Expression of Uncertainty in Qualitative Analysis

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Introduction

- What is “Qualitative Analysis”?
- Characterising uncertainty and method performance
- Qualitative response dependent on a concentration
- What can we expect from labs?

What is qualitative analysis?

- "Classification according to specific criteria"
  - "Above" or "Below" a limit
  - "Within Spec."
  - "Red"
  - Classification into ranges (<2; 2-5; 5-10; >10)
  - Molecular species by NMR, IR, MS…..
  - Material or ingredient ("Rubber", "Fat"…)
  - Origin or authenticity

Expression of uncertainty in qualitative analysis

- False response rates
  - What is a false response rate?
  - How is it determined?
- Alternative expressions of method performance or uncertainty
- Logistic regression for modelling performance

NOTE
Current literature refers to "nominal properties"

False response rates and derived indicators

		Actual (True) value: Negative	Actual (True) value: Positive
Observed	Negative	TN	FN
Observed	Positive	FP	TP

Alternative performance indicators (Single laboratory)

Reliability Measure	Formula
False positive rate	FP / (TN + FP)
False negative rate	FN / (TP + FN)
Sensitivity	TP / (TP + FN)
Specificity	TN / (TN + FP)
Positive predictive value	TP / (TP + FP)
Efficiency	(TP + TN) / (TP + TN + FP + FN)
Youden Index	Sensitivity + Specificity - 100
Likelihood ratio	(1-False neg. rate)/(False pos. rate)
Bayes posterior probability	Bayes rule (requires 'prior') - valuable for cumulative data

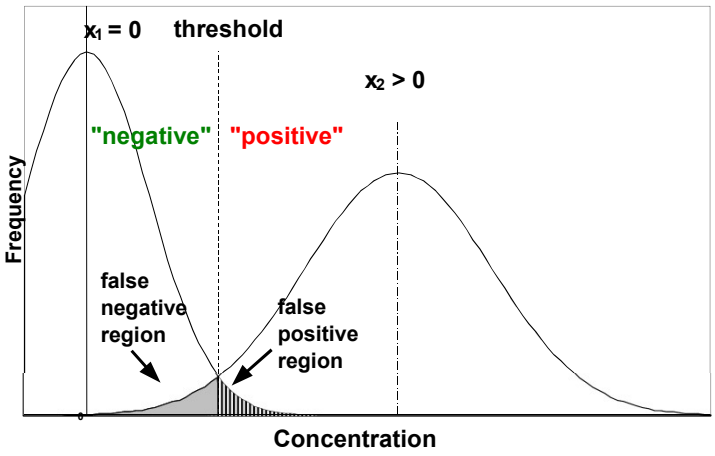
Proportion of positives that are correct

Uncertainty about the result

False response rates - how much data?

- Observed: 7/126 (5.6%)
- 95% confidence interval (binomial)
  - 1.6% to 9.5%
- 95% CI proportional to $1/\sqrt{n_{obs}}$
  - needs a LOT of false responses for precise figures
  - but false responses are rare for good methods….
- Most useful direct studies are 'worst case' or near 50% false response levels

False responses: Estimation from thresholds



False responses: From probabilities

- Spectroscopic identification study
  - S.L.R. Ellison, S.L. Gregory, *Anal. Chim. Acta.*, 1998 **370** 181.
- Calculated chance FT-IR match probabilities
  - probabilities based on “match-binning” - hits within set distance
  - required hypergeometric distribution (*n* matches of *m* taken from population)
- Compared with actual hits on IR database

False responses: From probabilities

- Theoretical predictions very sensitive to probability assumptions
  - 10% changes in *p* make large differences in predictions
- Best performance within factor of 3-10
  - (Improved over binomial probabilities by $>10^6$)
- Probability information must be excellent for good predictions

False response rates from databases

- Most spectral databases contain 1 of each material
  - most populations do not!
- Population data must account for sub-populations
  - cf. DNA profiles for racially inhomogeneous populations

