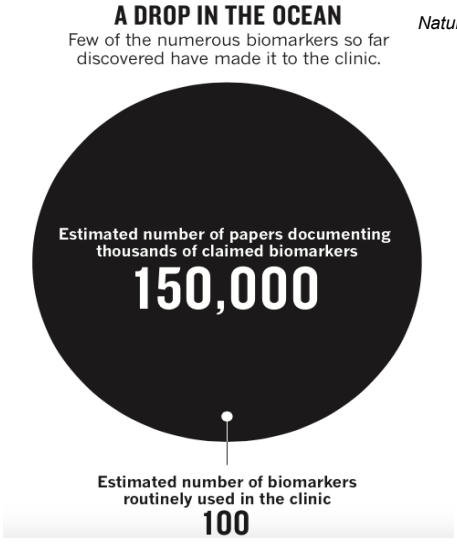




	$\bar{x} \pm s(x)$	$\frac{s^2(x)}{s^2(x^{hart})}$	$\bar{x} \pm s(x)$	$\frac{s^2(x)}{s^2(x^{hart})}$	$\bar{x} \pm s(x)$	$\frac{s^2(x)}{s^2(x^{hart})}$
$Sens^{(hart)}$	0,90 ± 0,030		0,90 ± 0,030		0,90 ± 0,030	
$Sens^{MSE}$	0,90 ± 0,030	1,00	0,92 ± 0,013	0,18	0,83 ± 0,006	0,04

CHEMO METRIX

Reproducibility!?



Nature **469**, 156-157

CHEMO METRIX

Validation: Questions

- Did you ask the right question?
- Or did you use a surrogate?
  - Is that surrogate appropriate?
  - What are the limits?
- Is your classifier set up correctly?
  - Is it really a classification problem?
  - one-class vs. discriminative?
  - open-world vs. closed-world?
- Do you use the correct controls/base class?
- What happens with out-of-spec cases (unknown class? bad measurements?)

Validation: Questions

- Bias introduced by data acquisition procedure?
  - Labeling procedure with self-fulfilling prophecies (e.g. cluster analysis as basis for labeling, semi-supervised label generation)?
- What about borderline cases?
  - Do your *labeled* cases correctly represent them?
  - No exclusion of “difficult” cases in the reference labeling step?
- What other confounders could exist?
- What are the limits of your method?
- reading:
  - **Buchen2011**
  - **Begley2012**
  - **Ioannidis2005**
  - …

Ruggedness: Perturb Data

- How robust are the predictions?
- Which factors (confounders) have most influence?
- Perturb Data
  - Repeated cross validation:
    How do predictions vary if *a few* training cases are exchanged?
    ⇝ stability of predictions
  - Simulate instrument related distortions:
    Measure respective drop in performance

Beleites2008
Sattlecker2010

CHEMO METRIX

Drift

- production use a model is almost always extrapolation in time!
  Training cases were collected *before* the prediction cases

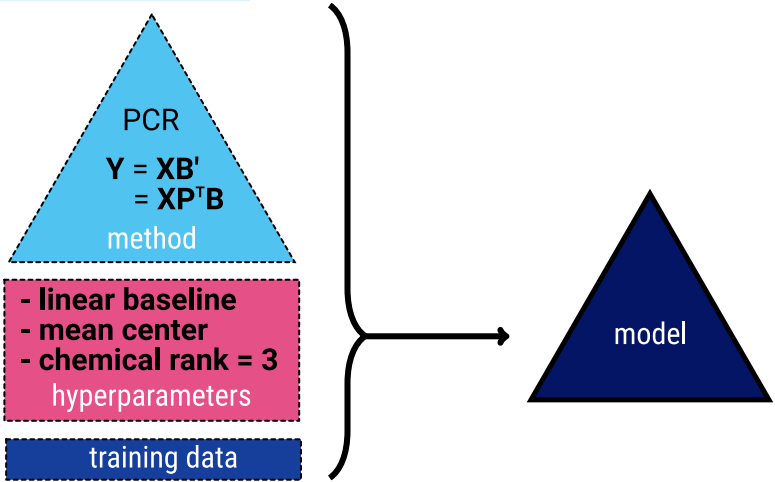
✘ Instrument drift

- Question: low long into the future does the model work well?
  ⇝ “recalibrate daily”

