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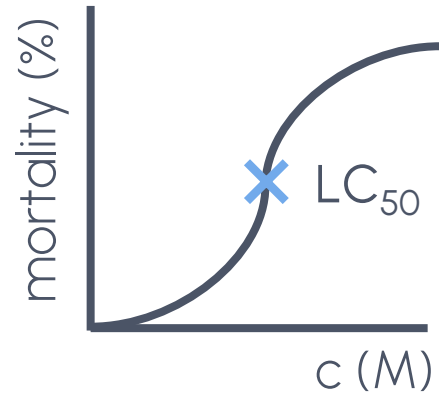


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Experimental validation of toxic unit predictions with MS^2 -based models

Helen Sepman, Lisa A. Baumann, Frederic Béen, Magnus Breitholtz,
Jonathan Martin, Matthew MacLeod, Anneli Kruve

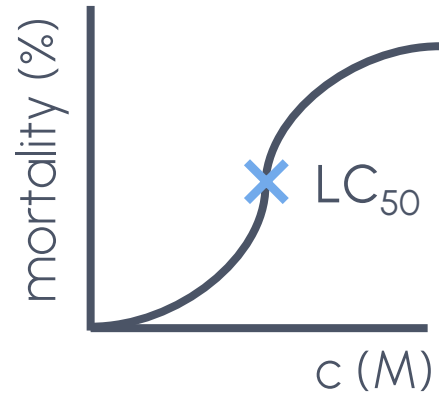
ENVIRONMENTAL RISK



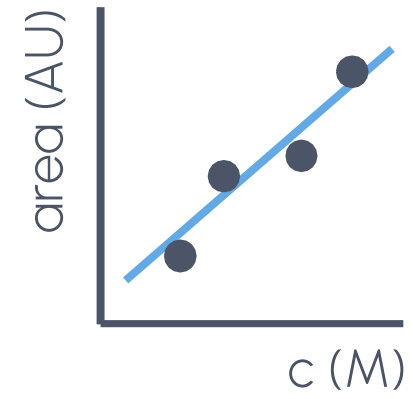
Toxicity



ENVIRONMENTAL RISK



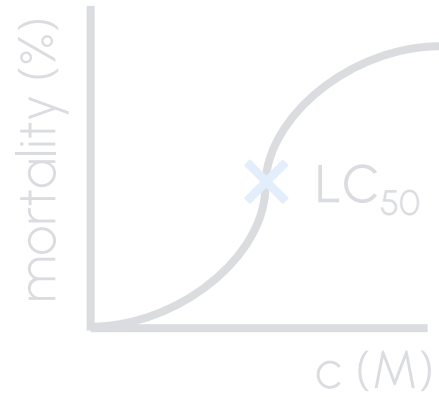
Toxicity



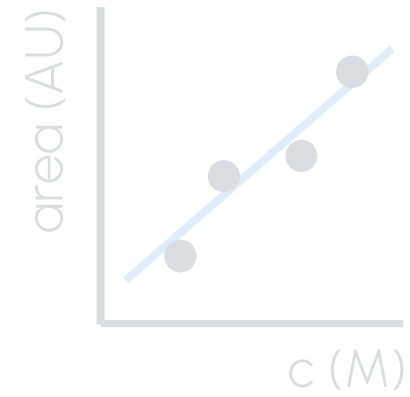
Exposure



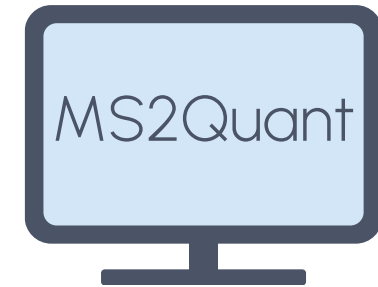
ENVIRONMENTAL RISK



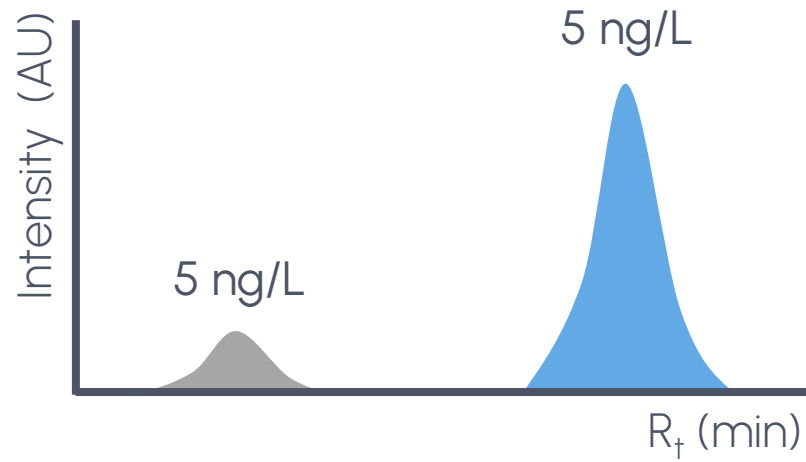
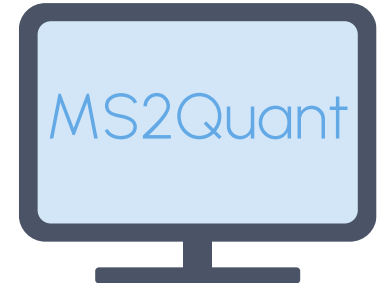
Toxicity



Exposure

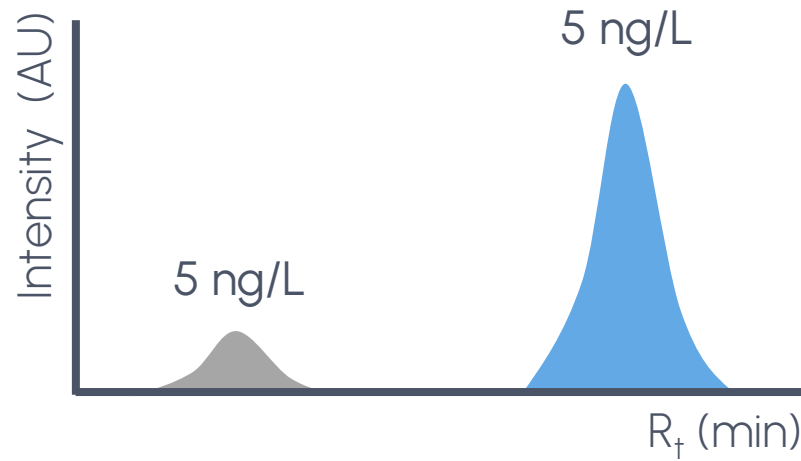
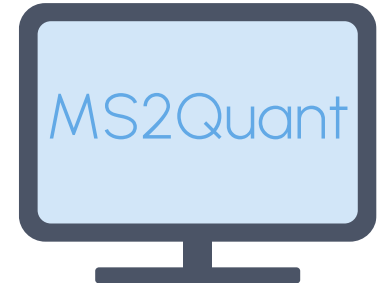


