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EQALM CENTRAL DATBASE: HALMA

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HALMA project

- Collaboration between the International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR) and EQALM
    - HALMA: **Harmonization of Measurands in Laboratory Medicine through Data Aggregation**
    - Aims at assessing harmonization between measurement procedures using EQA data
        - Commutability of samples
        - Selection of measurands
        - Selection of EQA providers
        - Uniform description of measurement procedures

https://www.eqalm.org/cooperations/halma

Data collection

Spring 2023: Selected EQA providers were asked to provide data

- Last EQA round
- No educative samples
- Albumin, Calcium, Creatinine

26099 results
59 different samples
11 EQA providers

CAP(USA)
Croqalm (Croatia)
Equalis (Sweden)
KEQAS (South-Korea)
Labquality (Finland)
NCCL (China)
Öquasta (Austria)
RCPAQAP (Australia)
SEQC (Spain)
SKML (The Netherlands)
WEQAS (United Kingdom)

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Assessing harmonization: including variability or not ?

- From a **metrological** point of view:

  Harmonized methods : no bias in between them

  If two methods follow the same traceability chain, there should be no bias

Only bias

- From an **outcome-oriented** point of view:

  Harmonized methods: measurements are alike

  Difference between two measurement results should be small
  Difference caused by bias and variability

Bias + variability

Quantification of metrological view

Maximum mean difference between methods:

- Method 1: maximum allowed positive bias
- Method 2: maximum allowed negative bias

- Maximum allowed difference:
- Harmonized if bias between methods is smaller than

Quantification of outcome-oriented view

Maximum difference between methods:

- Method 1: maximum allowed positive bias, maximum allowed variability
- Method 2: maximum allowed negative bias, maximum allowed variability

- Maximum allowed difference (Total deviation):
- $D_m = 2 \times maximum\ bias \pm 1.96 \times \sqrt{2} \times maximum\ variability$

- Observed maximum difference:
- $D_o = observed\ bias \pm 1.96 \times \sqrt{SD_1^2 + SD_2^2}$

  SD_1, SD_2 : standard deviation of respectively method 1 and method 2

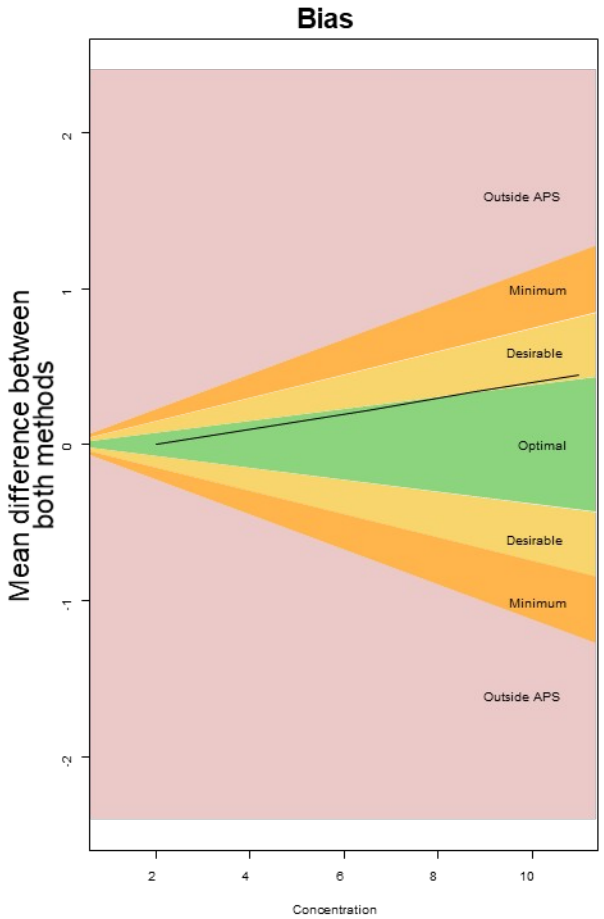
- Harmonized if $D_o < D_m$

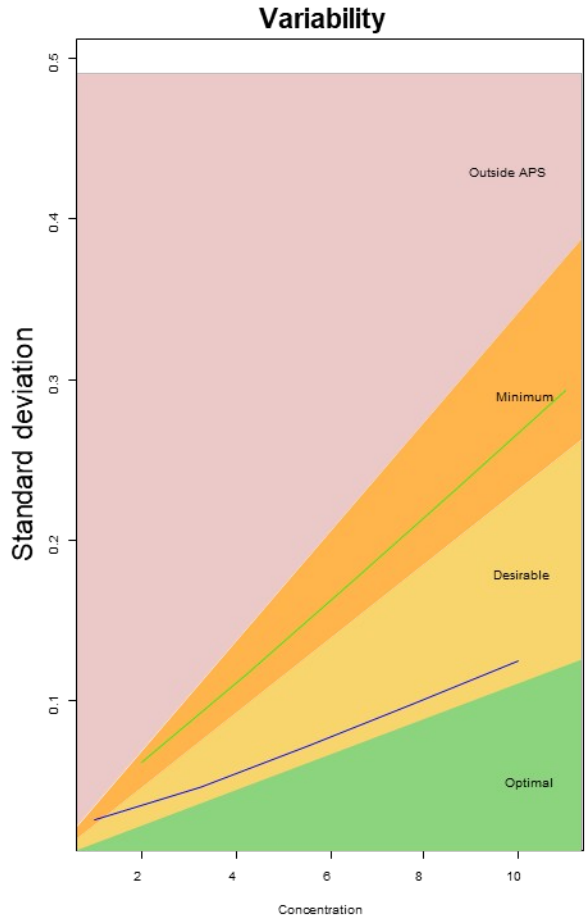
Matching with analytical performance specifications

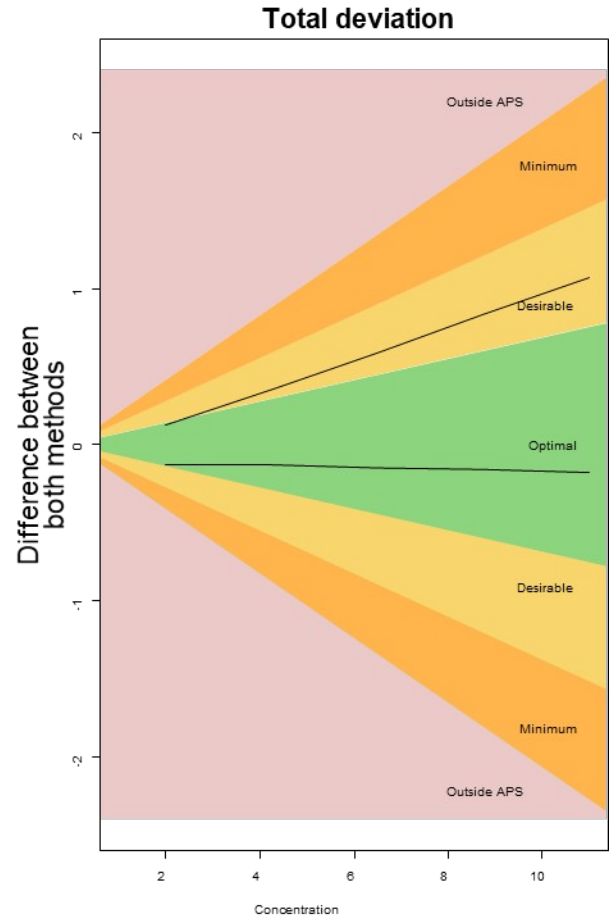
		Albumin	Calcium	Creatinine
Optimal	Variability	0.6%	0.5%	1.1%
Desirable		1.3%	0.9%	2.3%
Minimum		1.9%	1.4%	3.4%
Optimal	Bias	0.7%	0.4%	1.9%
Desirable		1.4%	0.8%	3.7%
Minimum		2.1%	1.2%	5.6%

