The Role of Retention Time in Untargeted Metabolomics

Caparica-Lisbon, 21st September 2015

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‡Department of Stress and Developmental Biology, Leibniz Institute of Plant Biochemistry, Halle, Germany

From feature to identified compound

Match to authentic standard

Orthogonal data: e.g. spectra + retention time

MSI LEVEL I

From feature to identified compound

Match to authentic standard

Orthogonal data: e.g. spectra + retention time

MSI LEVEL I

Match to public MS library

No orthogonal data: only spectra

MSI LEVEL II

From feature to identified compound

Match to authentic standard
Orthogonal data: e.g. spectra + retention time

MSI LEVEL I

Match to public MS library
No orthogonal data: only spectra

MSI LEVEL II

Compound not in any MS library

MSI LEVEL III/IV

From feature to identified compound

Match to public MS library

No orthogonal data: only spectra

MSI LEVEL II

MSI LEVEL II: match to public db

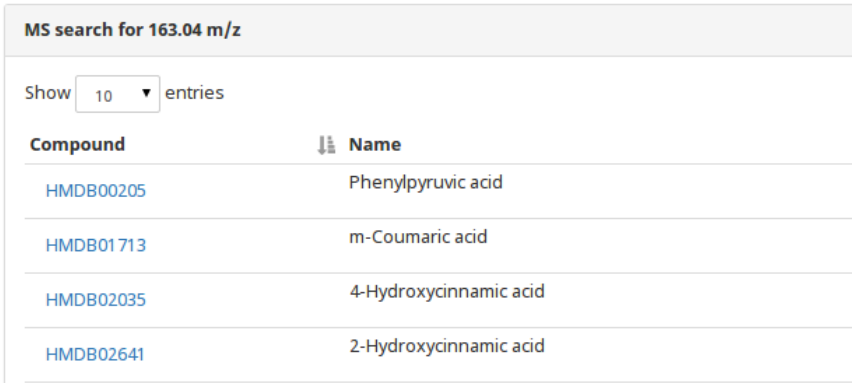
You got your match to a database spectra.

But are you sure that the spectra of your unknown couldn't match ***other*** isomers equally well?

MS search for 163.04 m/z

Show 10 entries

Compound	Name
HMDB00205	Phenylpyruvic acid
HMDB01713	m-Coumaric acid
HMDB02035	4-Hydroxycinnamic acid
HMDB02641	2-Hydroxycinnamic acid



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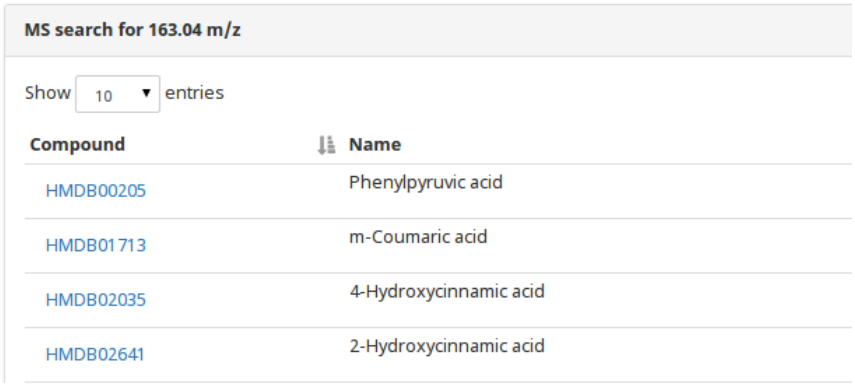
1) Examine mass spectra → No way to discriminate



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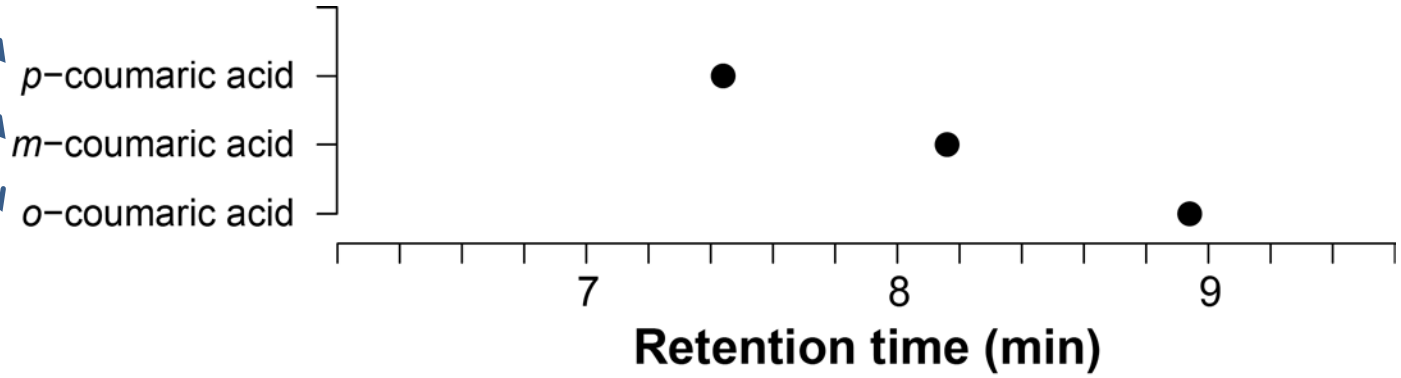

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So can we at least limit the number of isomers by using the information we already have?

Why retention time information is usually neglected

Retention time is specific to the chromatographic system and there are no RT references

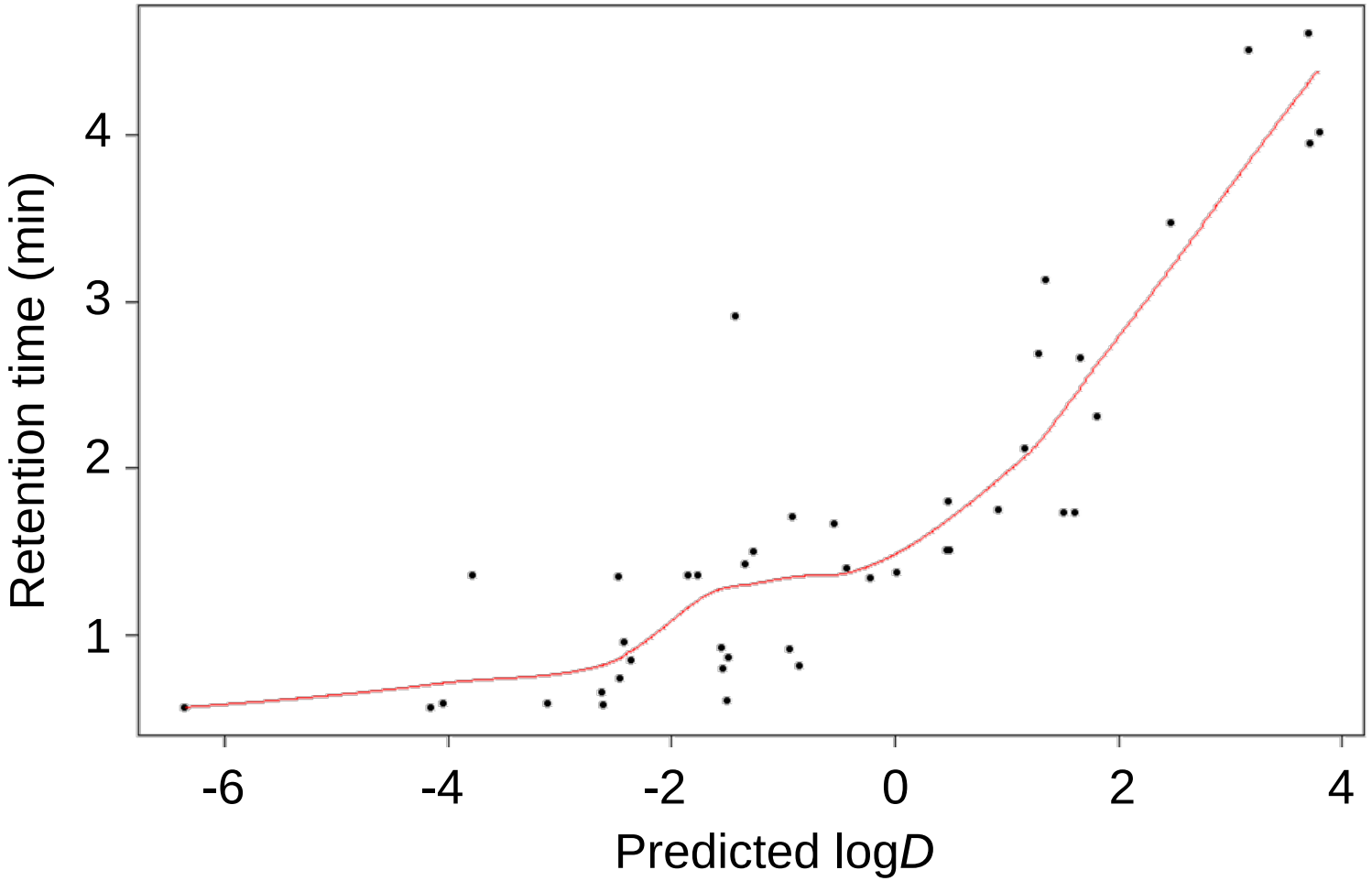
No coordinated efforts to share and exploit RT info.