EXPOSURE PREDICTION

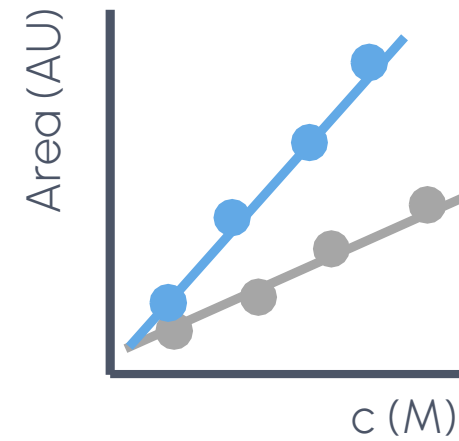


LC-ESI-MS features

EXPOSURE PREDICTION

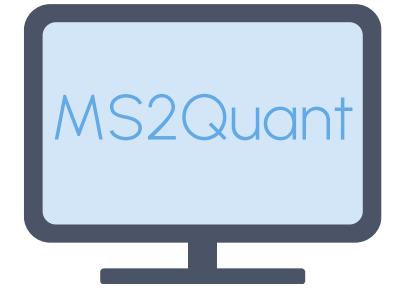


LC-ESI-MS features

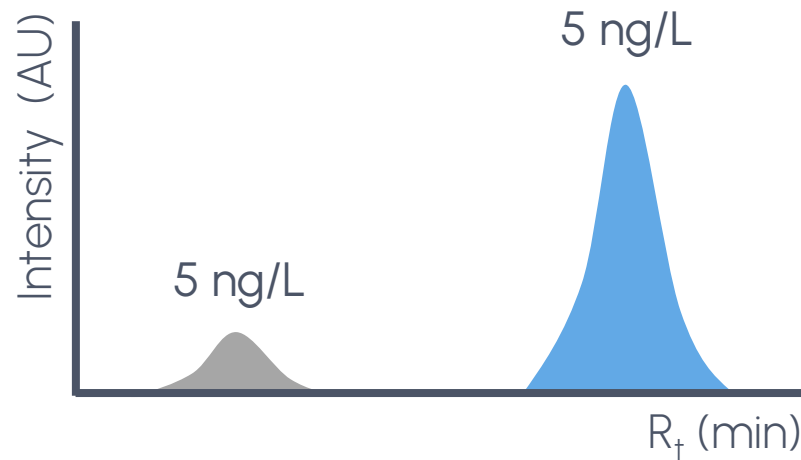


Slope = Response factor

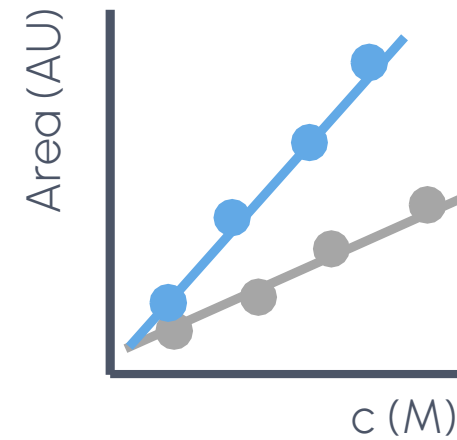
EXPOSURE PREDICTION



MS2Quant2

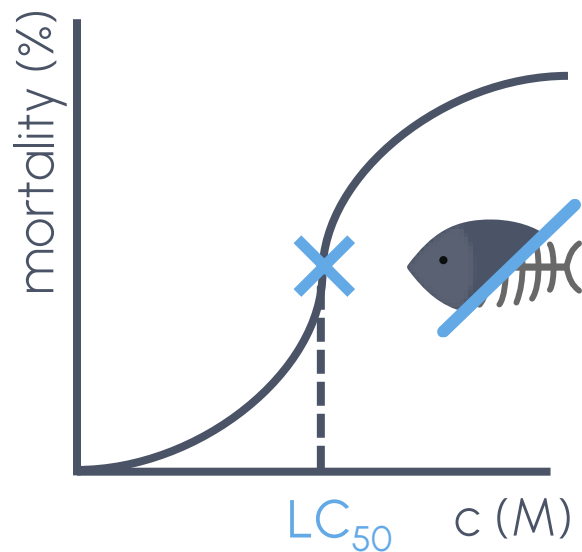


LC-ESI-MS features



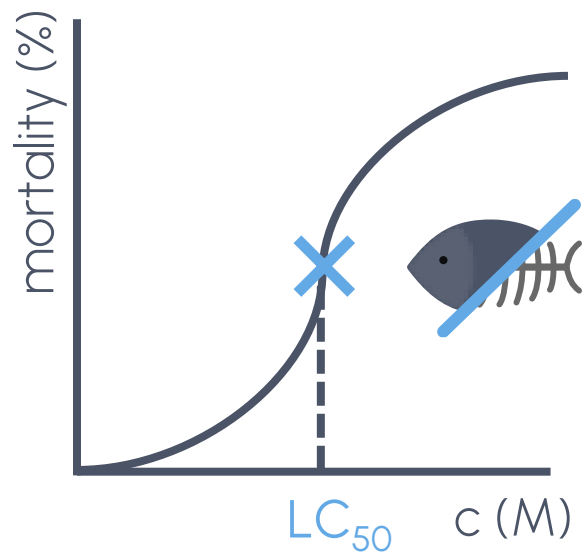
Slope = Response factor

TOXICITY PREDICTION

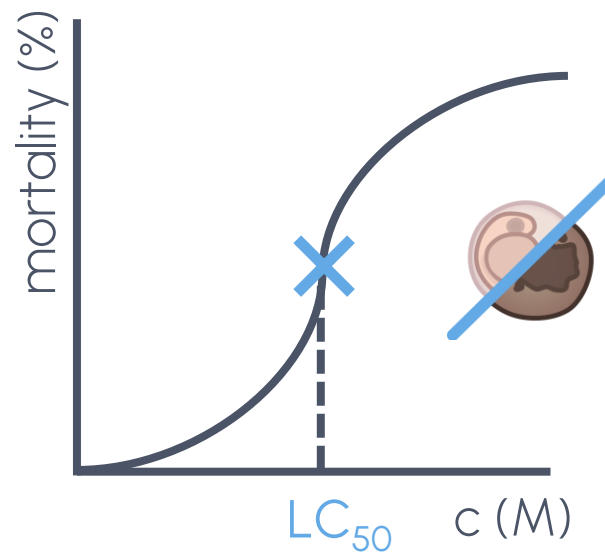


Adult fish toxicity