Matching with analytical performance specifications

Combining results for various samples by regression lines



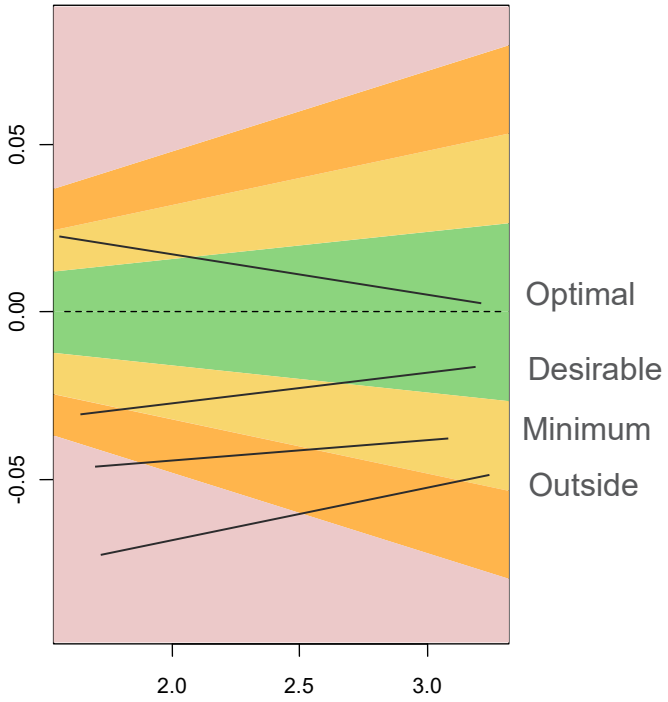




$$B = c + d * concentration \quad SD = \sqrt{a + b.concentration^2} \quad TD = B \pm 1.96\sqrt{SD_1^2 + SD_2^2}$$

Assessment of bias

- Outside if more than 20% of range is outside limits, else
- Minimum if more than 40% of range is outside or minimum limits, else
- Desirable if more than 50% of range is in desirable, minimum or outside region
- Else optimal



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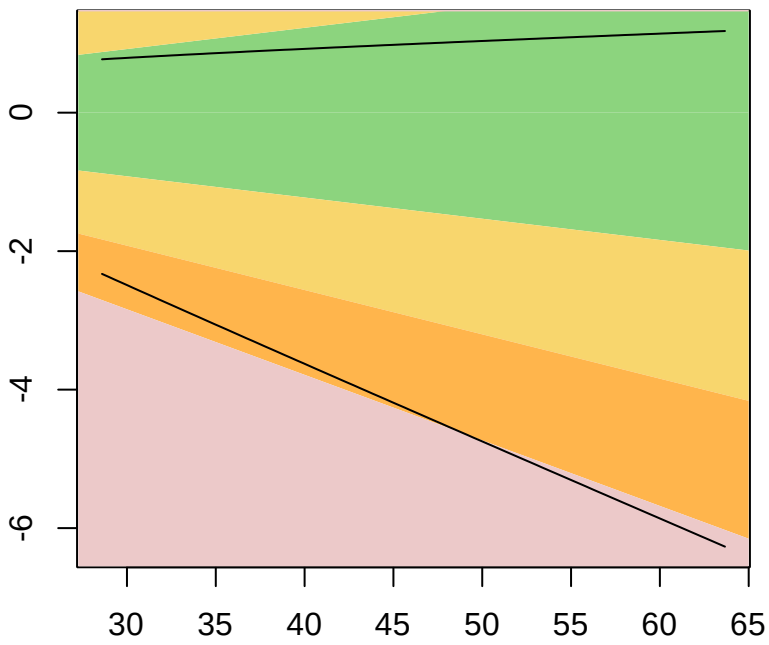
Total deviation between methods