✔ dedicated experiments to check long-term stability

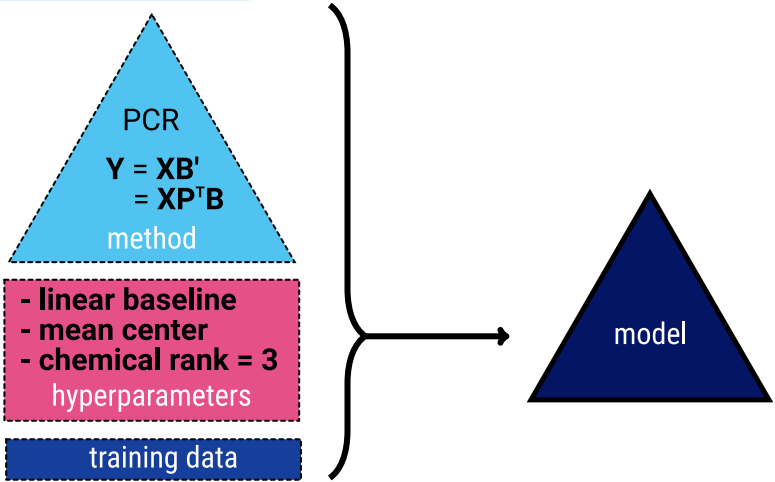
✘ Influence of drift/aging *cannot* be estimated by resampling
  glimpse at drift: look at splits where model is trained on old cases, tested on new cases

Hyperparameters



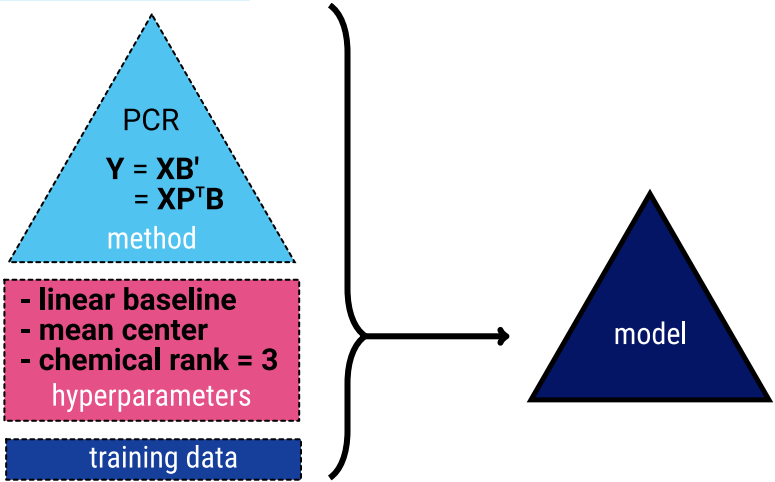
CHEMO METRIX

Hyperparameters



- available: PCR (**$X_{train,preprocessed}$**, `m, center = TRUE`)

Hyperparameters



- available: PCR ($\mathbf{X}_{\mathtt{train,preprocessed}}$, m, center = TRUE)
- wanted: tuned.PCR ($\mathbf{X}_{\mathtt{train}}$)

CHEMO METRIX

Data-driven Model Optimization

training data

Idea:

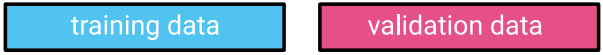
1. sensible range of hyperparameters
2. build covering this search space
3. validate them ⇝ figure of merit (performance)
4. take the best

⇒ **Optimize predictive performance**

✔ Large variety of numerical optimizers available

exhaustive grid search, genetic optimizers, simulated annealing, …

Data-driven Model Optimization



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CHEMO METRIX

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⇒ **Optimize predictive performance**

✔ Large variety of numerical optimizers available
exhaustive grid search, genetic optimizers, simulated annealing, …

✘ Careful: valdiation data enters model building process
⇒ need another independent set to validate the *final* model

Data-driven Model Optimization

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2. build covering this search space
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4. take the best