Peets et al. 2023

TOXICITY PREDICTION

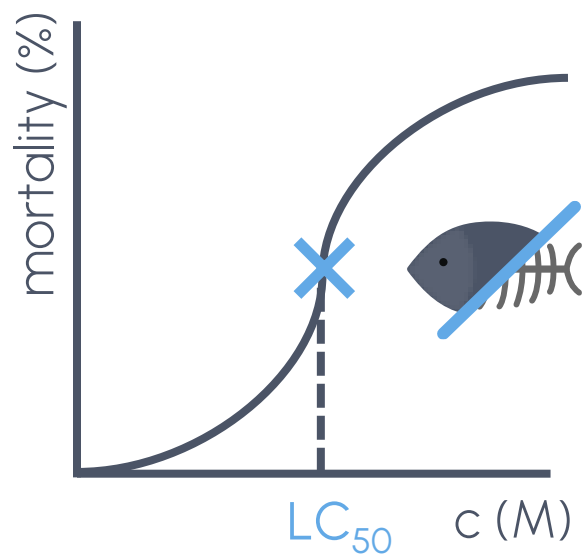


Adult fish toxicity
Peets et al. 2023

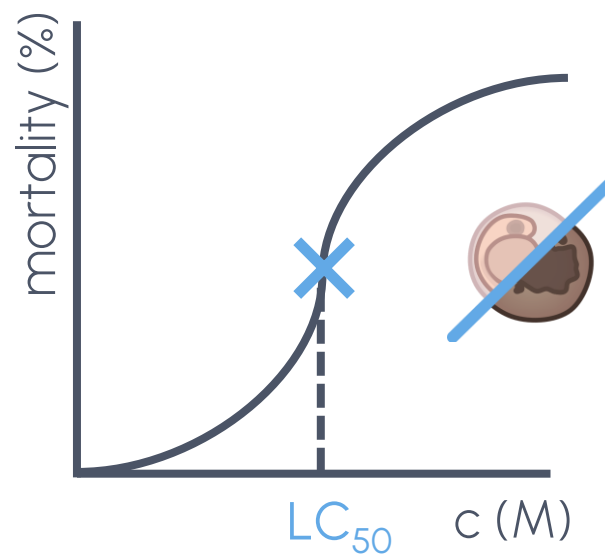


Fish embryo toxicity
Sepman et al. unpublished

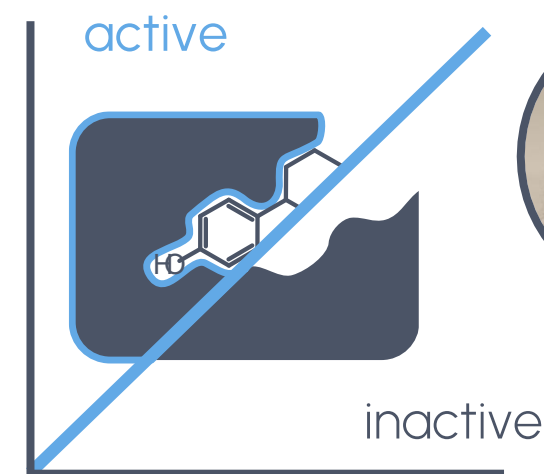
TOXICITY PREDICTION



Adult fish toxicity
Peets et al. 2023



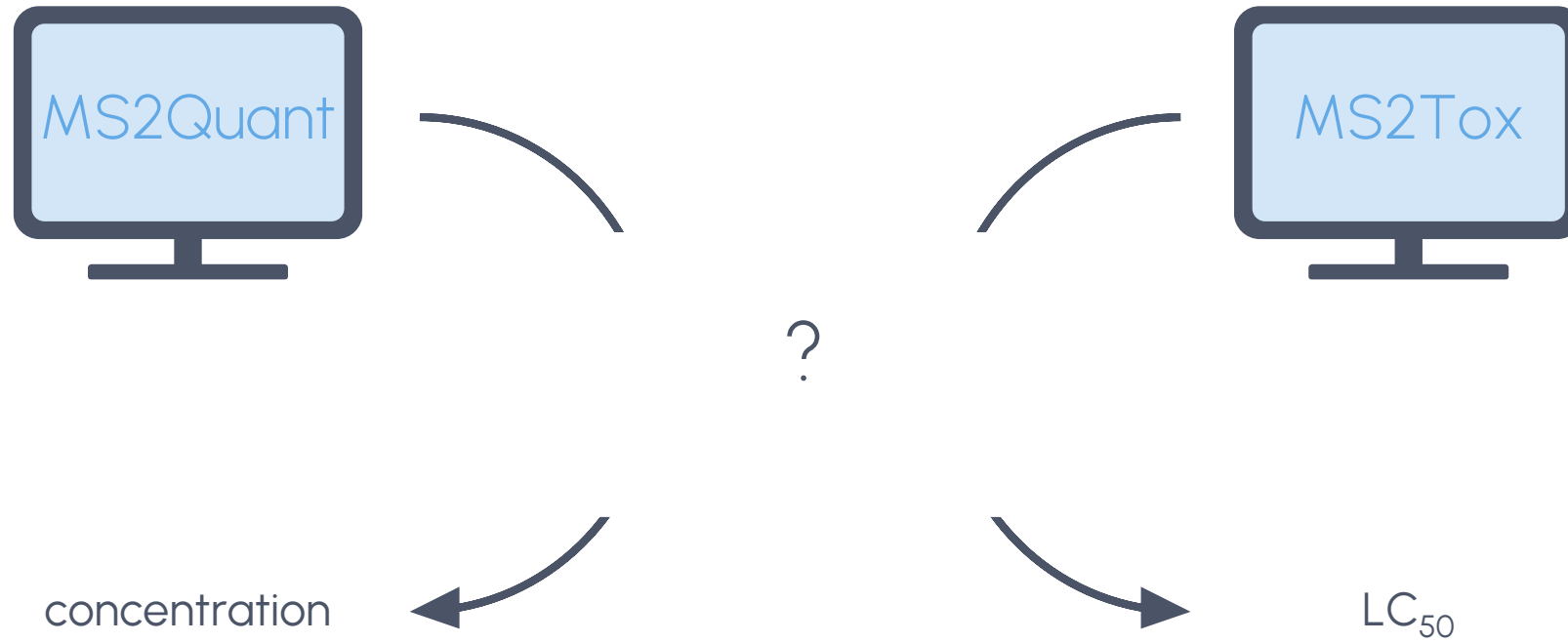
Fish embryo toxicity
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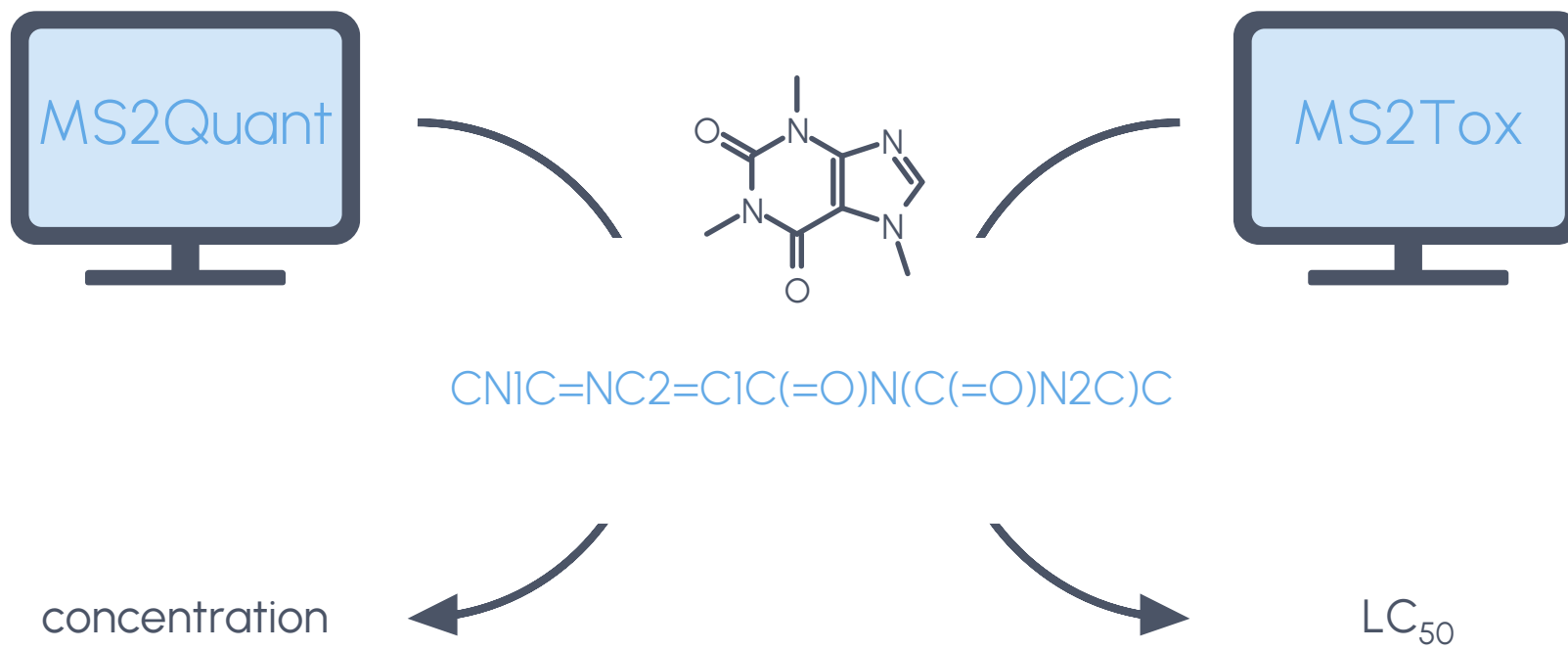
Bioassay activity
Rahu et al. 2024