Current approaches to retention time prediction and their characteristics

	Prediction from structure (QSRR)	**Projection from isocratic runs**[a]
Accuracy	Low	Very high
Universality (any structure)	High	Low
Additional lab work	None	Lots
Model complexity	High	Low

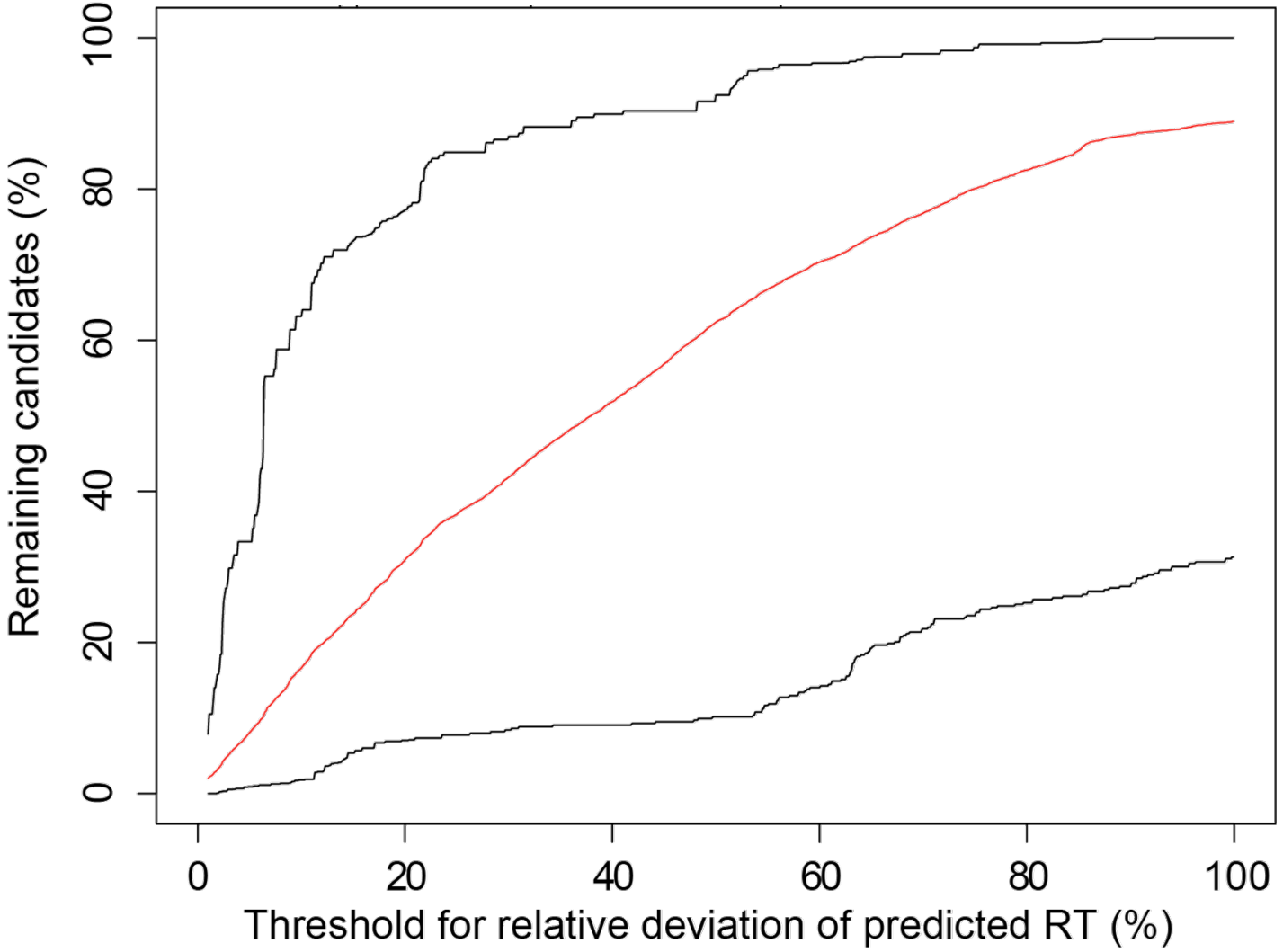
[a]Abate-Pella D, et al. (2015). Retention Projection Enables Accurate Calculation of Liquid Chromatographic Retention Times Across Labs and Methods. *J Chromatogr.*

Simplest QSRR model



Stanstrup, J., Gerlich, M., Dragsted, L. O., & Neumann, S. (2013). Metabolite profiling and beyond: Approaches for the rapid processing and annotation of human blood serum mass spectrometry data Metabolomics and Metabolite Profiling. *Analytical and Bioanalytical Chemistry*, *405*(15), 5037–5048.

Candidates after filtering as a function of prediction accuracy



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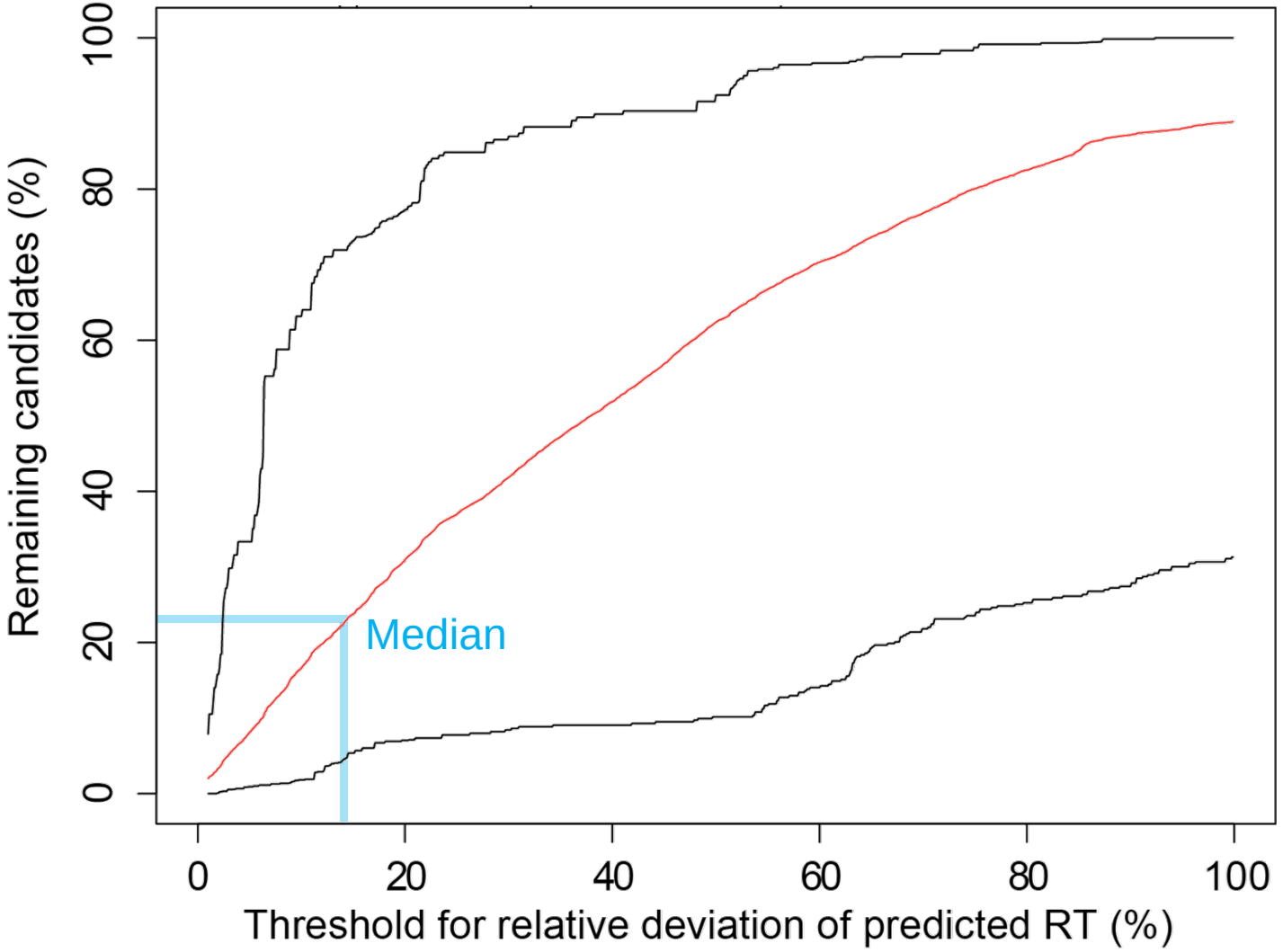