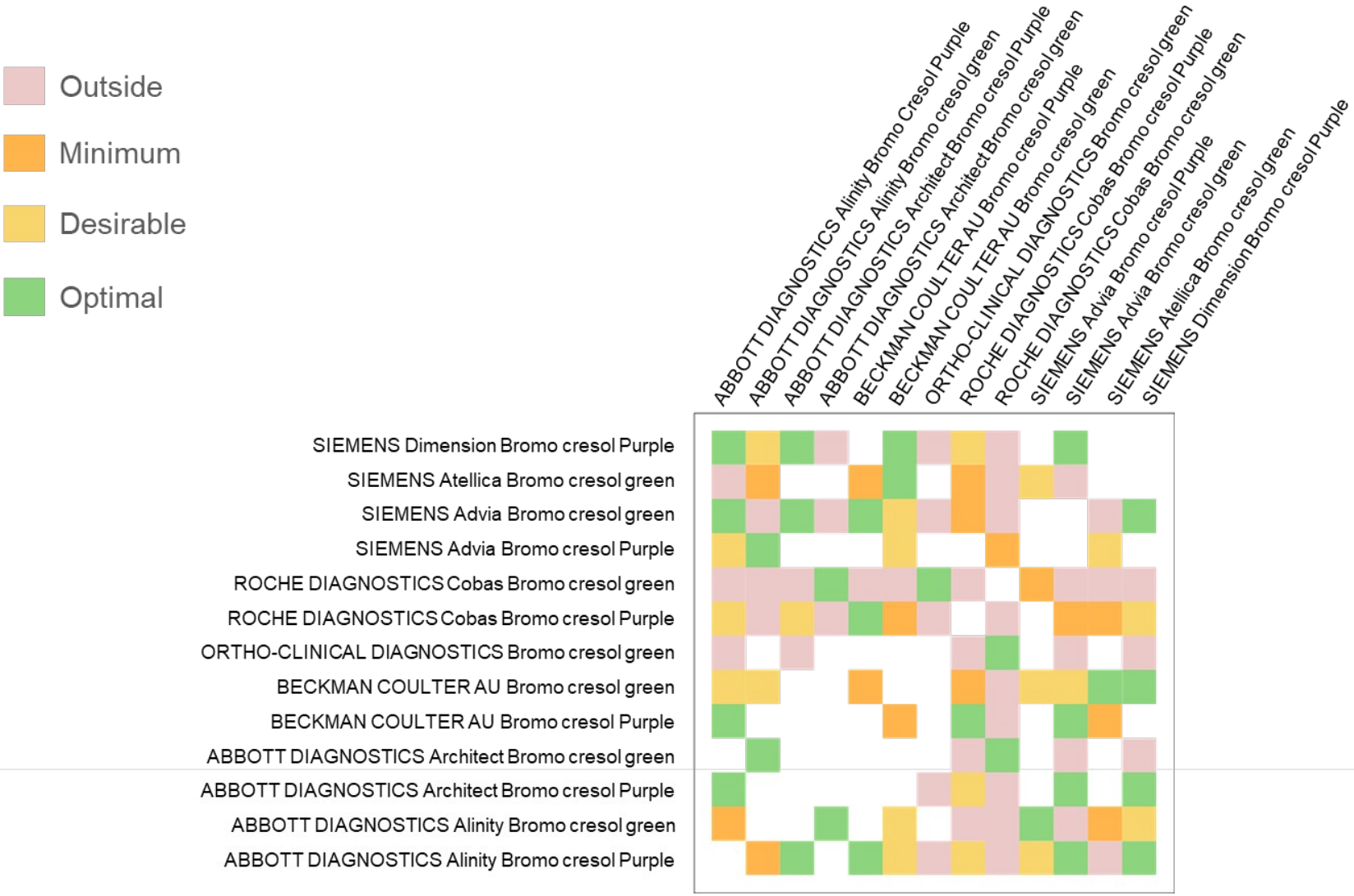
Bias + 1.96*combined SD

Bias - 1.96*combined SD

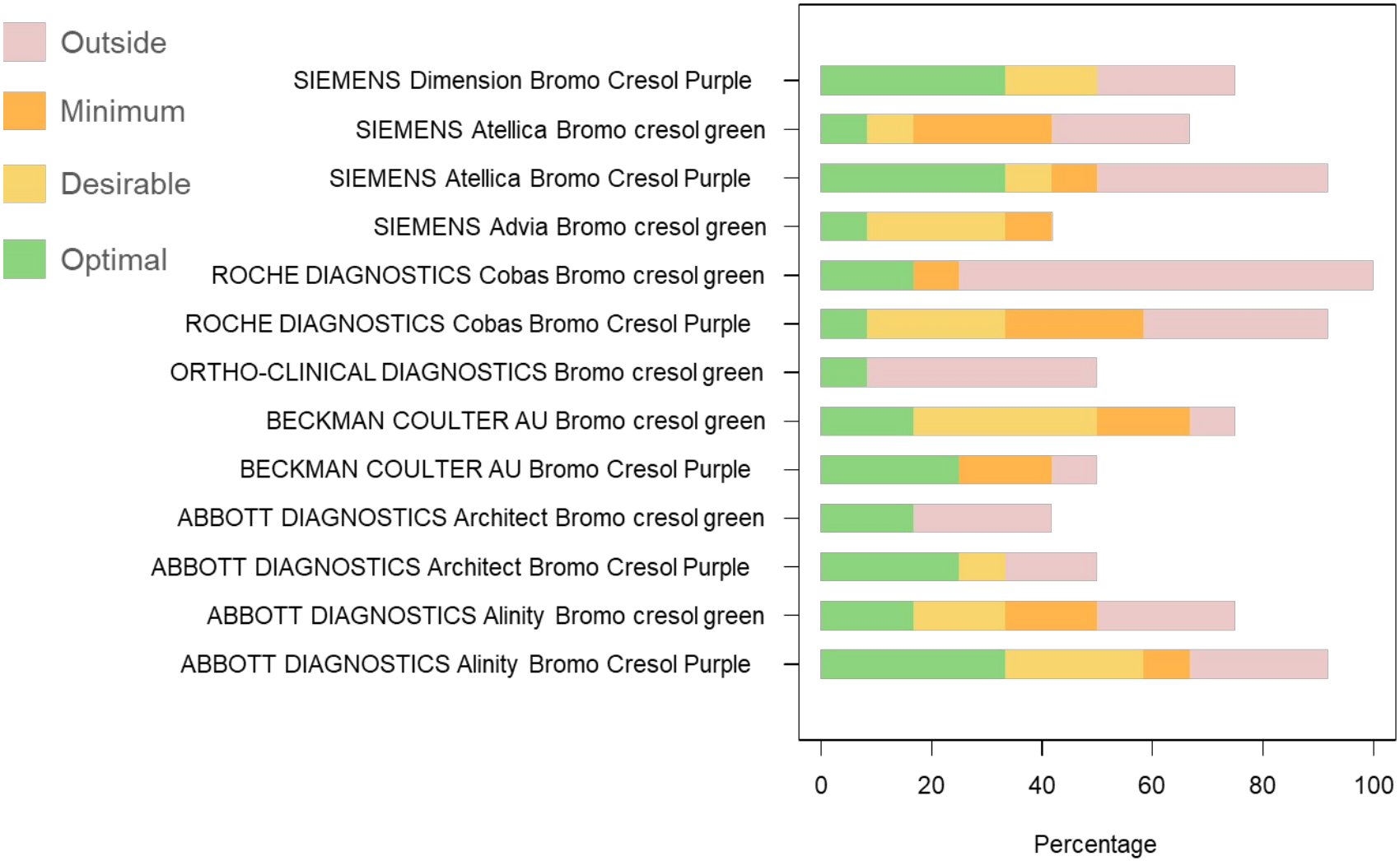
- Outside if more than 20% of range is outside limits, else
- Minimum if more than 40% of range is outside or minimum limits, else
- Desirable if more than 50% of range is in desirable, minimum or outside region
- Else optimal