⇒ **Optimize predictive performance**

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CHEMO METRIX

Data-driven Model Optimization

- fit normal parameters (coefficients) with *training* set
- fit hyperparameters with validation set
- validate chosen model with test set

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✔ resampling version: nested/double cross validation

Data-driven Model Optimization

- fit normal parameters (coefficients) with *training* set
- fit hyperparameters with ~~validation set~~ optimization set
- validate chosen model with ~~test set~~ final verification set

✔ resampling version: nested/double cross validation

✔ `train (X, hyperparameters)` vs. `tuned.train (X)`
  - tuned training function: additional internal split for tuning

CHEMO METRIX

Data-driven Model Optimization

- fit normal parameters (coefficients) with *training* set
- fit hyperparameters with ~~validation set~~ optimization set
- validate chosen model with ~~test set~~ final verification set

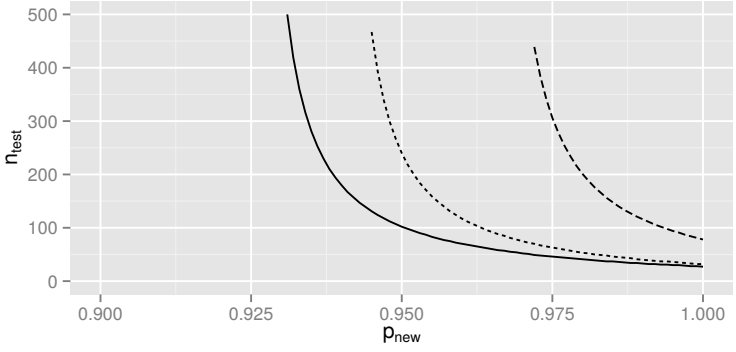
✔ resampling version: nested/double cross validation

✔ `train (X, hyperparameters)` vs. `tuned.train (X)`
  - tuned training function: additional internal split for tuning
  - ✔ treat `tuned.train (X)` like any other training function

CHEMO METRIX

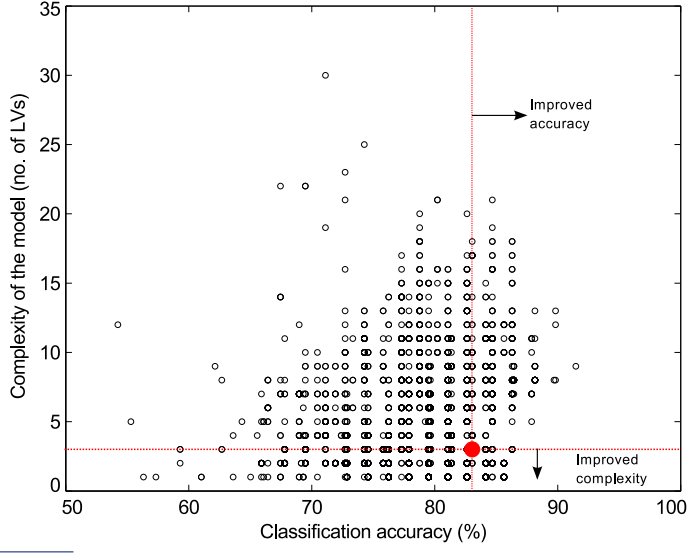
Sample Number Planning: Model Comparison as Statistical Test

		accepted risk		
Type I error	α =	5 %	10 %	5 % wrongly reject non-superiority hypothesis
Type II error	β =	20 %	10 %	5 % wrongly accept non-superiority hypothesis



Assume: old model $p = \frac{19}{25} \approx 75\,\%$

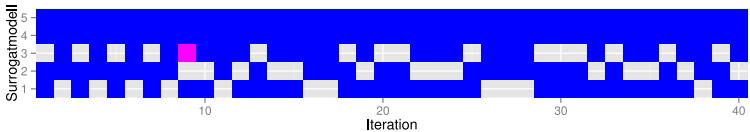
Autotuning: Preprocessing, method selection