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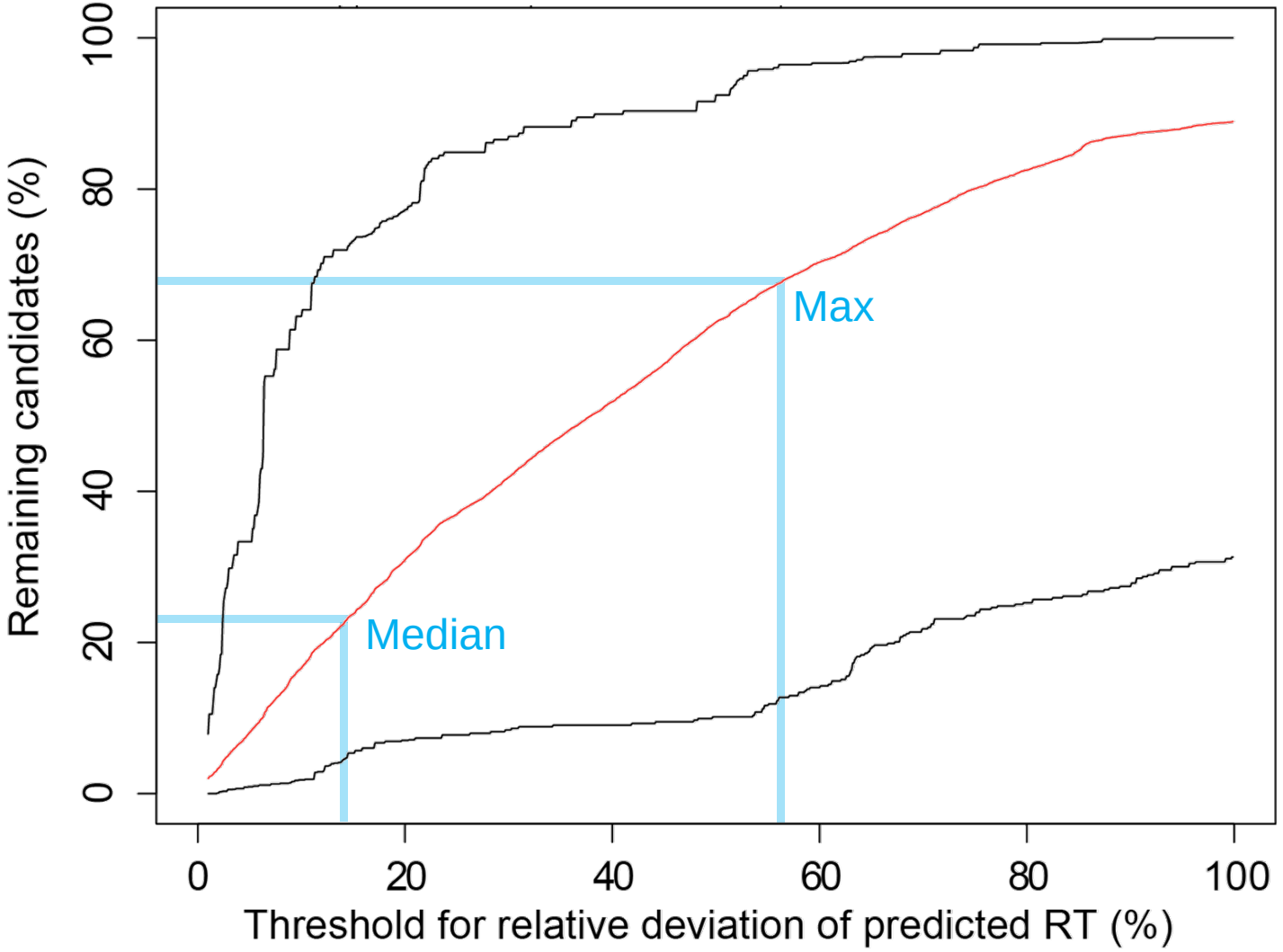

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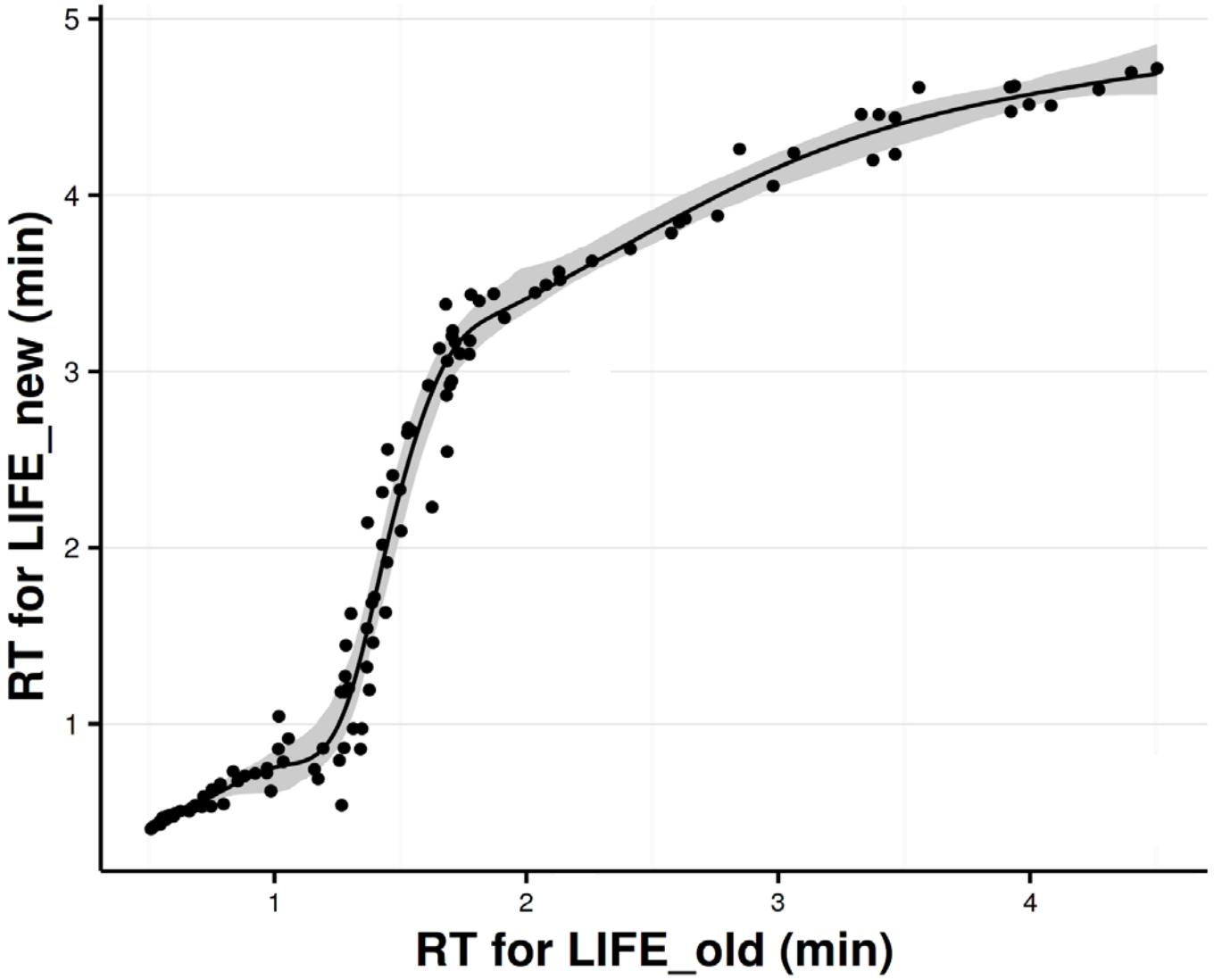
Previous approaches to retention time prediction