RESULTS

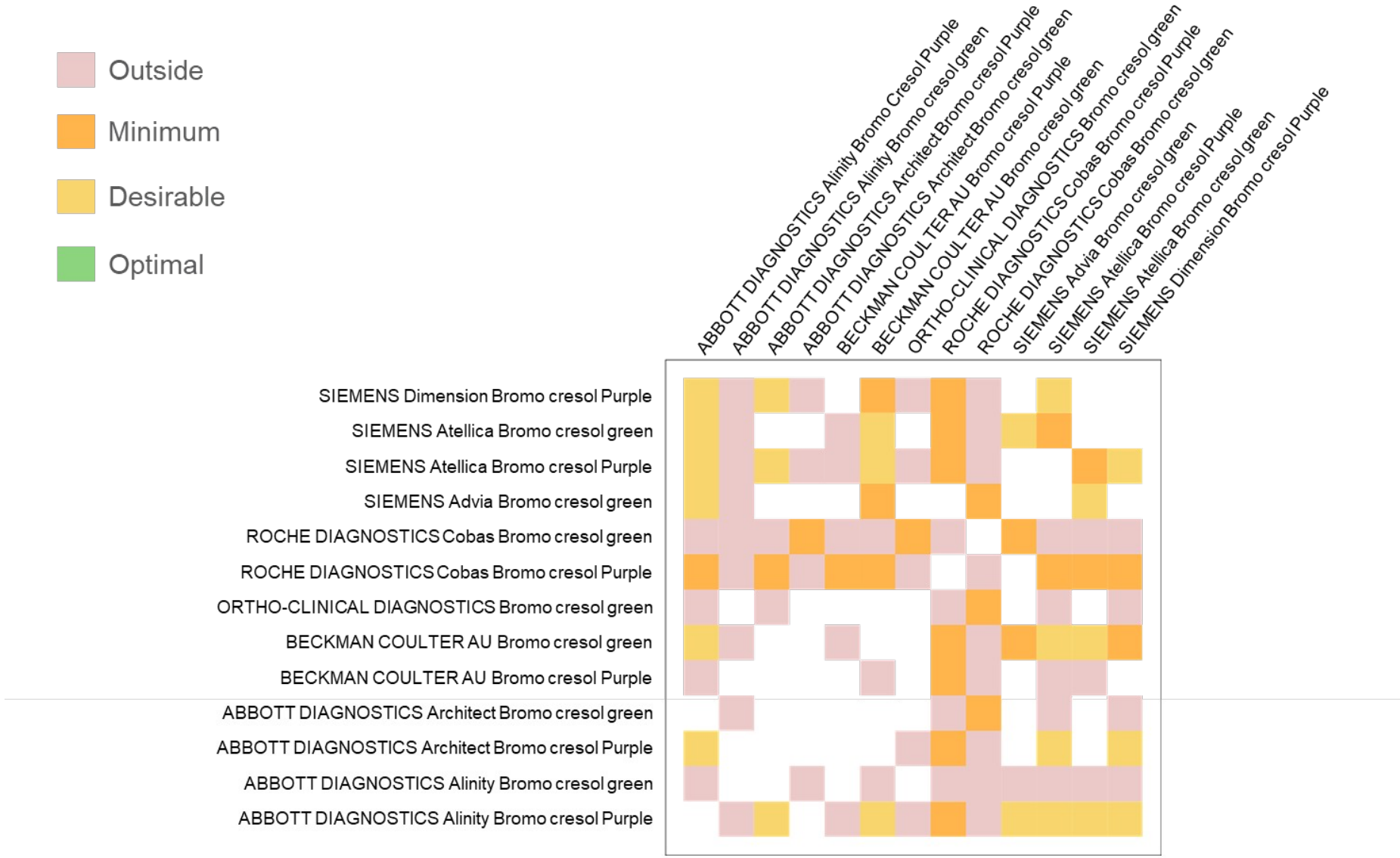
Bias between methods: albumin



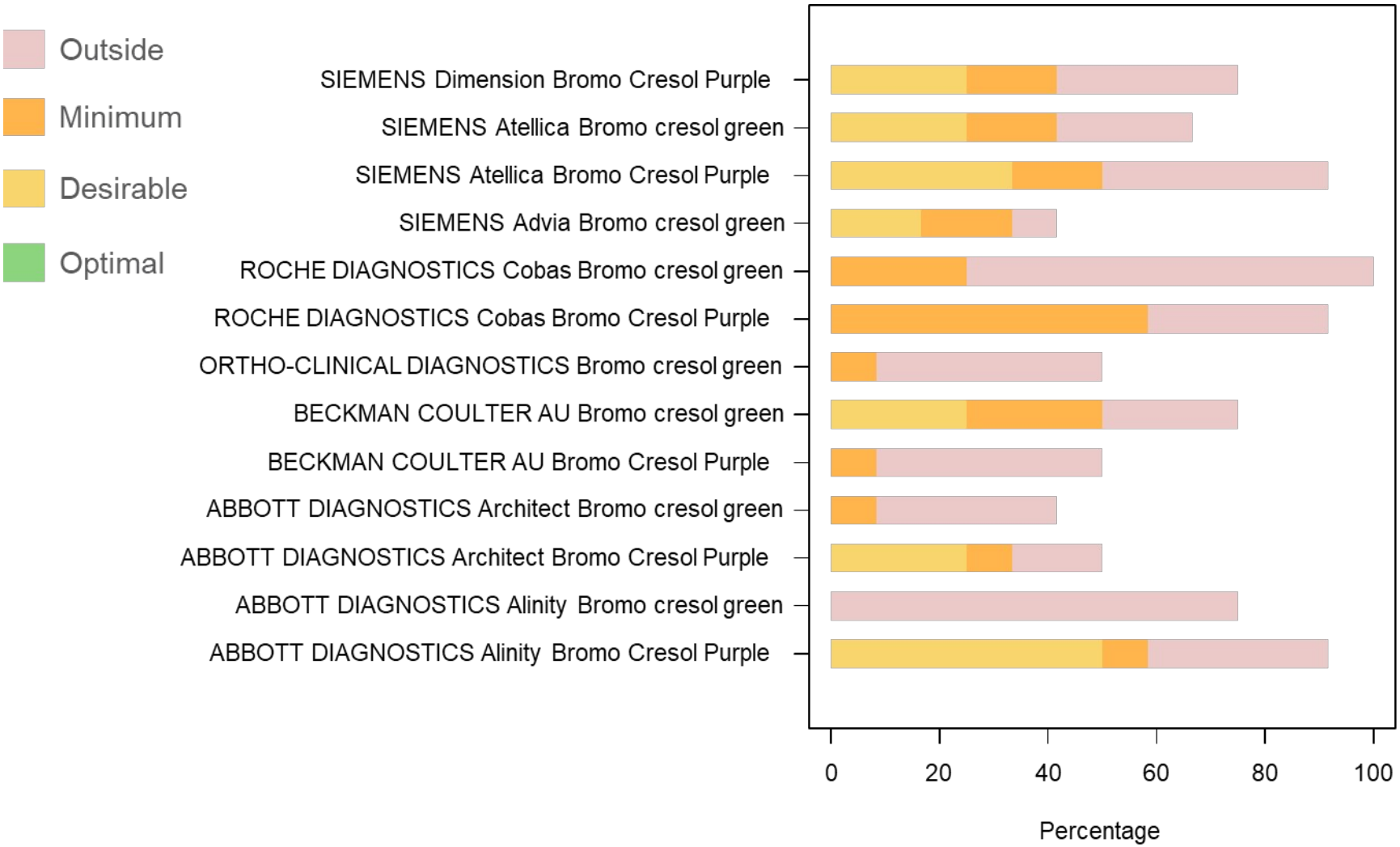
Bias between methods: Albumin- summary



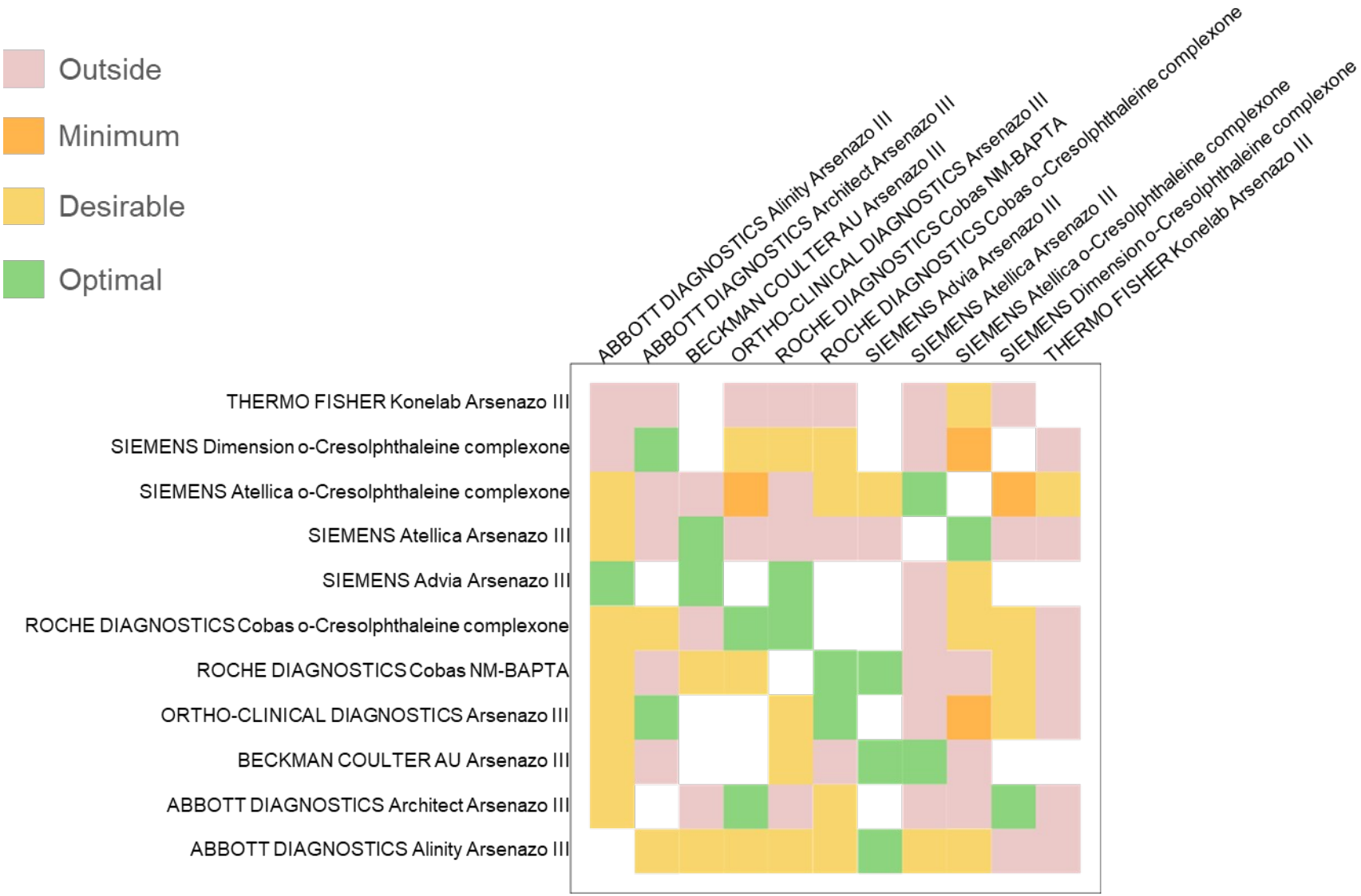
Total deviation between methods: Albumin