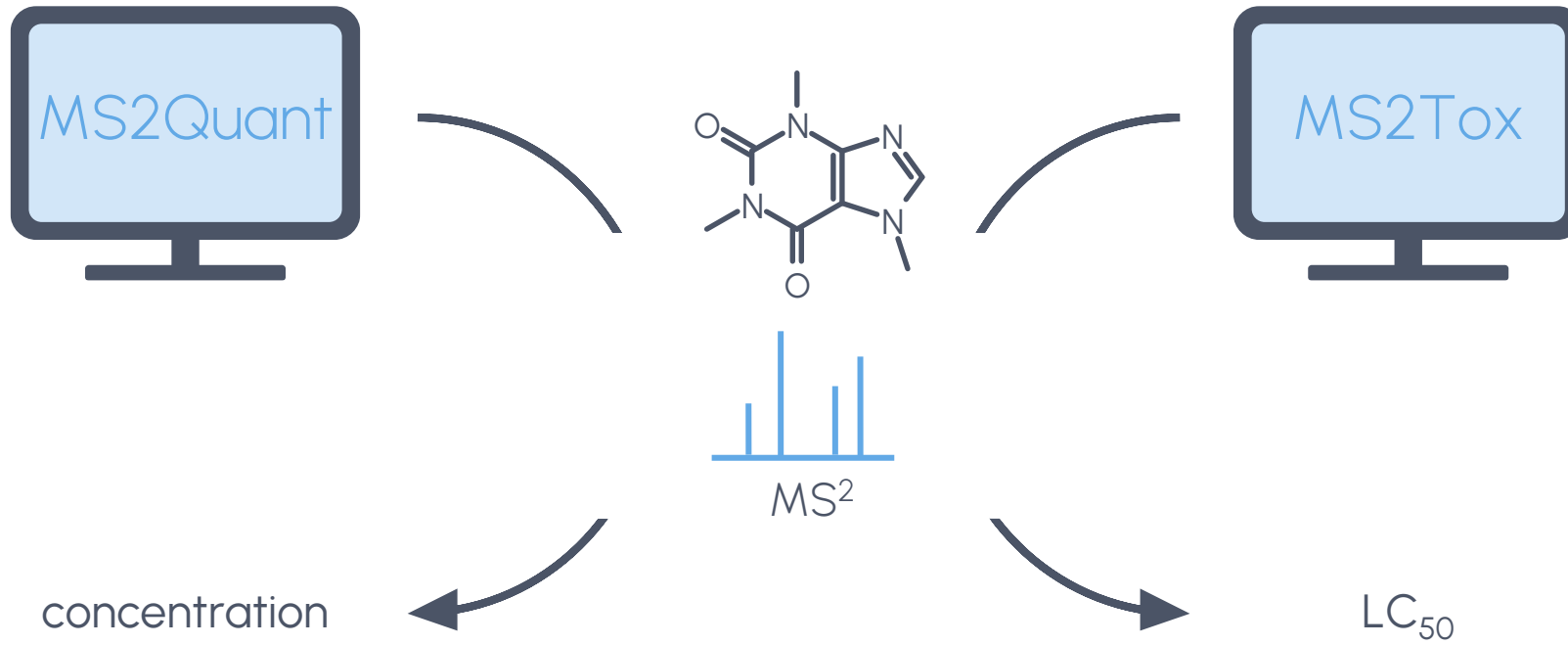
RISK PREDICTIONS



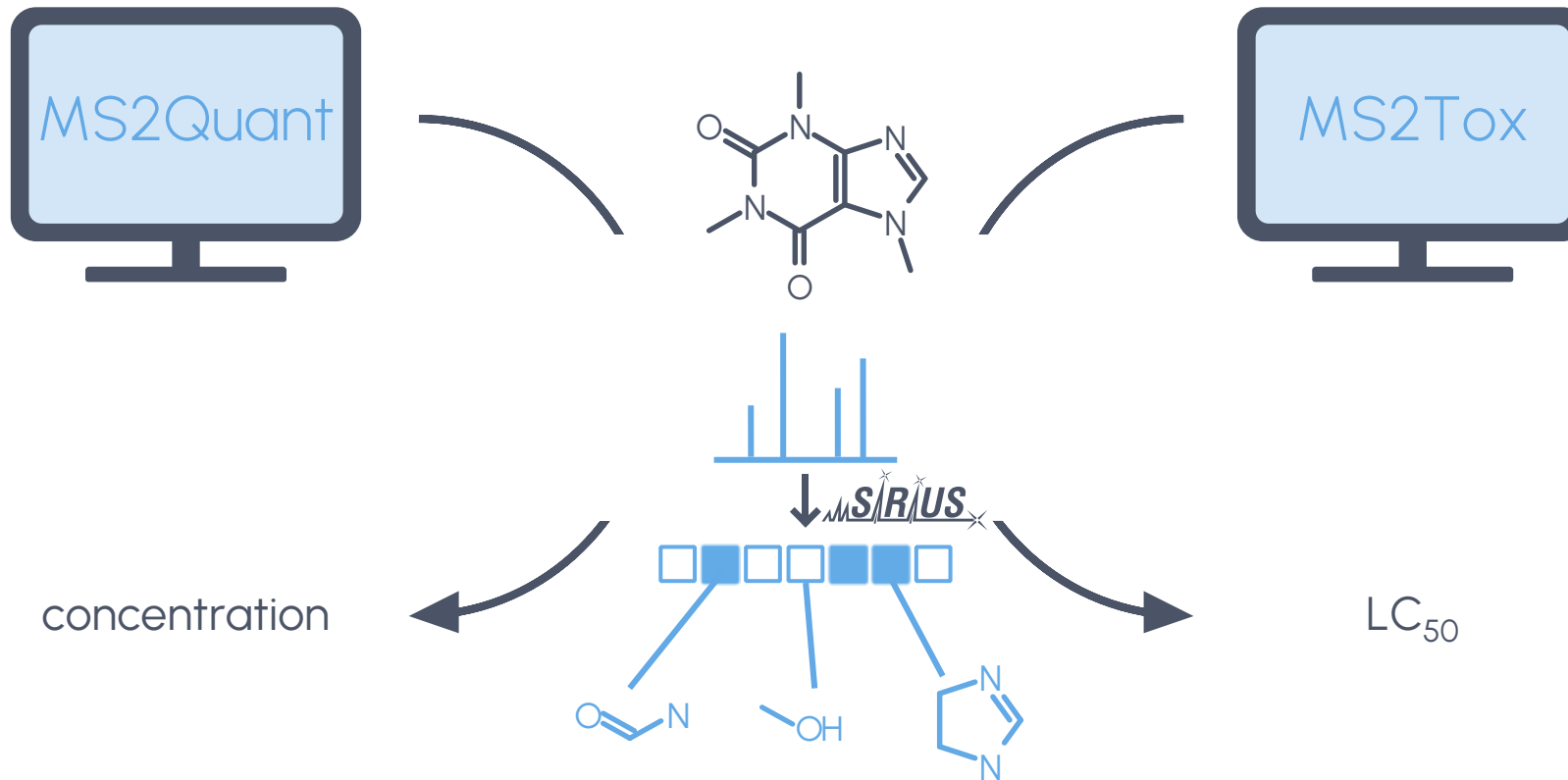
RISK PREDICTIONS



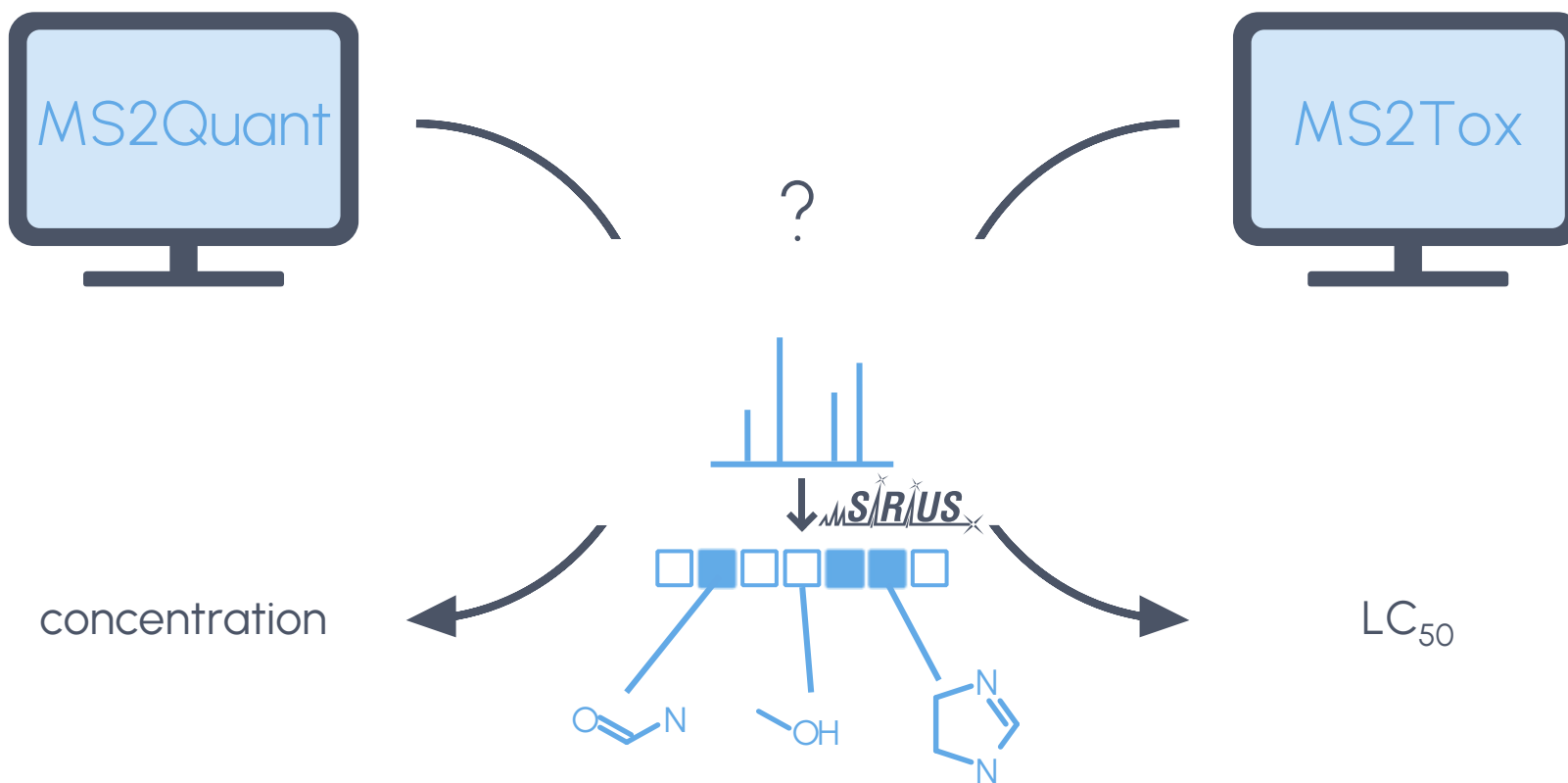
RISK PREDICTIONS



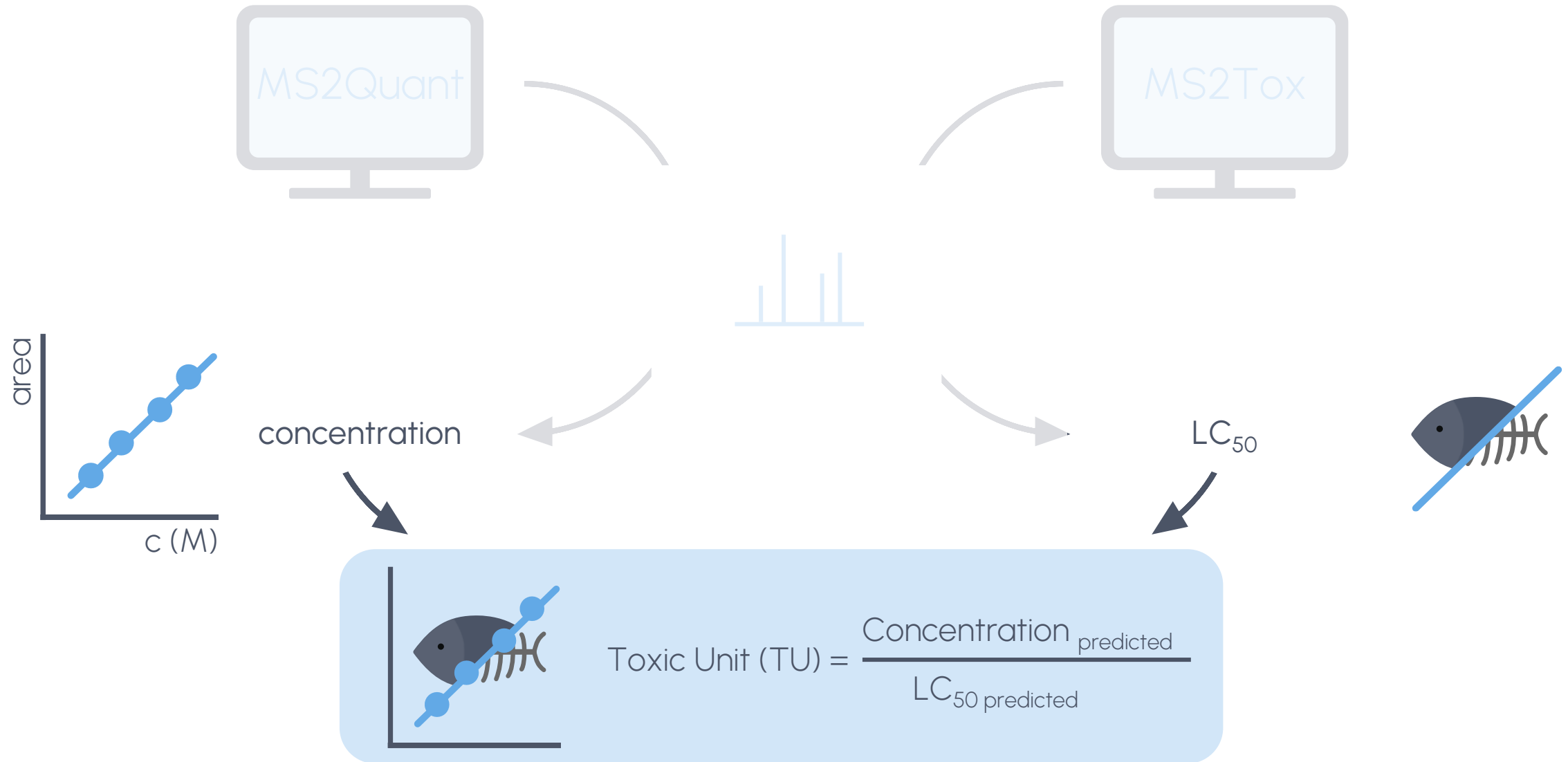
RISK PREDICTIONS



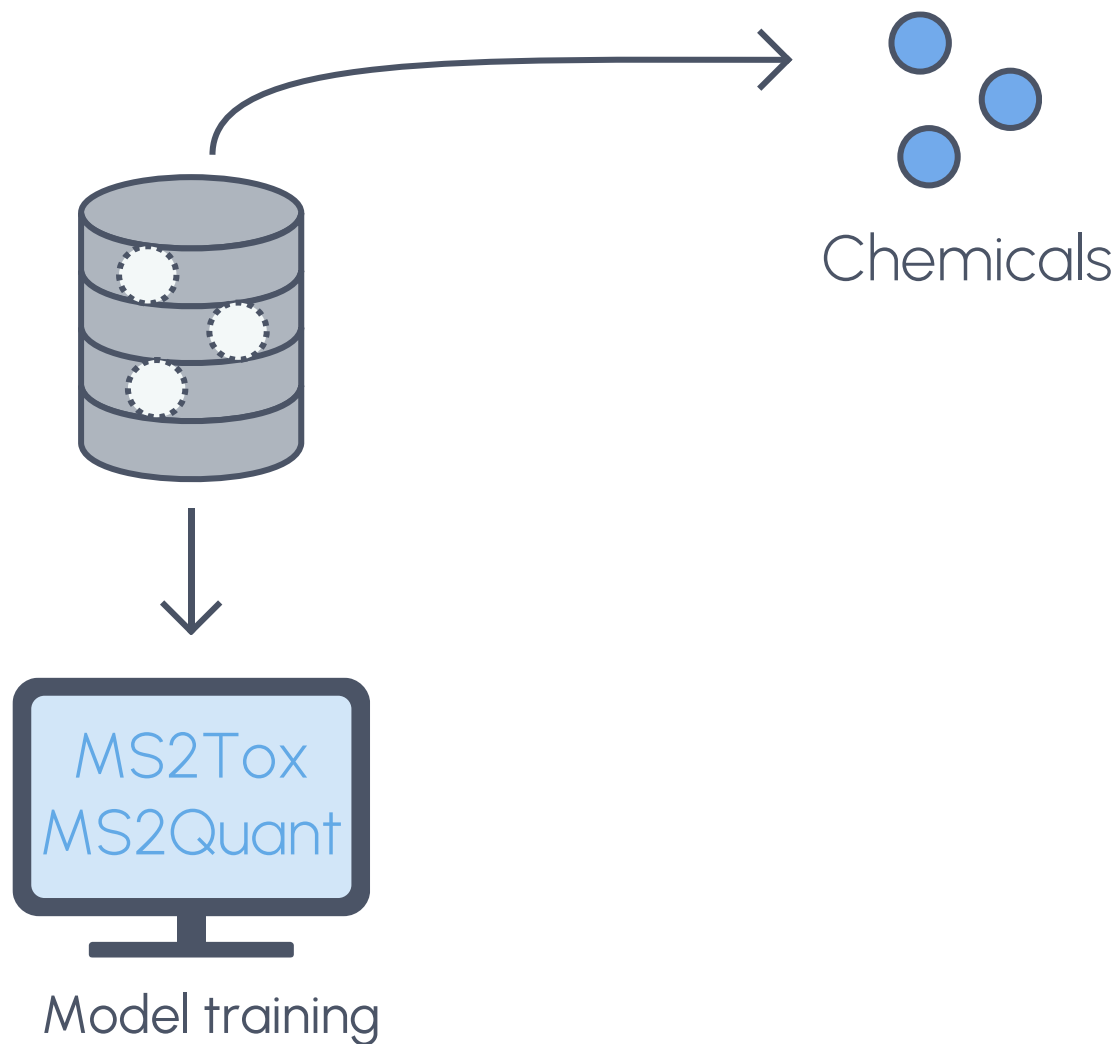
RISK PREDICTIONS