	Prediction from structure (QSRR)	**Projection from isocratic runs**[a]	**PredRet**[b]
Accuracy	Low	Very high	Medium to high
Universality (any structure)	High	Low	Low to medium
Additional lab work	None	Lots	None
Model complexity	High	Low	Low

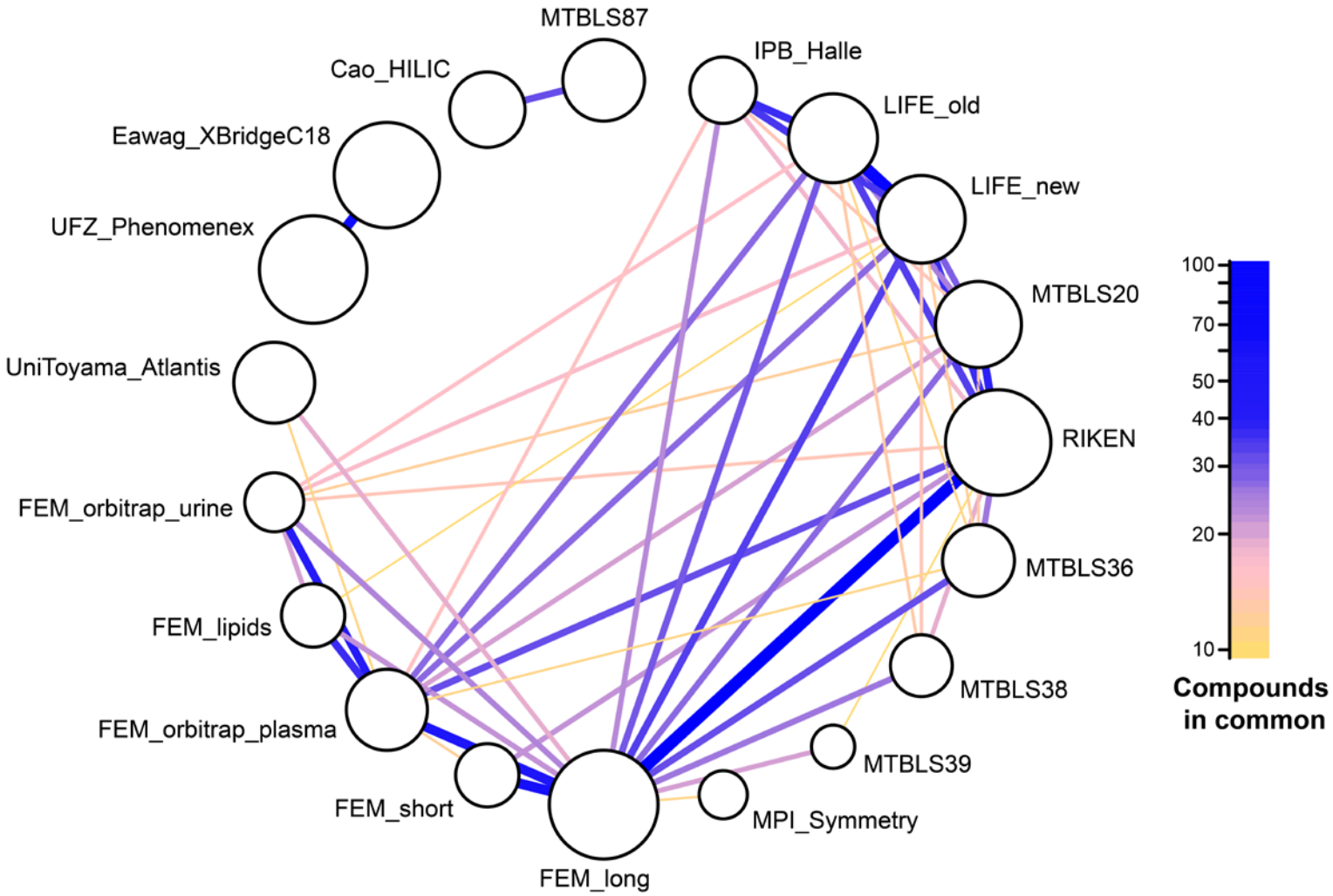
[a]Abate-Pella D, et al. (2015). Retention Projection Enables Accurate Calculation of Liquid Chromatographic Retention Times Across Labs and Methods. *J Chromatogr.*

[b]Stanstrup, J., Neumann, S., & Vrhovsek, U. (2015). PredRet: Prediction of Retention Time by Direct Mapping between Multiple Chromatographic Systems. *Analytical Chemistry*.