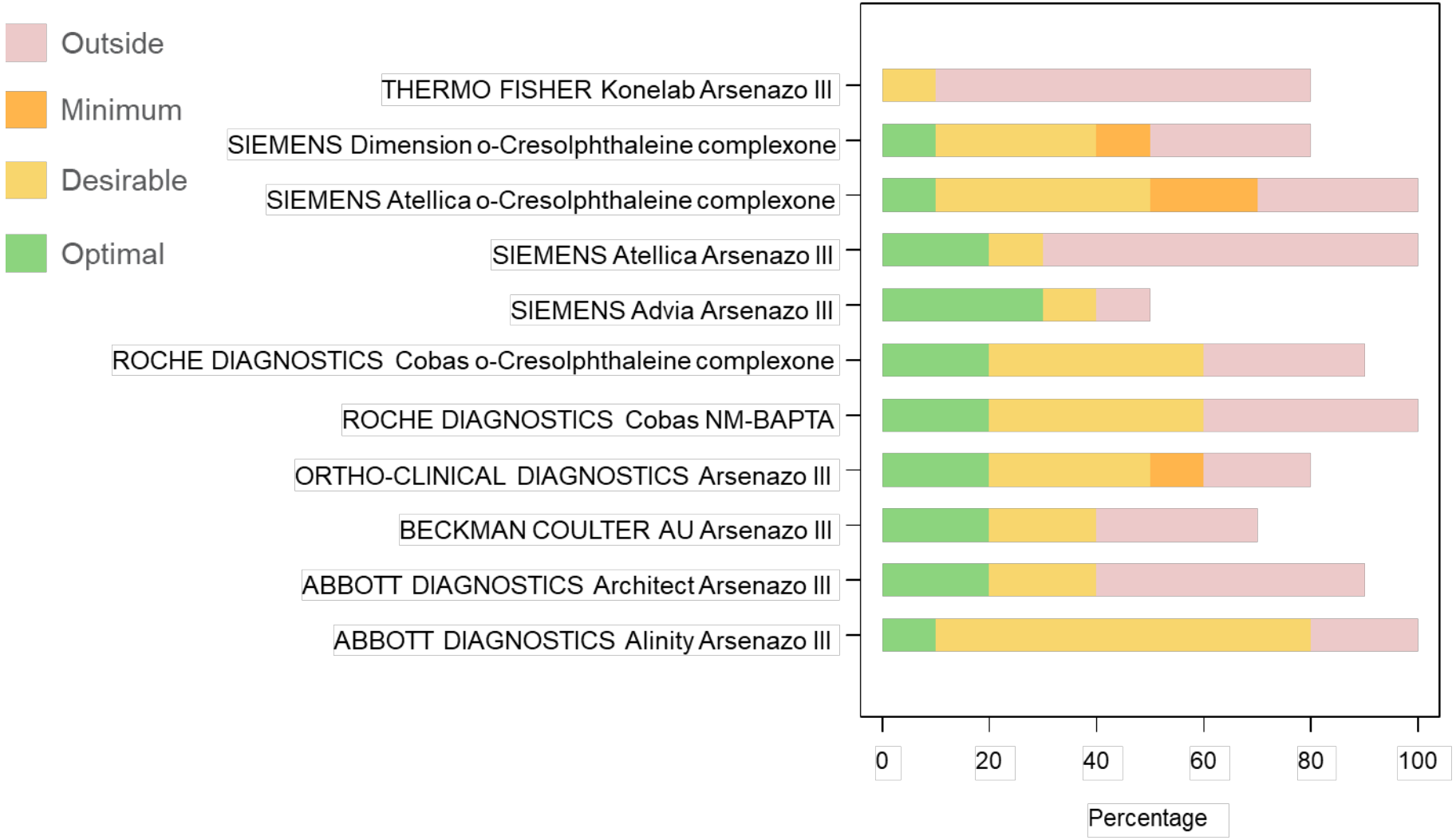
Total deviation between methods: Albumin - summary