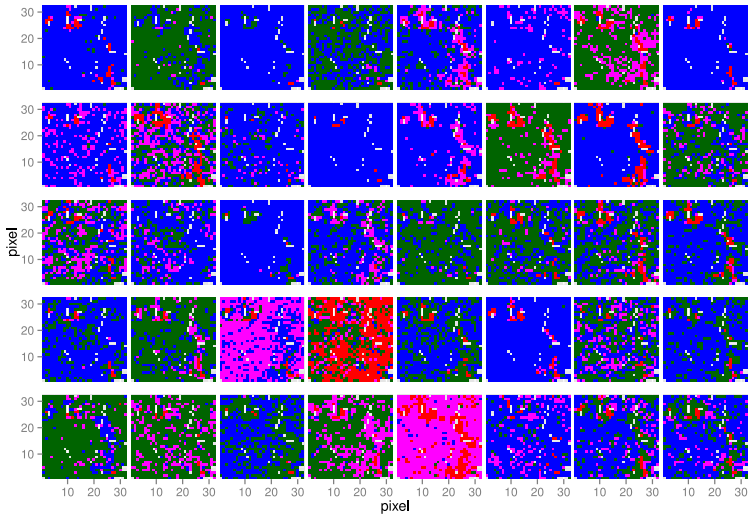
J. Engel et al., Trends in Analytical chemistry 50 (2013) 96 – 106.