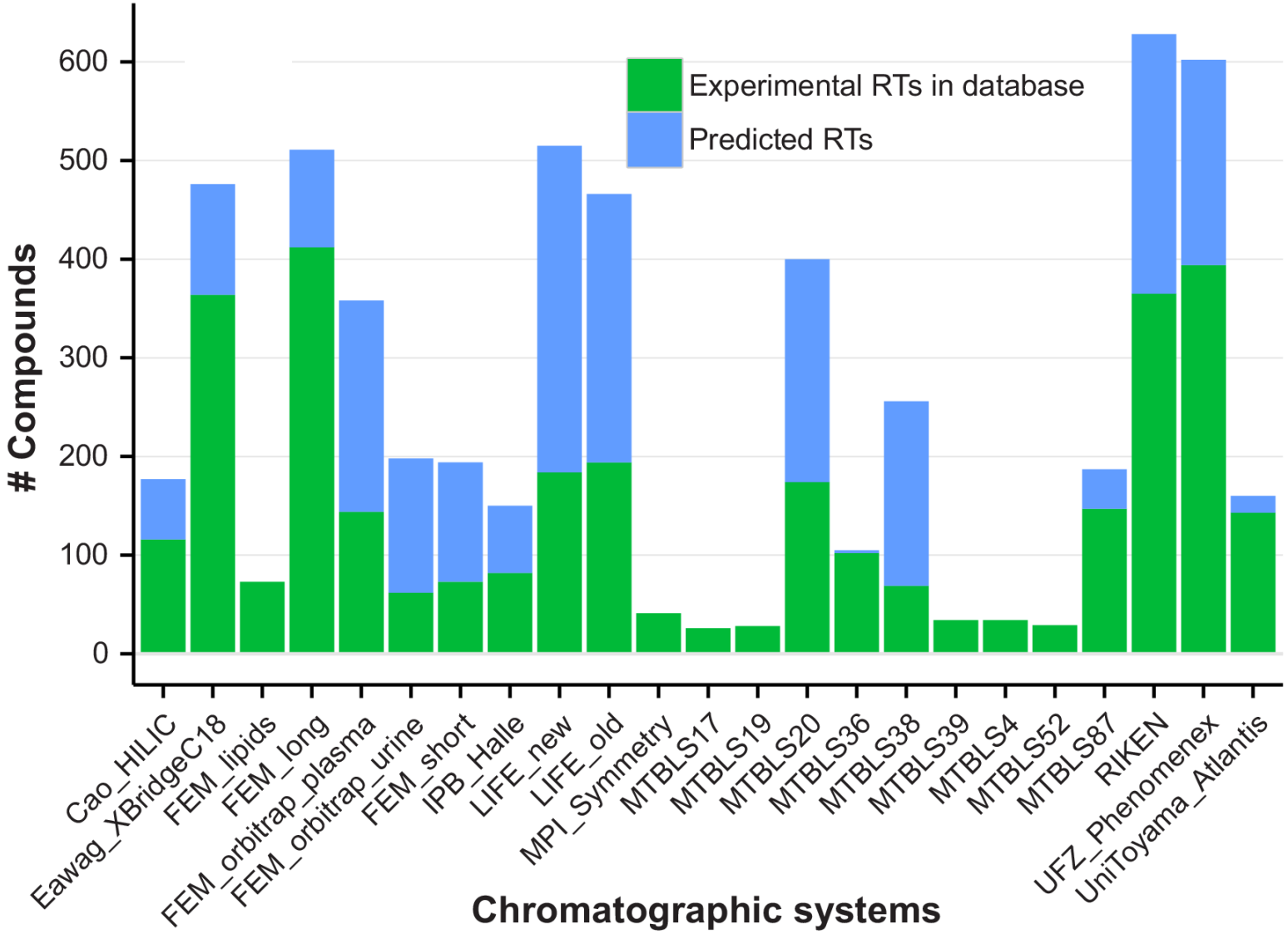
PredRet models



Compound overlap between systems in PredRet



Number of RTs in database and predictions made



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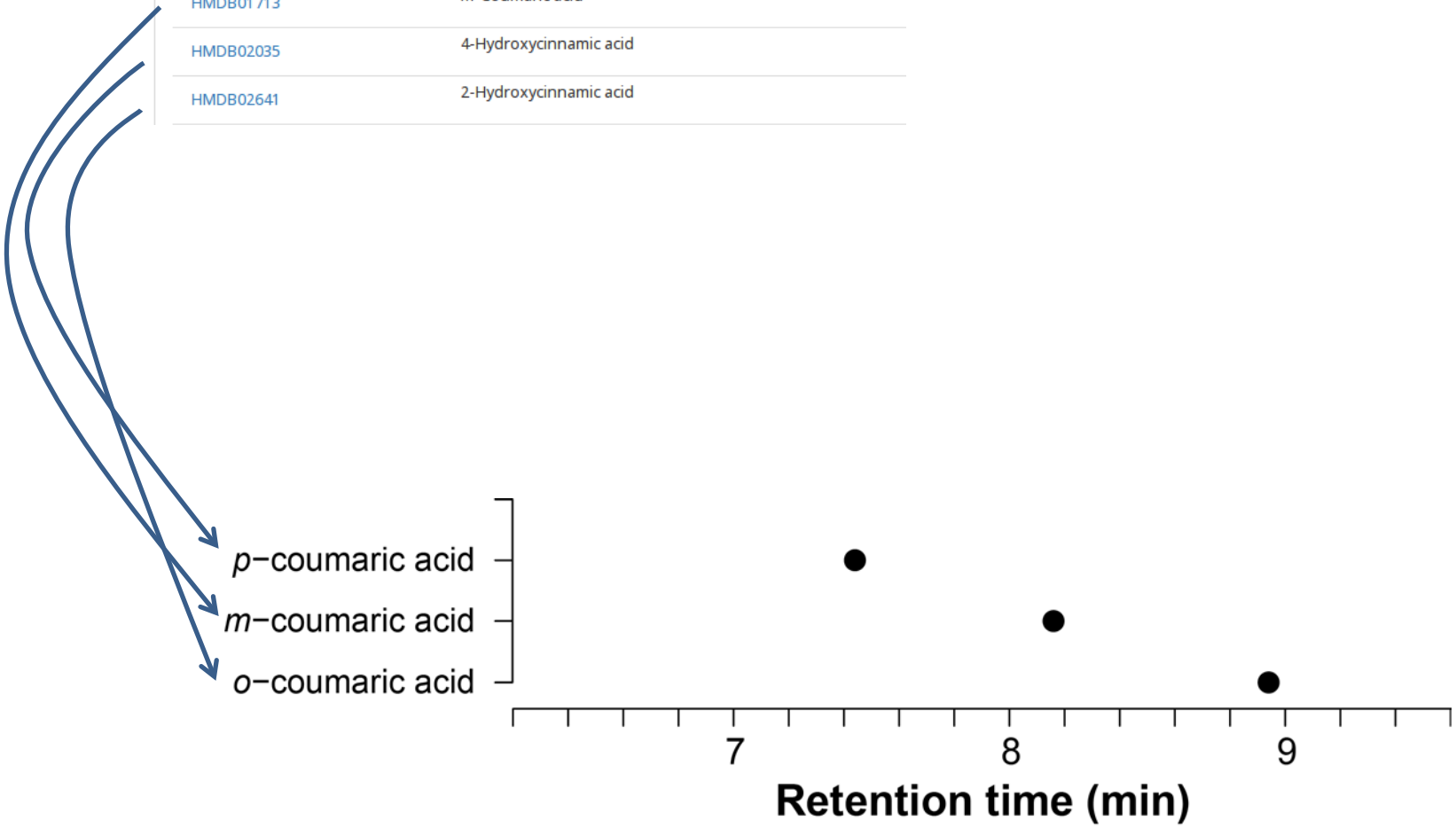

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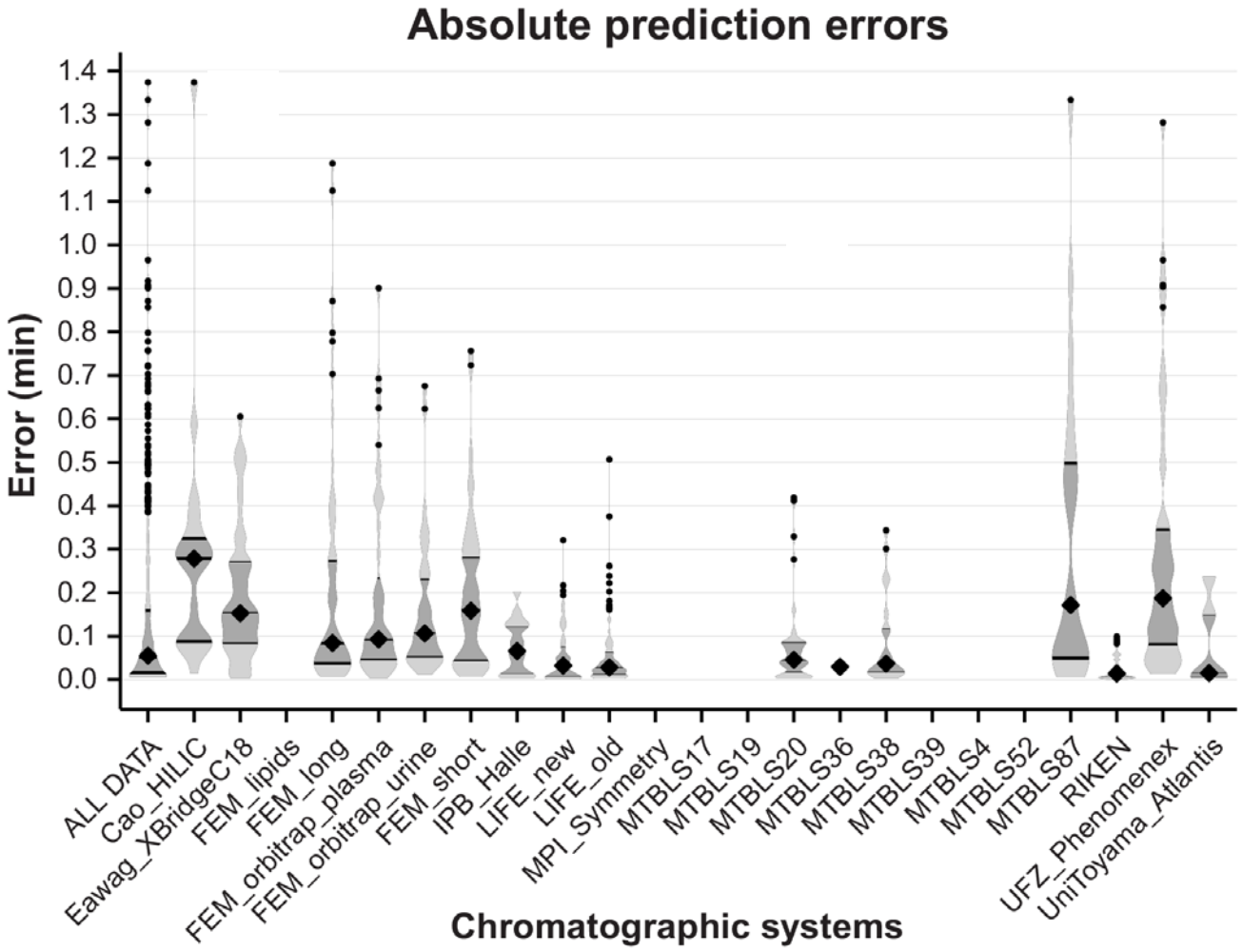
Accuracy of PredRet predictions