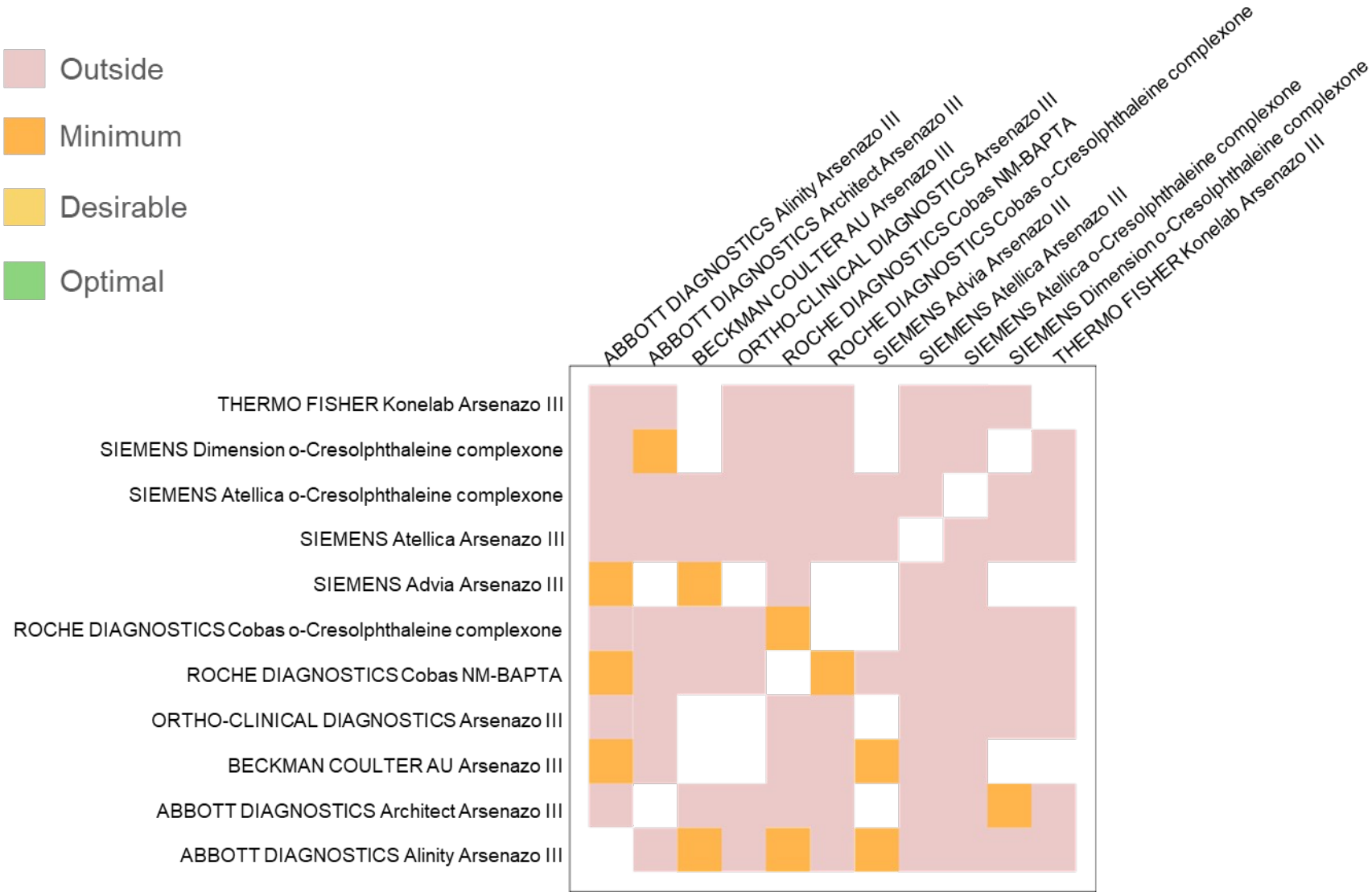
Bias between methods: Calcium



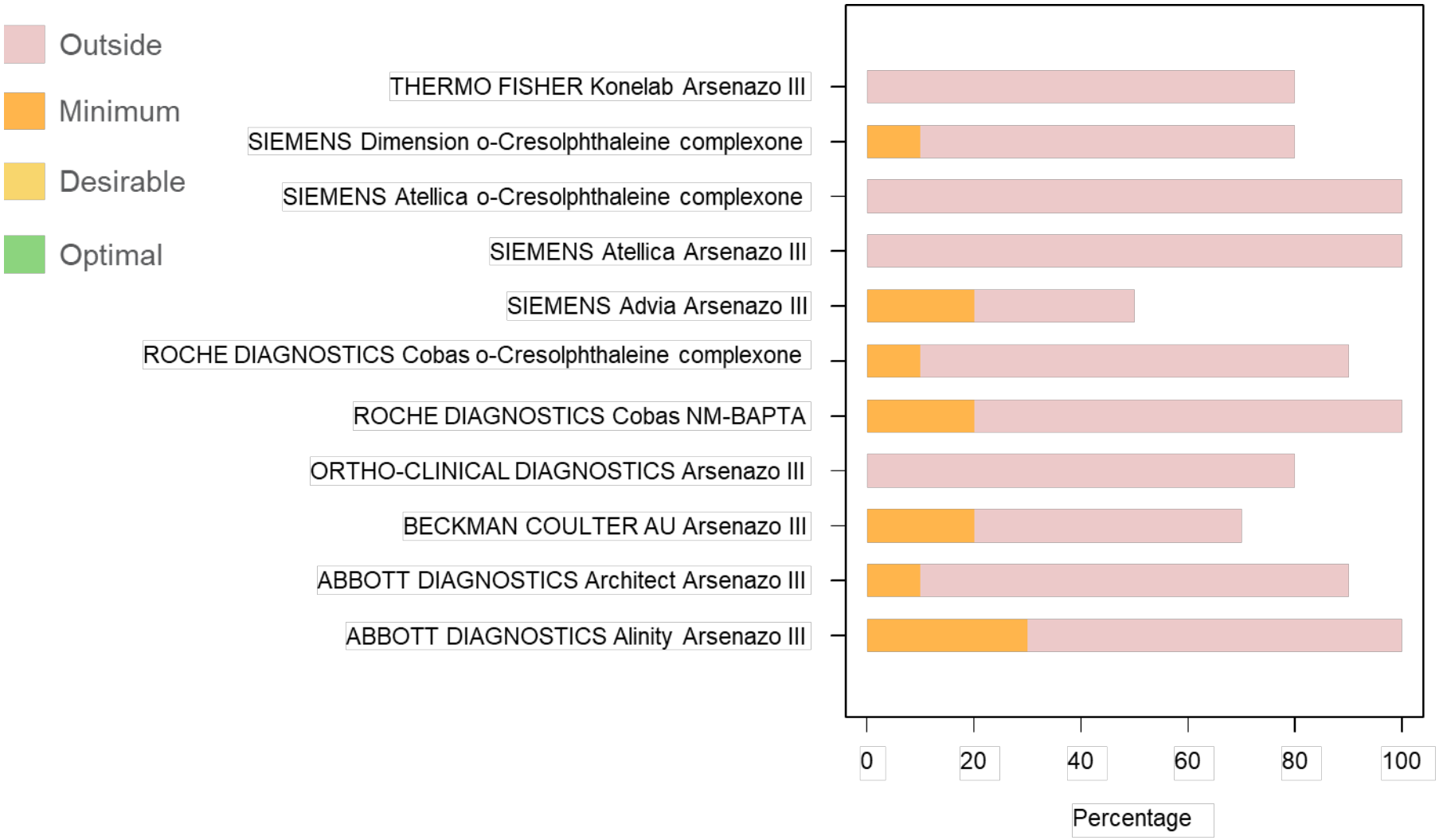
Bias between methods: Calcium - summary



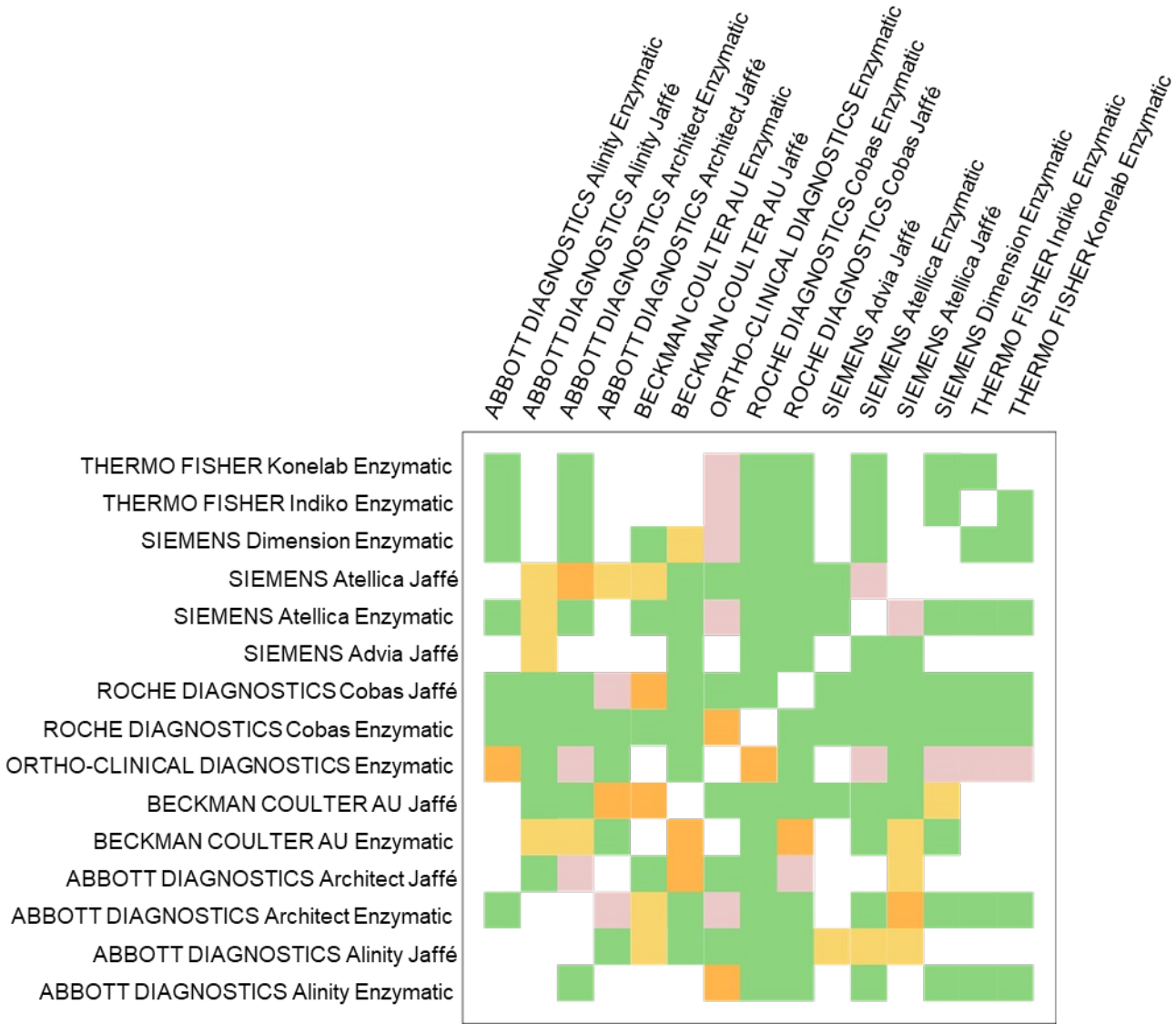
Total deviation between methods: Calcium



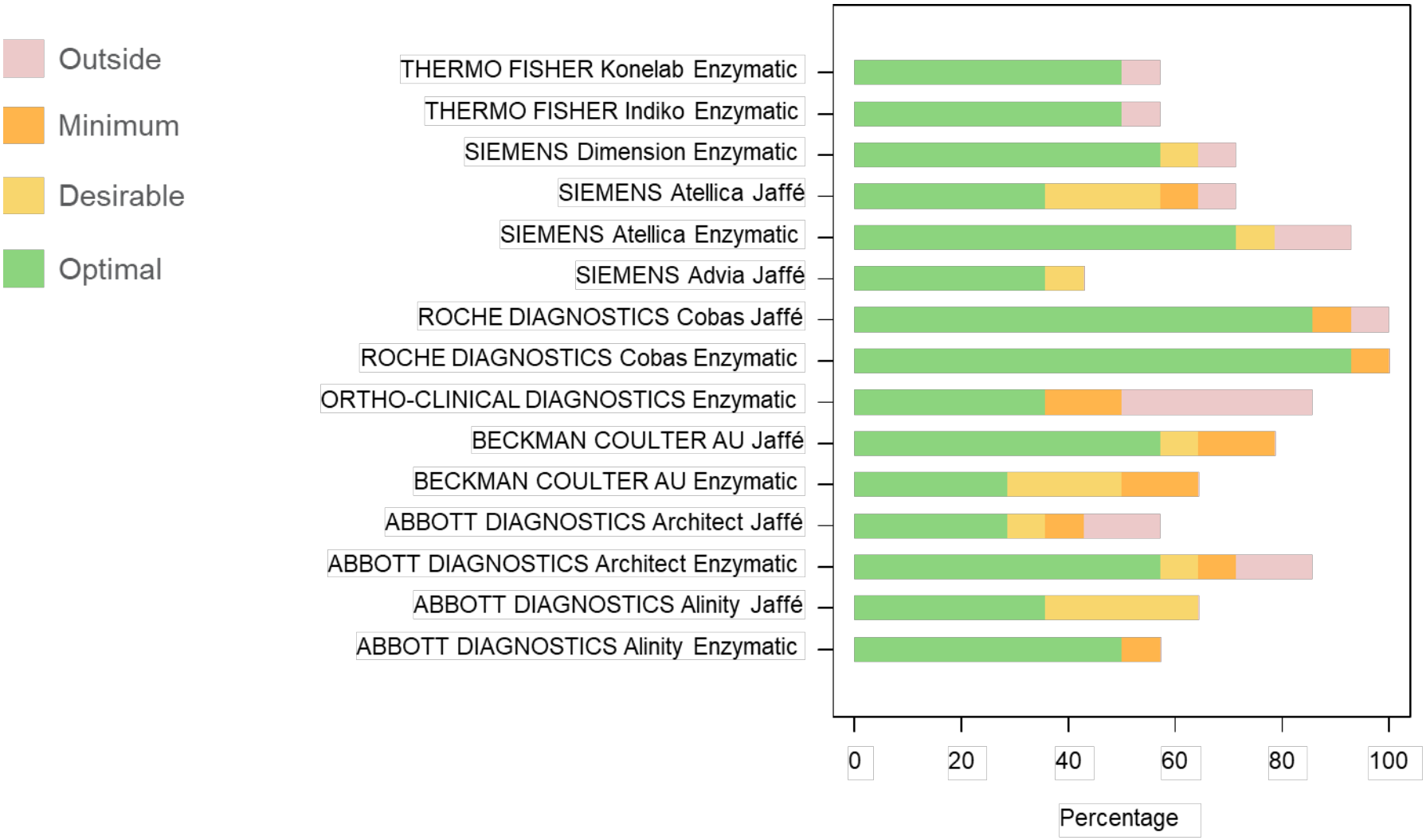
Total deviation between methods: calcium – summary