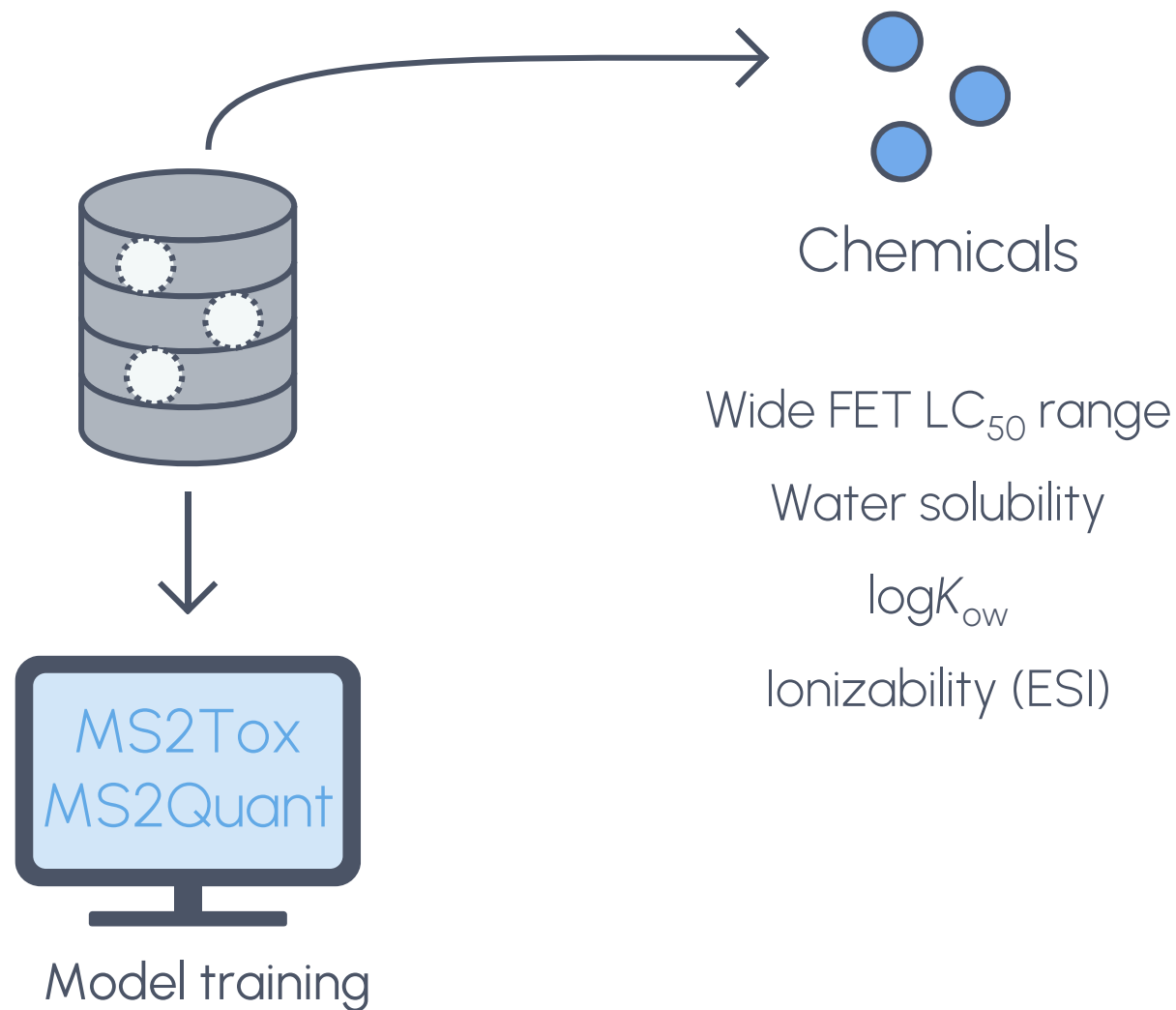
RISK PREDICTIONS



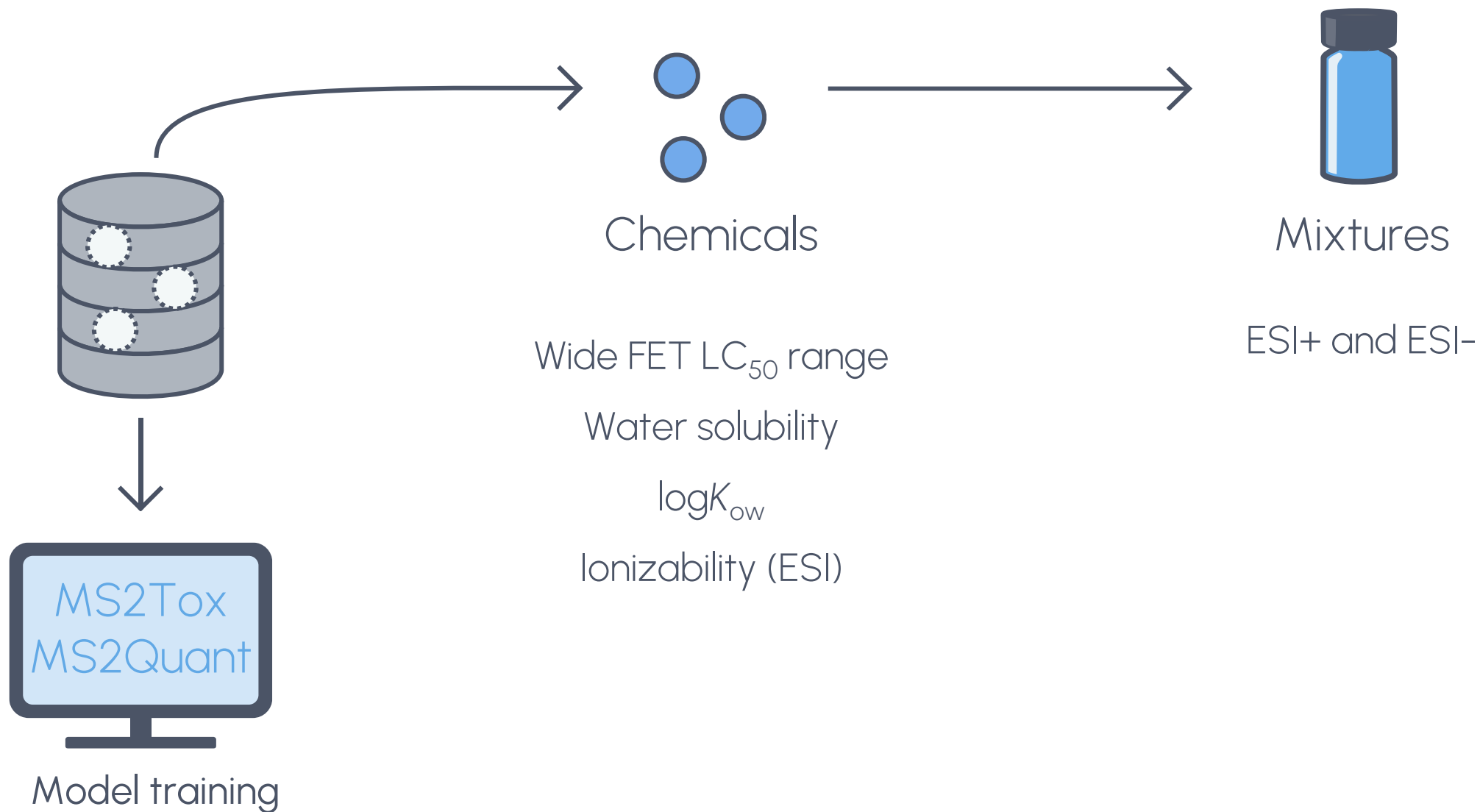
VALIDATION WORKFLOW



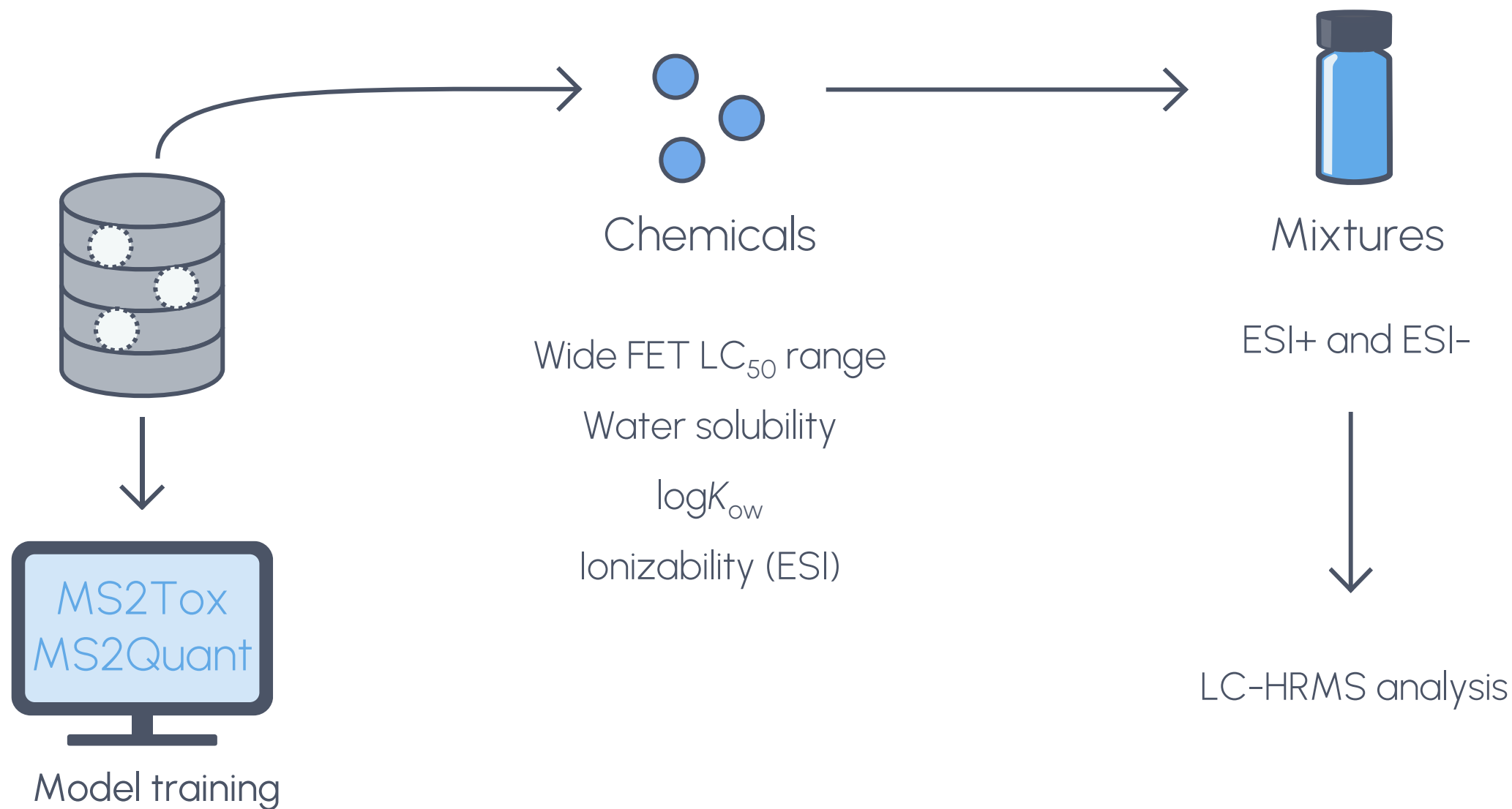
VALIDATION WORKFLOW



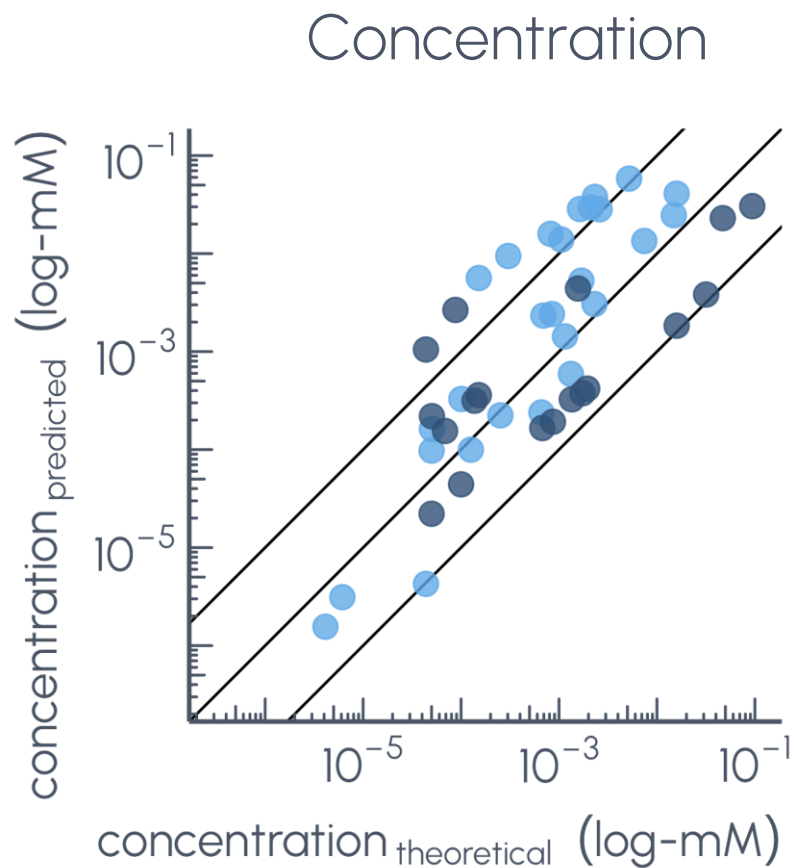
VALIDATION WORKFLOW



VALIDATION WORKFLOW

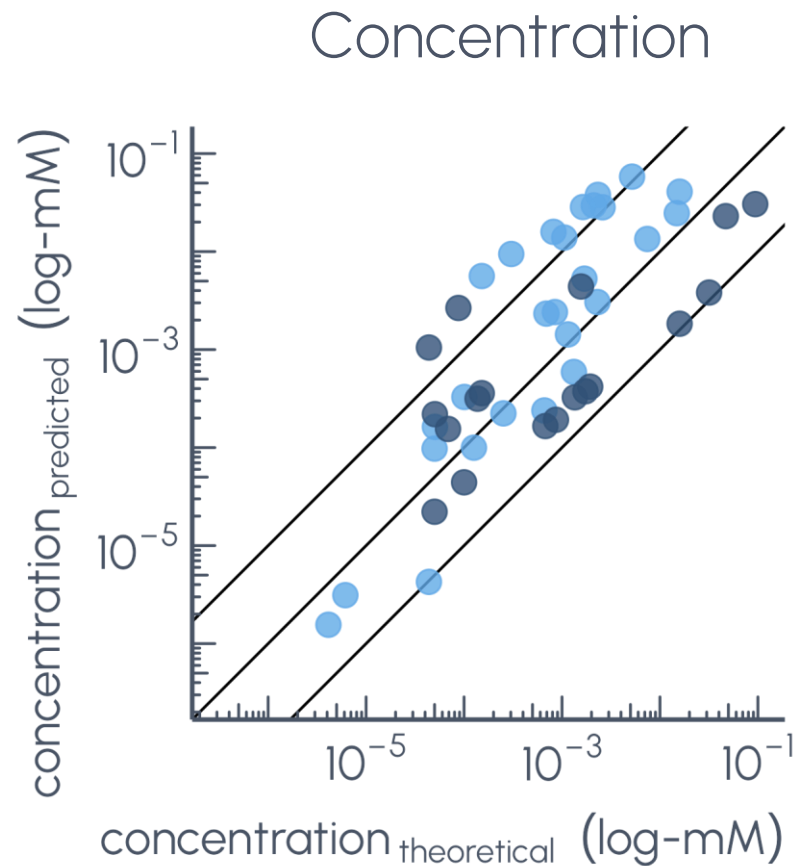


MS²-BASED PREDICTIONS