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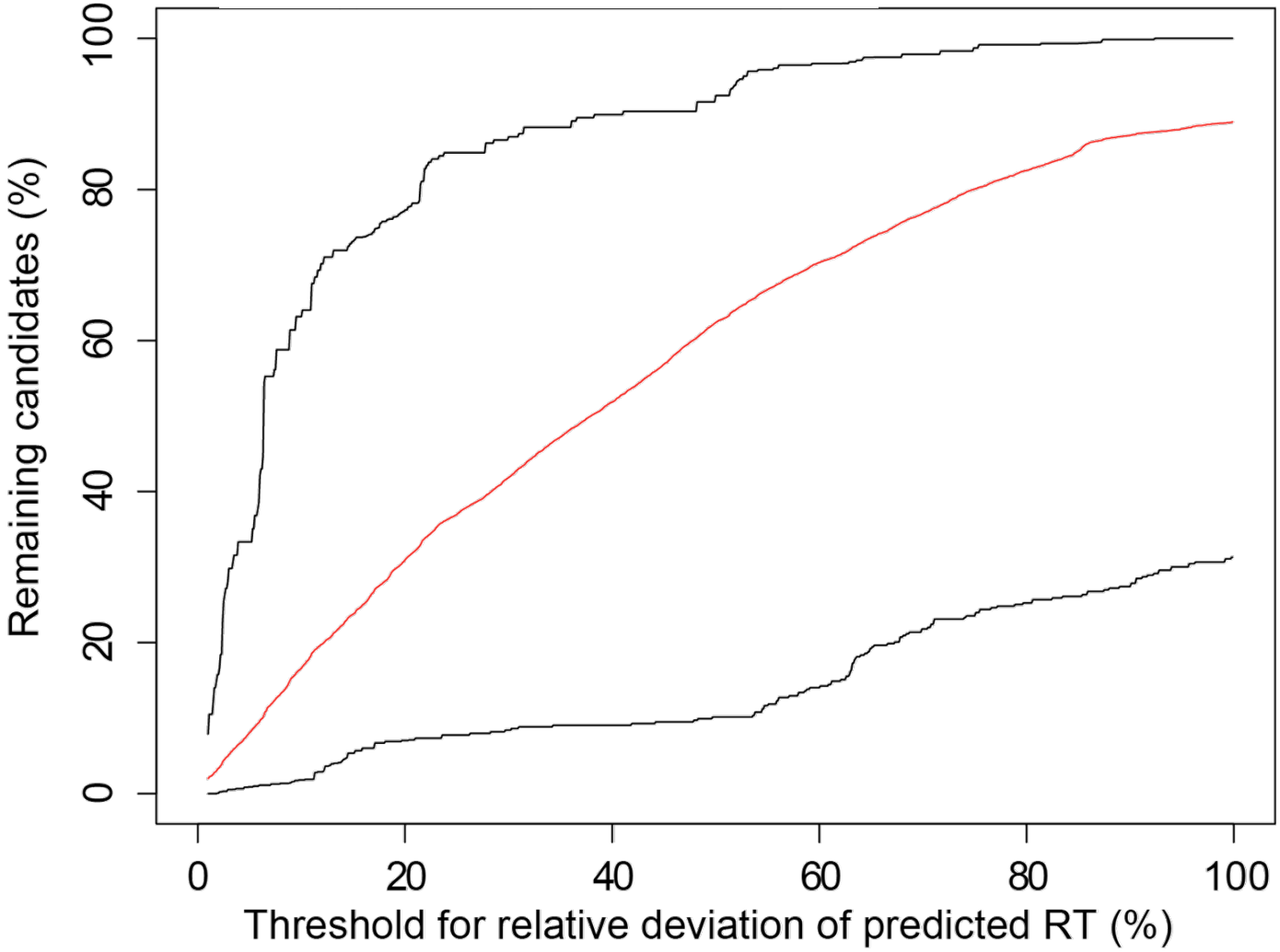

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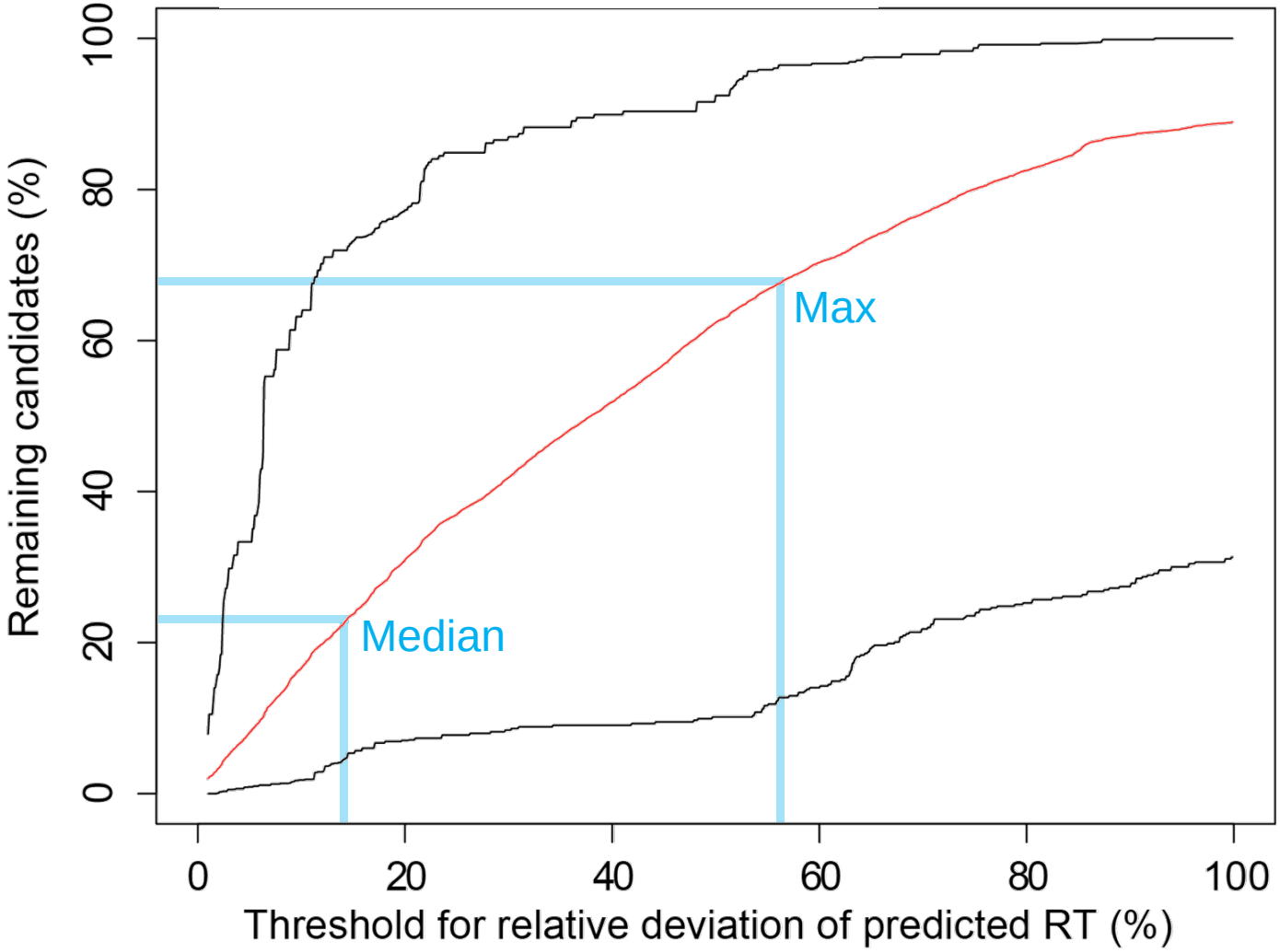