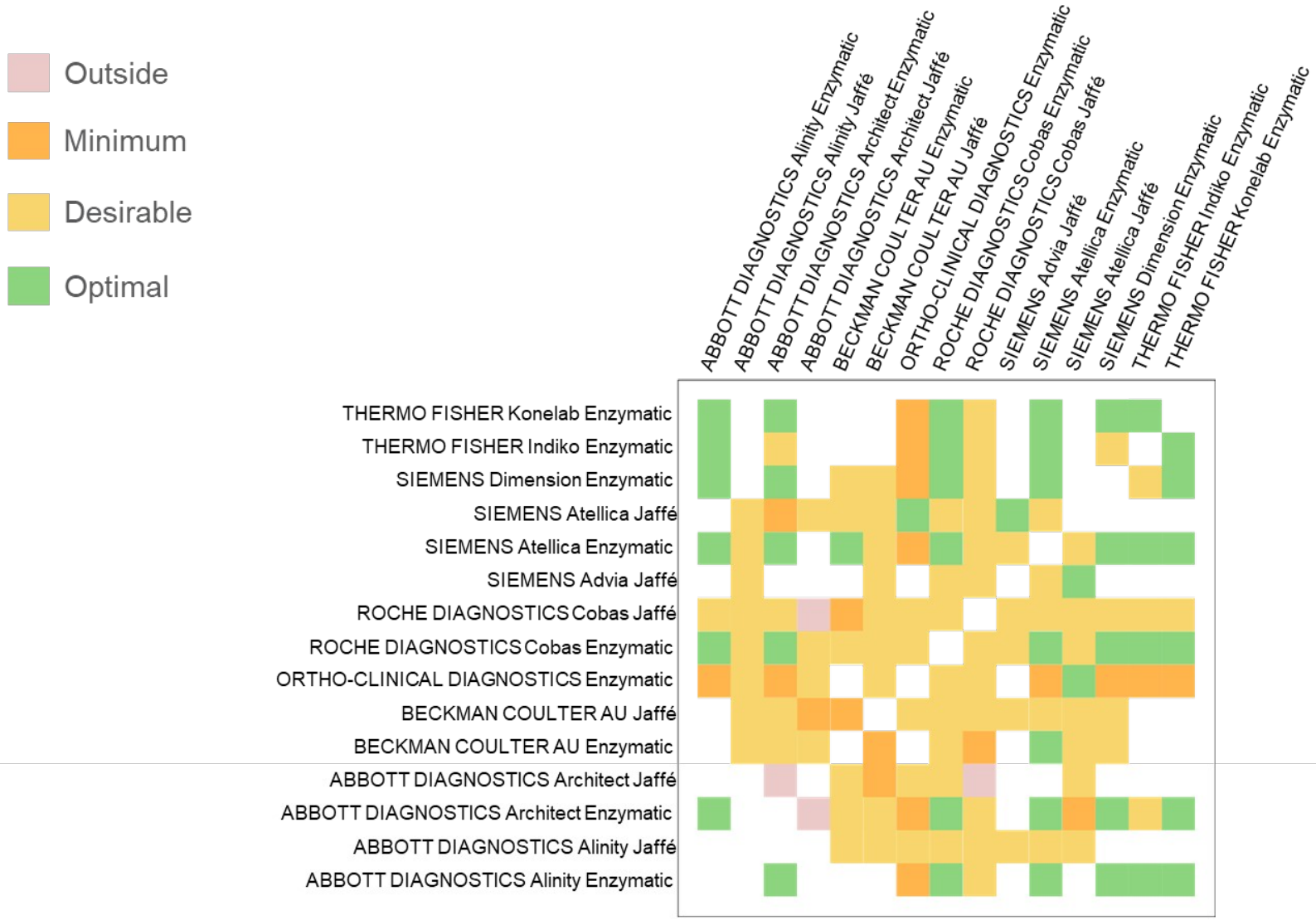
Bias between methods: Creatinine



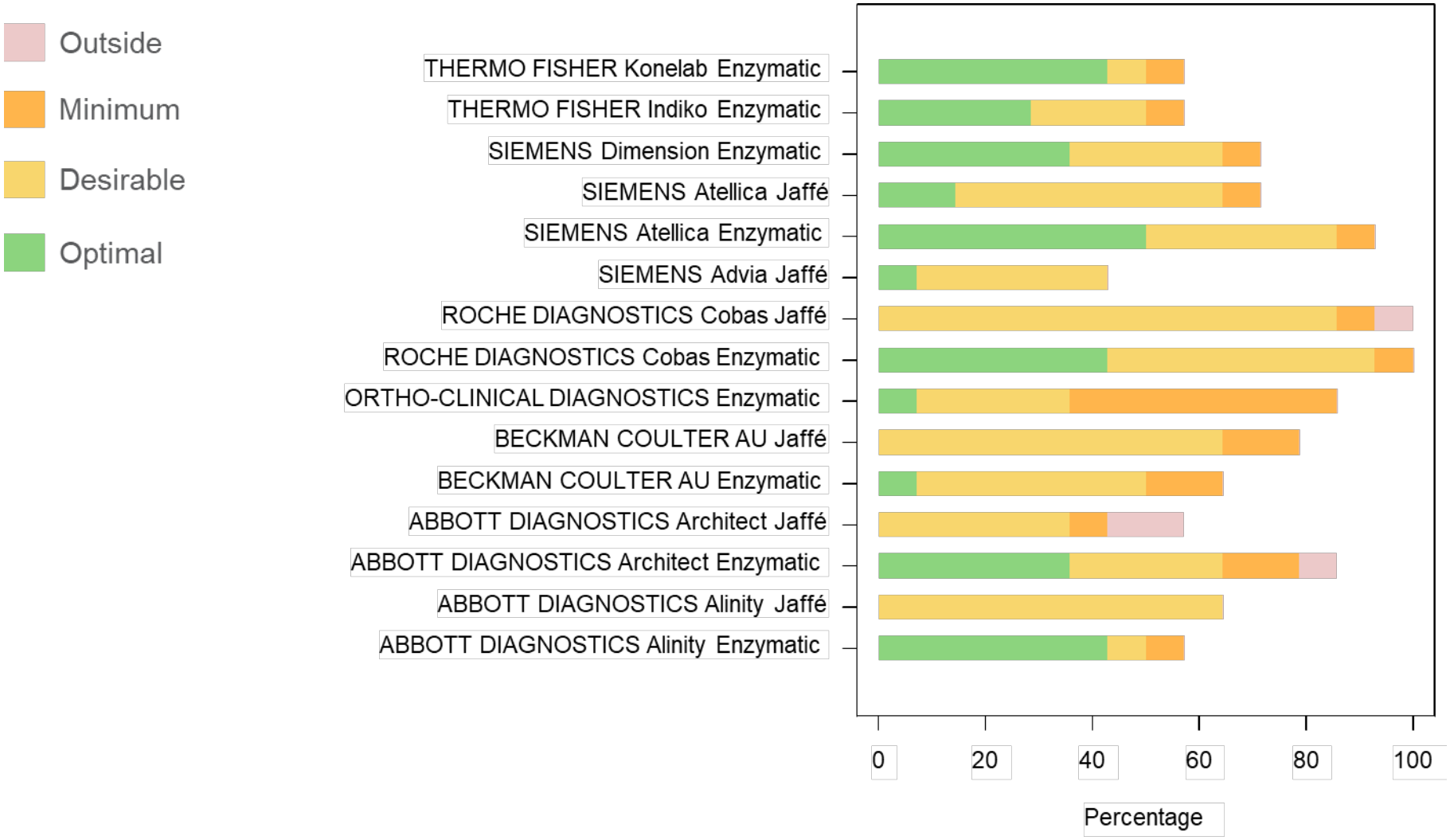
Bias between methods: Creatinine - summary