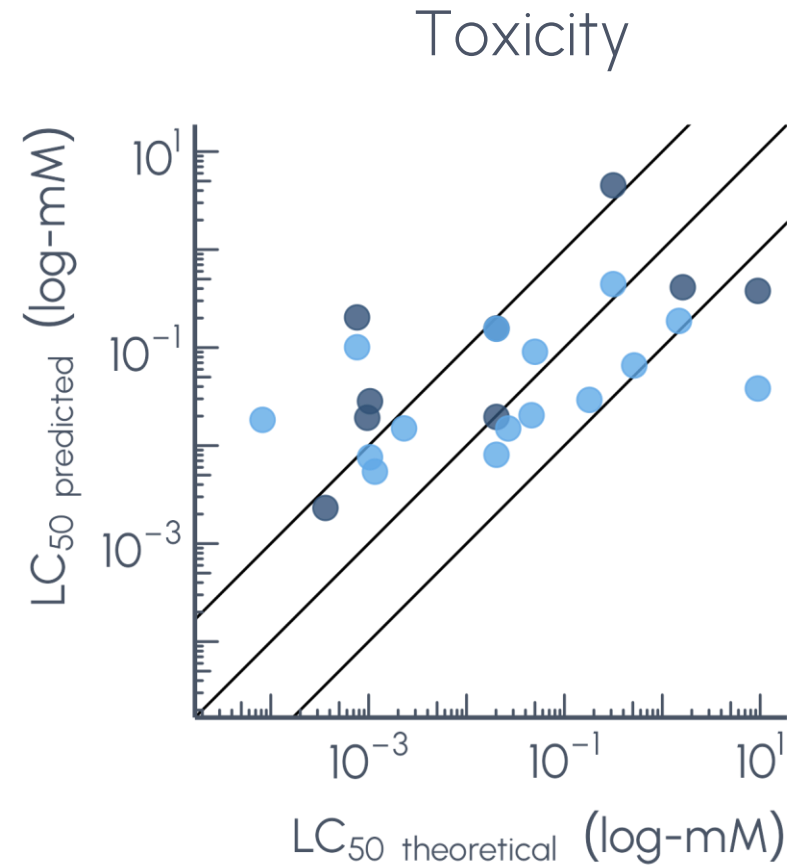


$$\begin{aligned} \text{RMSE}_{\text{ESI}+} &= 0.72 \text{ log-mM} & R^2_{\text{ESI}+} &= 0.71 \\ \text{RMSE}_{\text{ESI}-} &= 0.75 \text{ log-mM} & R^2_{\text{ESI}-} &= 0.50 \end{aligned}$$

MS²-BASED PREDICTIONS



$RMSE_{ESI+} = 0.72 \text{ log-mM}$ $R^2_{ESI+} = 0.71$