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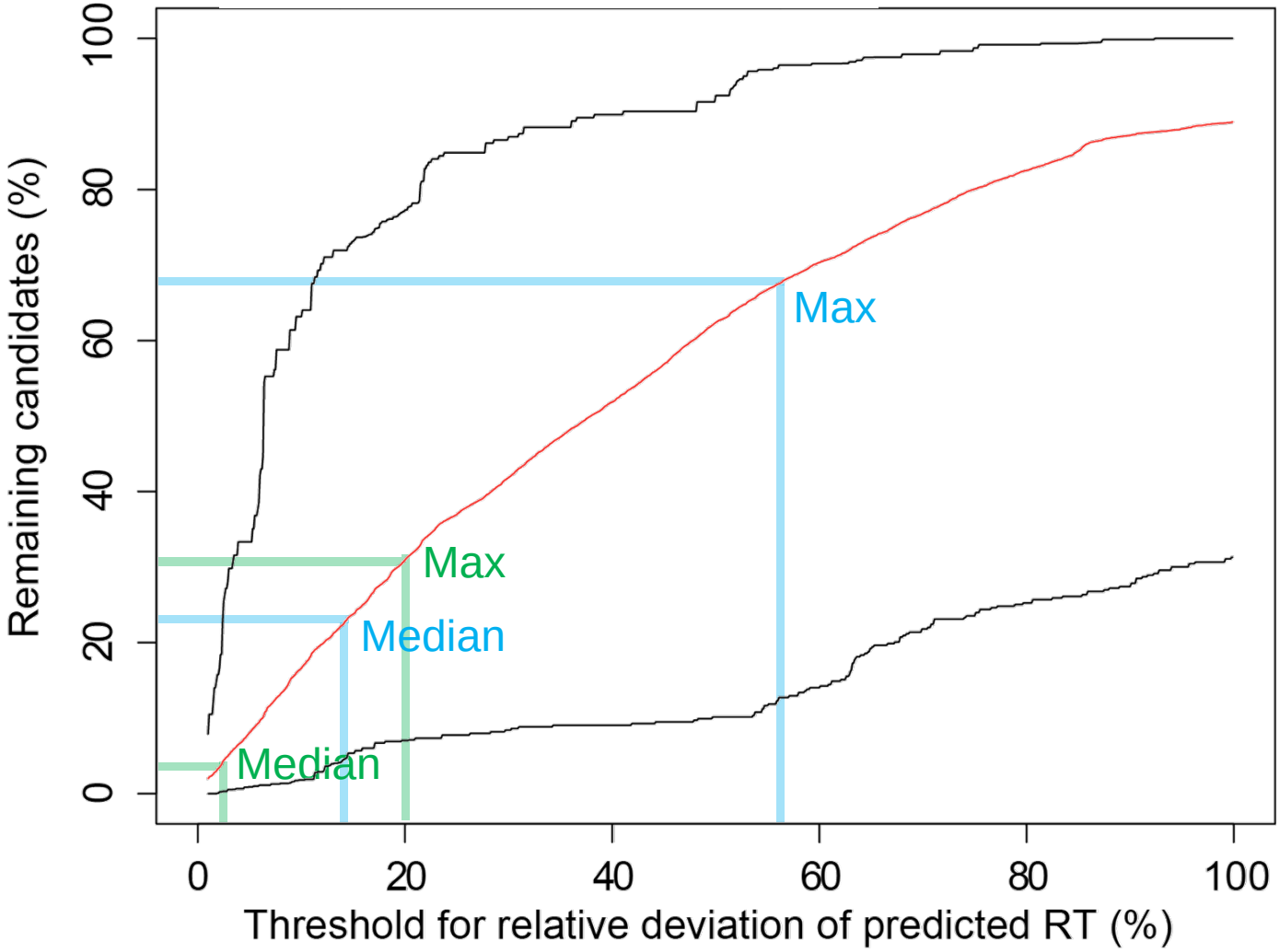

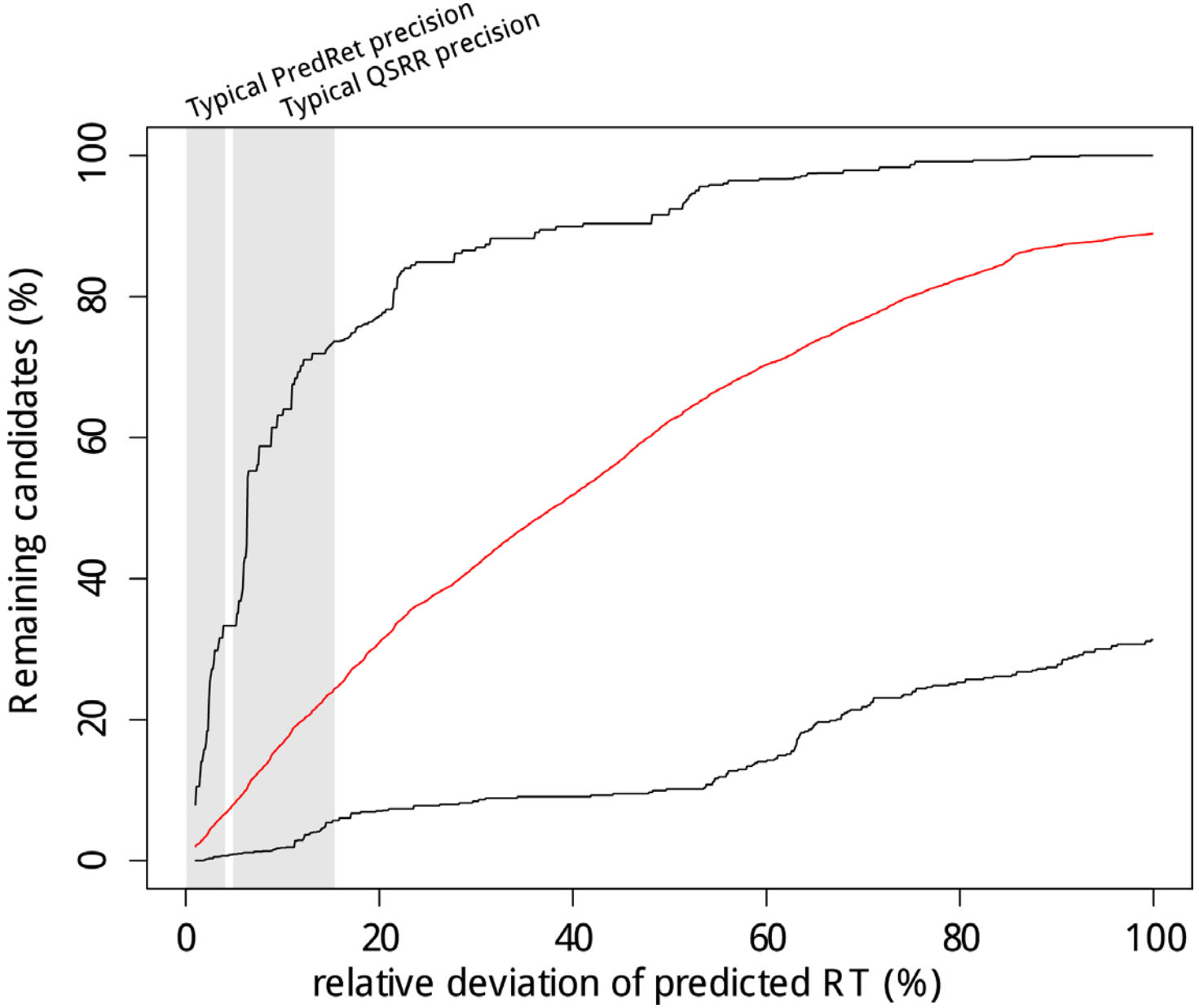
Typical PredRet precision
Typical QSRR precision
Remaining candidates (%)
0
20
40
60
80
100
0
20
40
60
80
100
relative deviation of predicted RT (%)