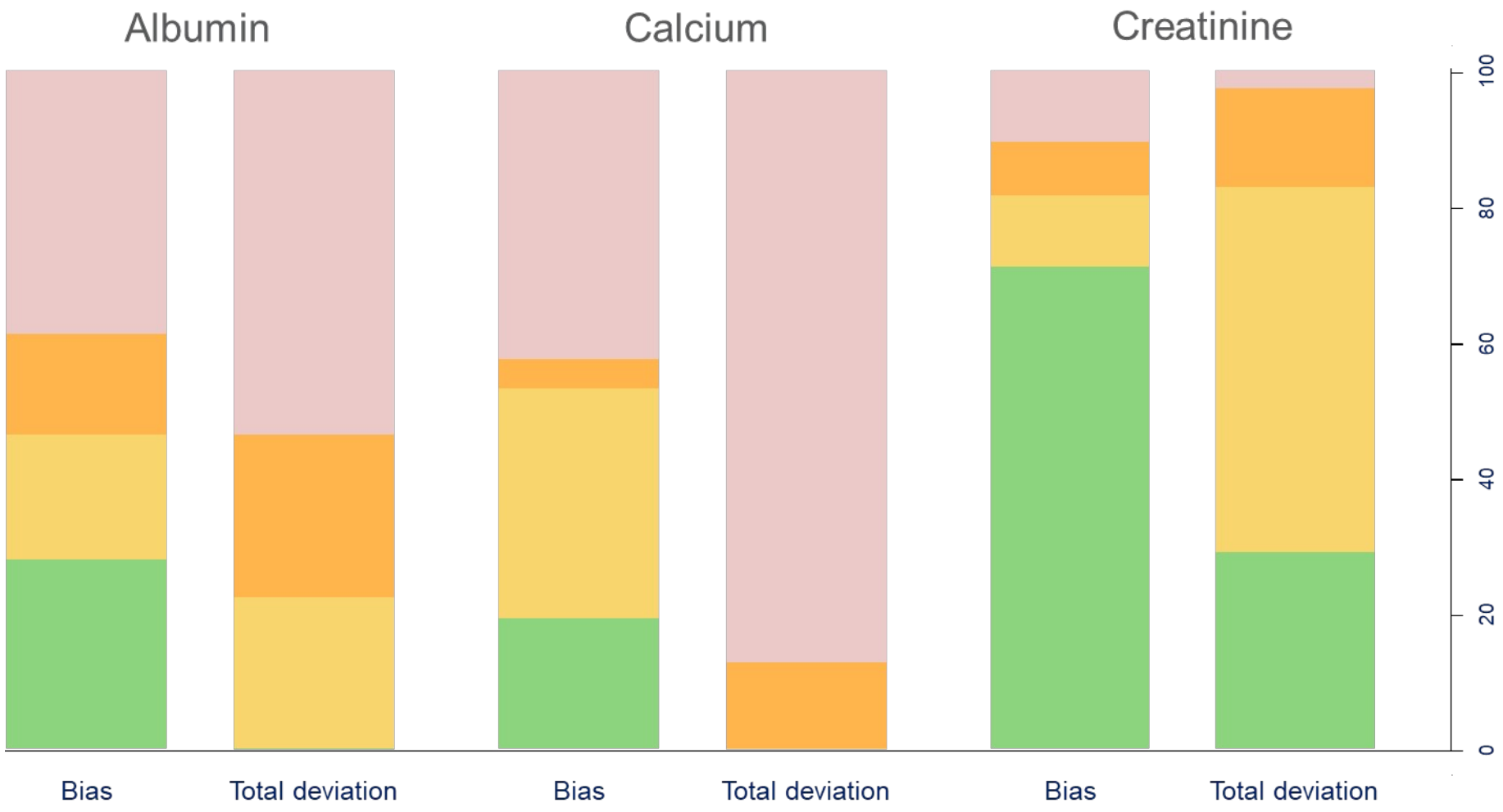
Total deviation between methods: Creatinine



Total deviation between methods: creatinine - summary

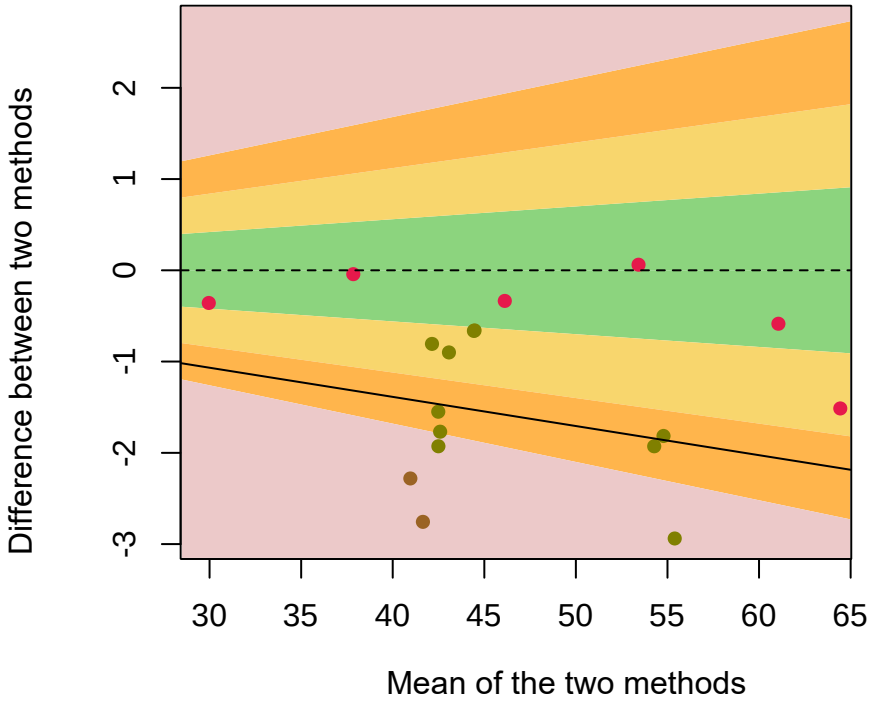


Summary per measurand



Discussion - disclaimer

- Correctness depens on commutability of sample material



Questionnable commutability of individual samples will be assessed by HALMA

Discussion - disclaimer

- Correctness depends on homogeneity of peer groups
  - Effect on variability
  - Will be investigated further by HALMA

- Correctness depends on chosen evaluation limits
  - Biological variation from HALMA has originally not been designed for this kind of studies
  - Maximum bias between two methods, total deviation still under discussion

Conclusion

- Matching with EFLM's analytical performance specifications leads to weak harmonization for Albumin and Calcium, moderate harmonization for Creatinine

- Including variability: although limits are wider, harmonization becomes worse for Albumin and Calcium
  - Many methods do not attain even minimal requirements for variability
  - Or: measurement procedure definition is too coarse

Anyone knows how to use automated methods to classify measurement procedures ?