CHEMO METRIX

Internal vs. External Performance Estimate

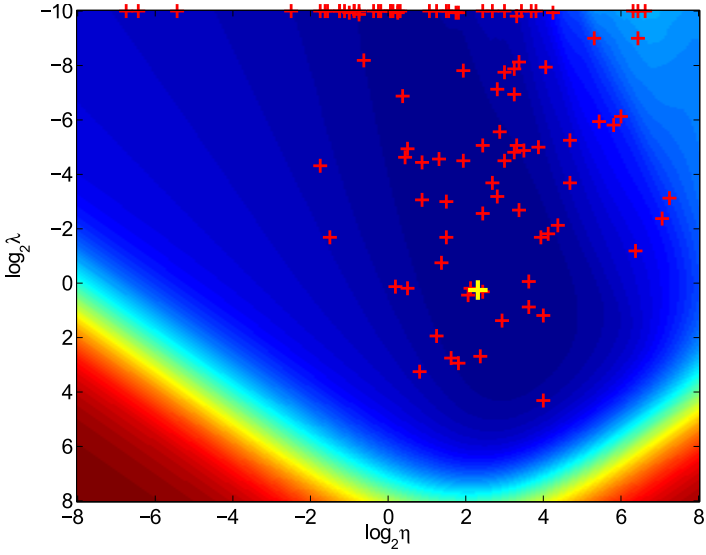


Internal vs. External Performance Estimate



CHEMO METRIX

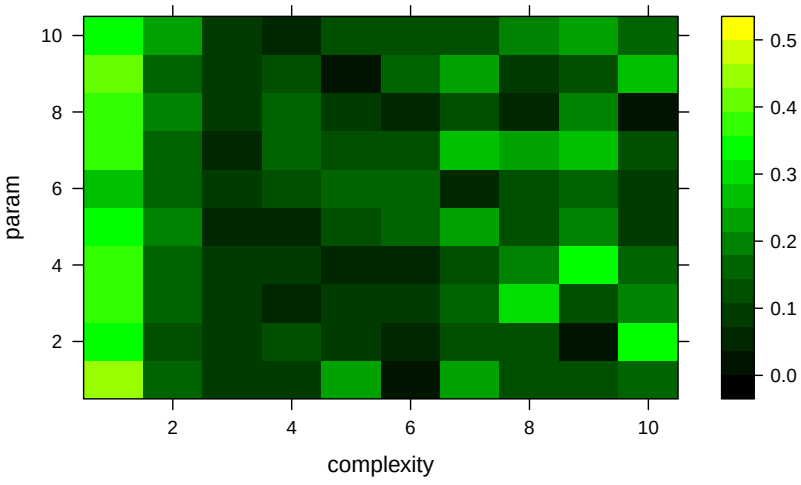
Grid Search



Cawley2010

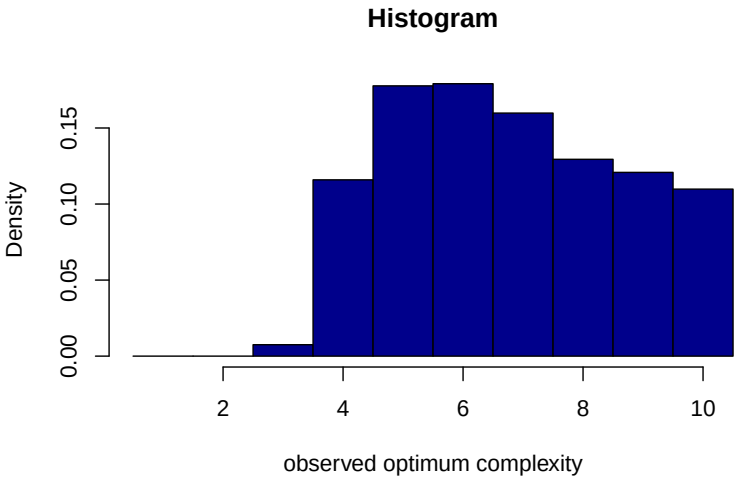
CHEMO METRIX

Grid search



CHEMO METRIX

Grid search: Stability of Solution



CHEMO METRIX

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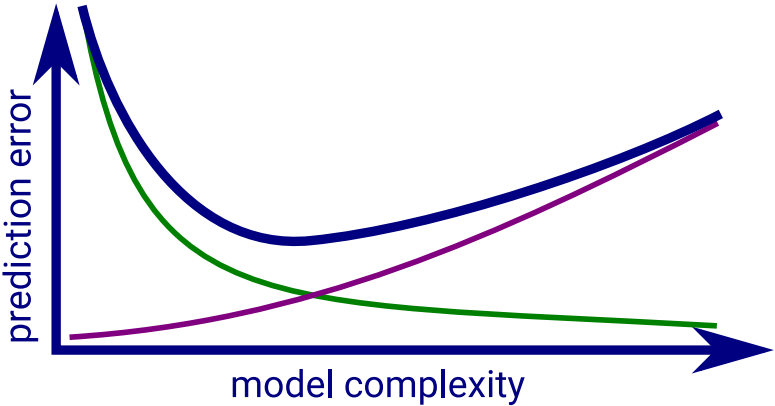

CHEMO METRIX

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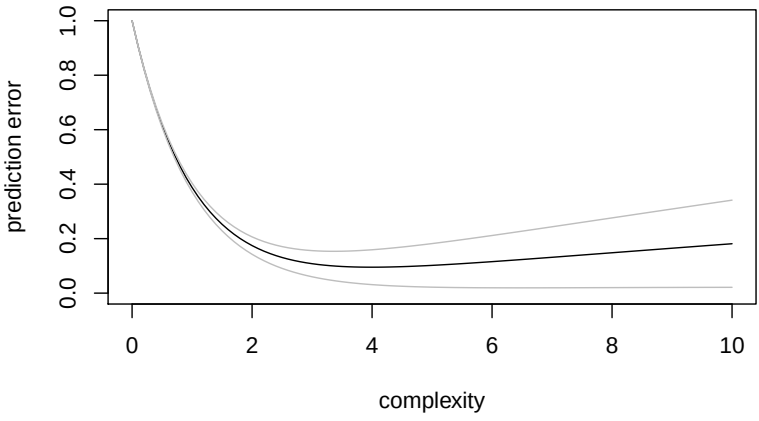