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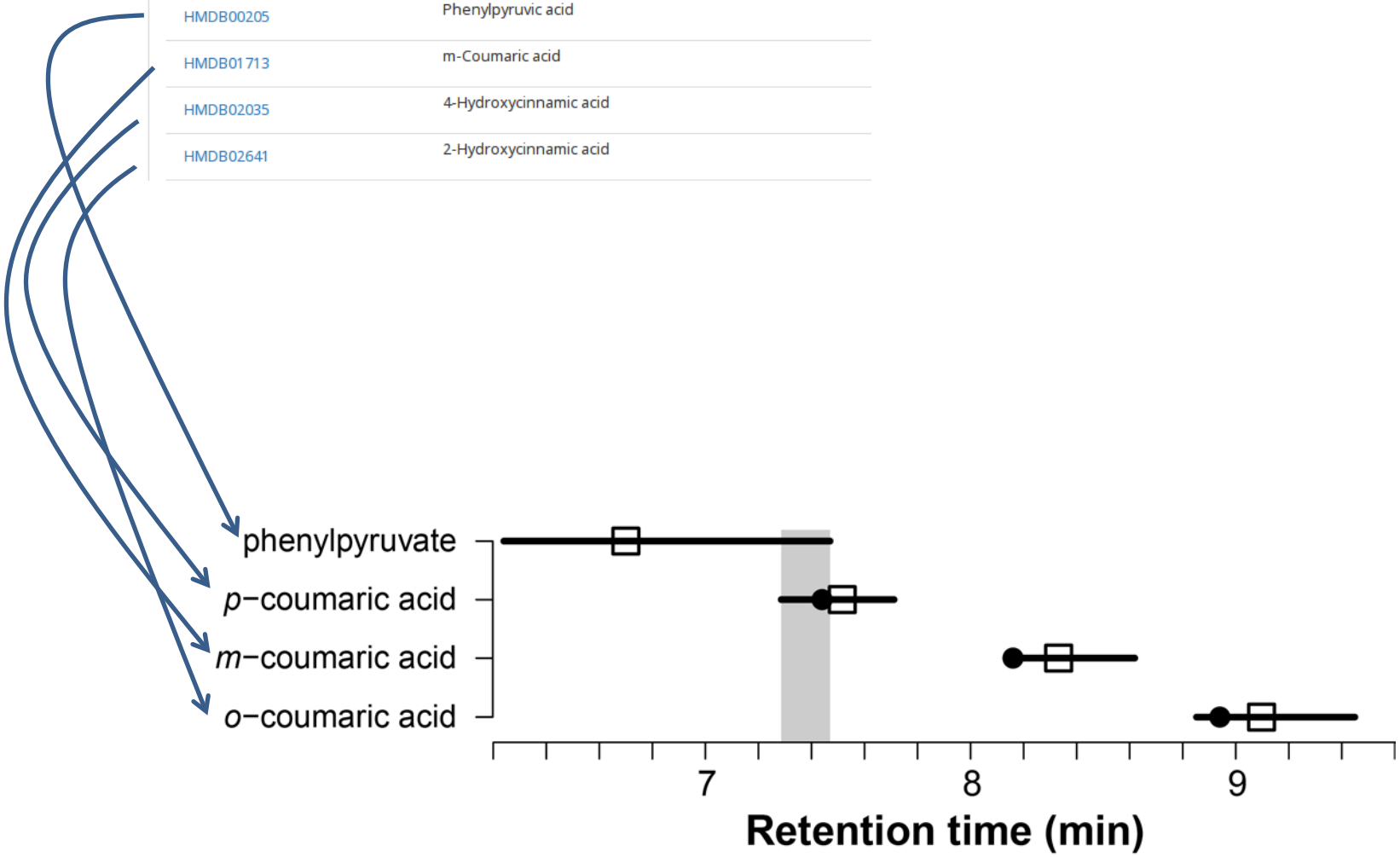

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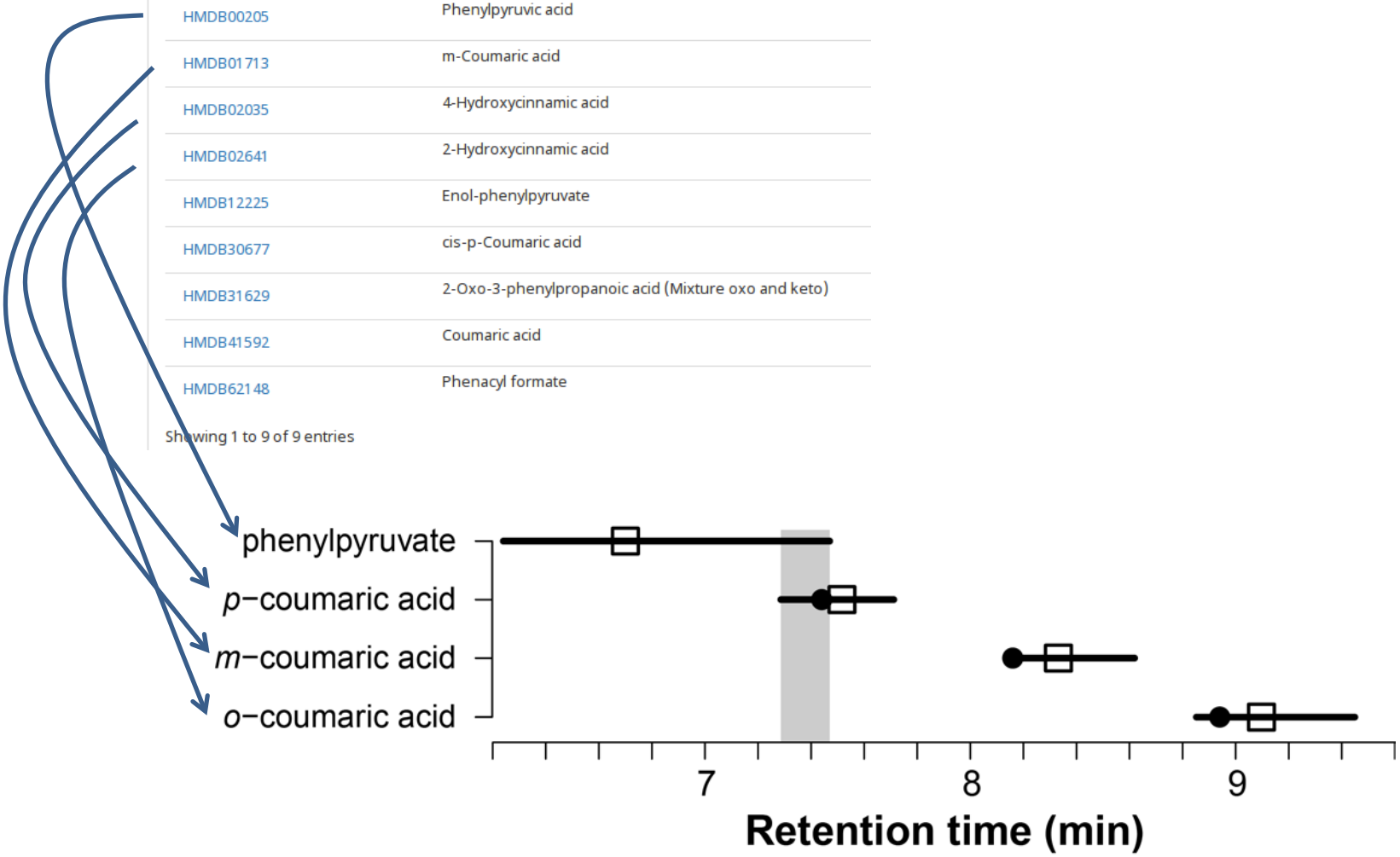
HMDB12225	Enol-phenylpyruvate
HMDB30677	cis-p-Coumaric acid
HMDB31629	2-Oxo-3-phenylpropanoic acid (Mixture oxo and keto)
HMDB41592	Coumaric acid
HMDB62148	Phenacyl formate

Showing 1 to 9 of 9 entries



Conclusions

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- When people use PredRet the database expands

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Thank you for your attention

Share the RTs!