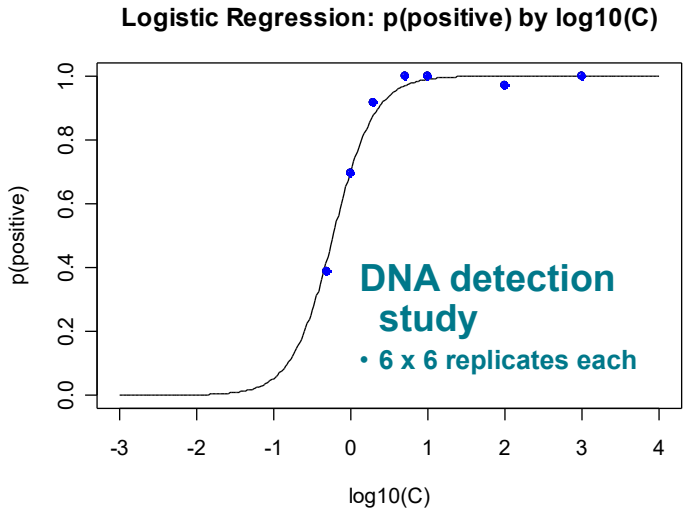
Using Logistic Regression

- Logistic regression models *probability* as a function of a continuous variable

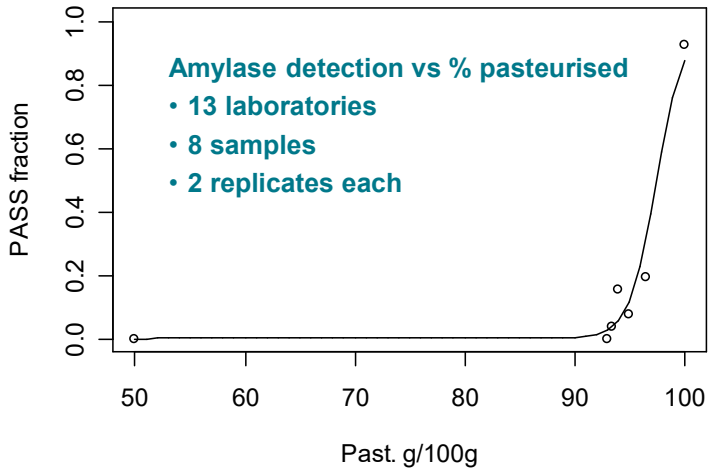
$$E(Y \mid x) = \frac{e^{\beta_0 + \beta_1 x}}{1 + e^{\beta_0 + \beta_1 x}}$$

- Example:
  - p(DNA found) vs DNA concentration

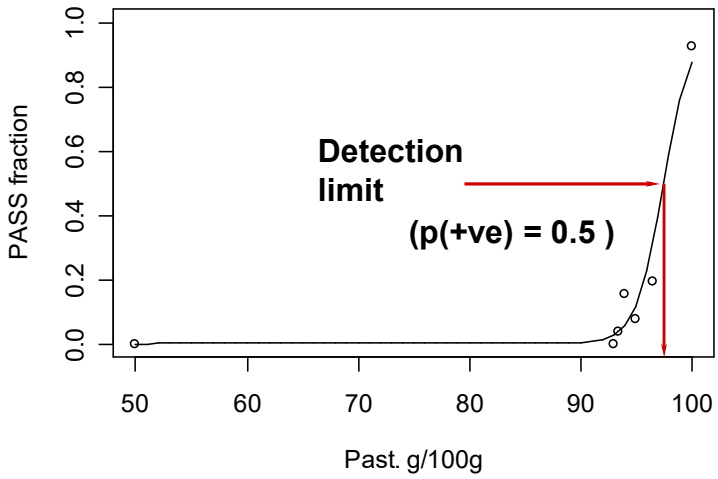
Logistic regression and performance assessment



Logistic regression and method performance



Logistic regression and method performance



Problems for qualitative "uncertainty"

- Hard to estimate low false response rates
  - May take hundreds of experiments
- Harder to estimate population probabilities
- Harder still to evaluate joint probabilities
  - … and these have large effects on calculation
- Prior probabilities are very rarely available

Recommendations*

- It is realistic to expect that testing laboratories have qualitative test method parameters (conditions of testing) under adequate control. Evidence will typically involve
  - evidence of traceability for the values of important control parameters prescribed by the method
  - evidence that uncertainties in these parameters are sufficiently small for the purpose
- It is important for laboratories to check at least the most critical false response rate for a qualitative test.
- It is reasonable to expect laboratories to be following published codes of best practice in qualitative testing where they are available.
- Quantitative (i.e. numerical) reports of uncertainties in qualitative test results should not generally be expected.

***Eurachem position paper:**
Accreditation and Quality Assurance 5, 346–348(2000)