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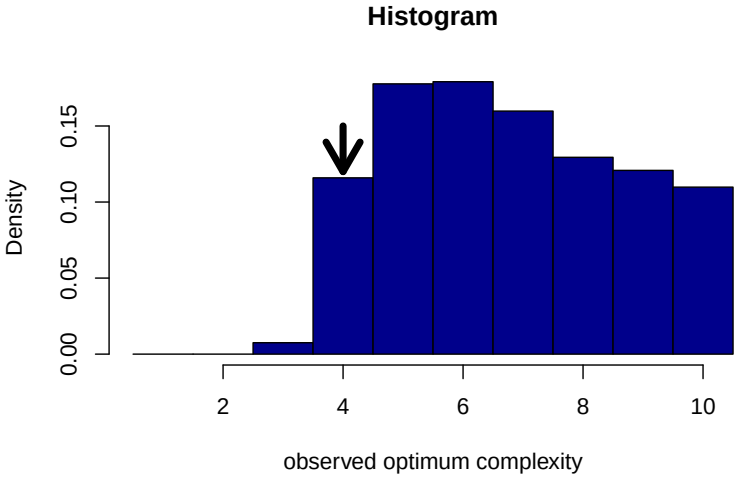

CHEMO METRIX

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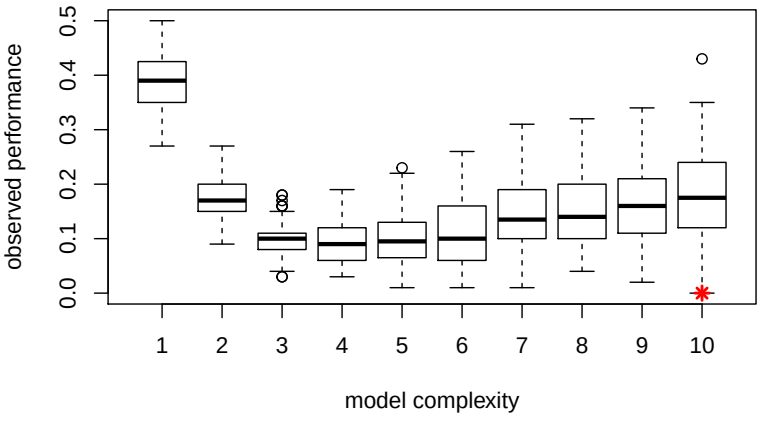
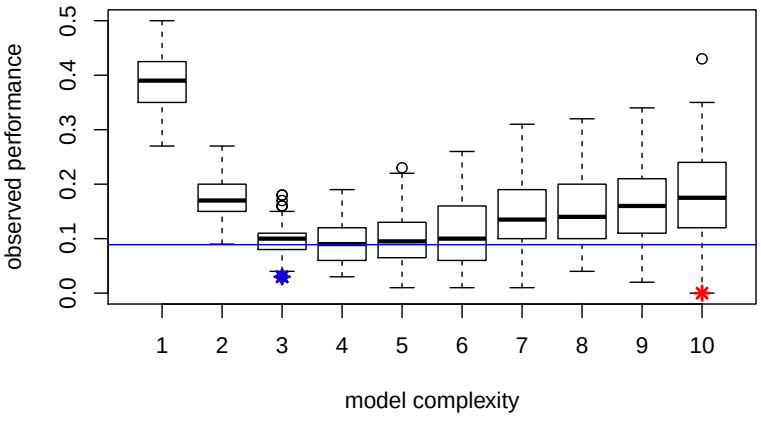


Grid search: Stability of Solution



CHEMO METRIX

Summary: Validation

- ✔ Think hard about your data, model, and application!
- ✔ Randomize (and block) your measurements
- ✔ Sample size planning: calculate from required precision of validation results
- At some point, validation studies are needed.
  Before that, use repeated cross validation or out-of-bootstrap.
- ✔ Use DoE (Hasse diagram) to determine independent splitting
- ✔ Check stability of predictions and – if possible – model parameters
- ✔ Aggregation improves *unstable* models
- ✘ Resampling cannot detect drift
- ✘ Hold-out is inefficient and prone to the same errors as resampling!

CHEMO METRIX

Summary: Data-driven model Optimization

- ✔ Needs internal performance estimate plus outer independent validation
- ✘ ⇝ large sample size required
- ✔ wrap optimization in `autotuned.model` function
- ✔ validate output of `autotuned.model` like any other model training function
- ✔ Check stability of optimization
- ✔ Use 1-sd-rule to guard against overfitting
- ✔ Class membership probability predicted: MSE (Brier's Score) has low variance and is proper scoring rule
  ⇝ suitable for optimization