 $RMSE_{ESI-} = 0.75 \text{ log-mM}$ $R^2_{ESI-} = 0.50$

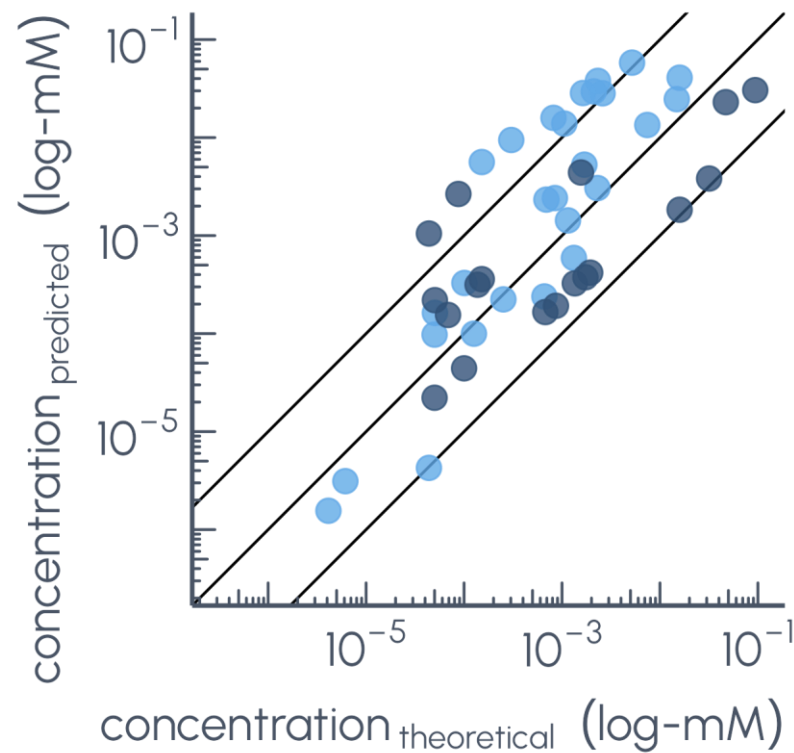


$RMSE_{ESI+} = 1.18 \text{ log-mM}$ $R^2_{ESI+} = 0.26$
 $RMSE_{ESI-} = 1.28 \text{ log-mM}$ $R^2_{ESI-} = 0.54$

MS²-BASED PREDICTIONS

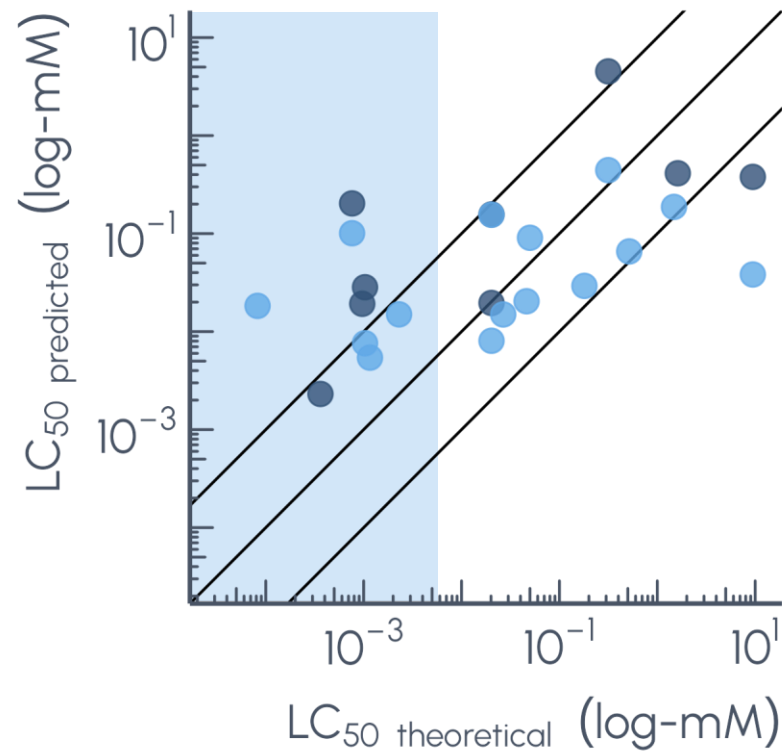


Concentration



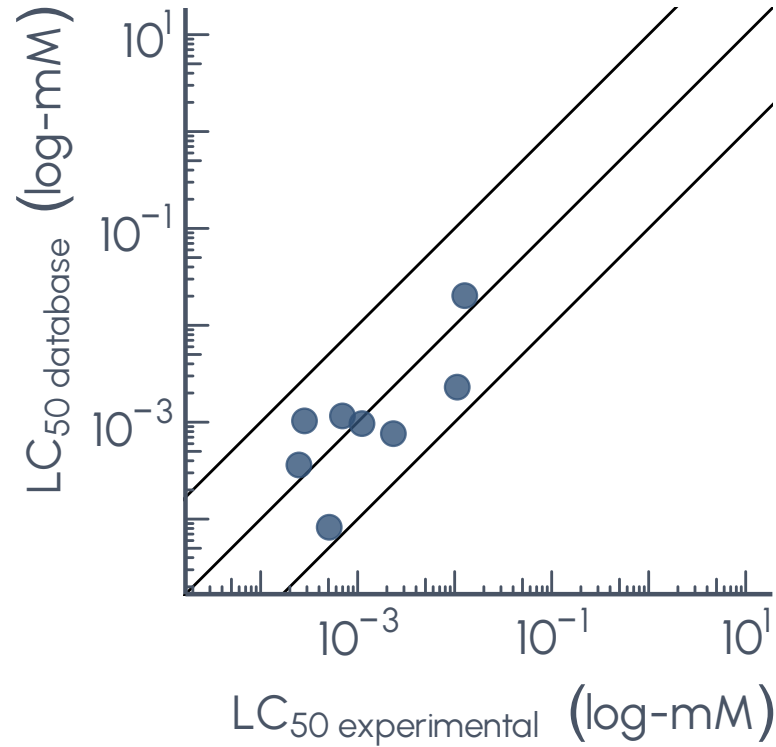
$RMSE_{ESI+} = 0.72 \text{ log-mM}$ $R^2_{ESI+} = 0.71$
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Toxicity



$RMSE_{ESI+} = 1.18 \text{ log-mM}$ $R^2_{ESI+} = 0.26$
 $RMSE_{ESI-} = 1.28 \text{ log-mM}$ $R^2_{ESI-} = 0.54$

EXPERIMENTAL TOXICITY (OECD TG 236)



RMSE = 0.47 log-Mm

$R^2 = 0.55$

VU

 $R^2 = 0.55$

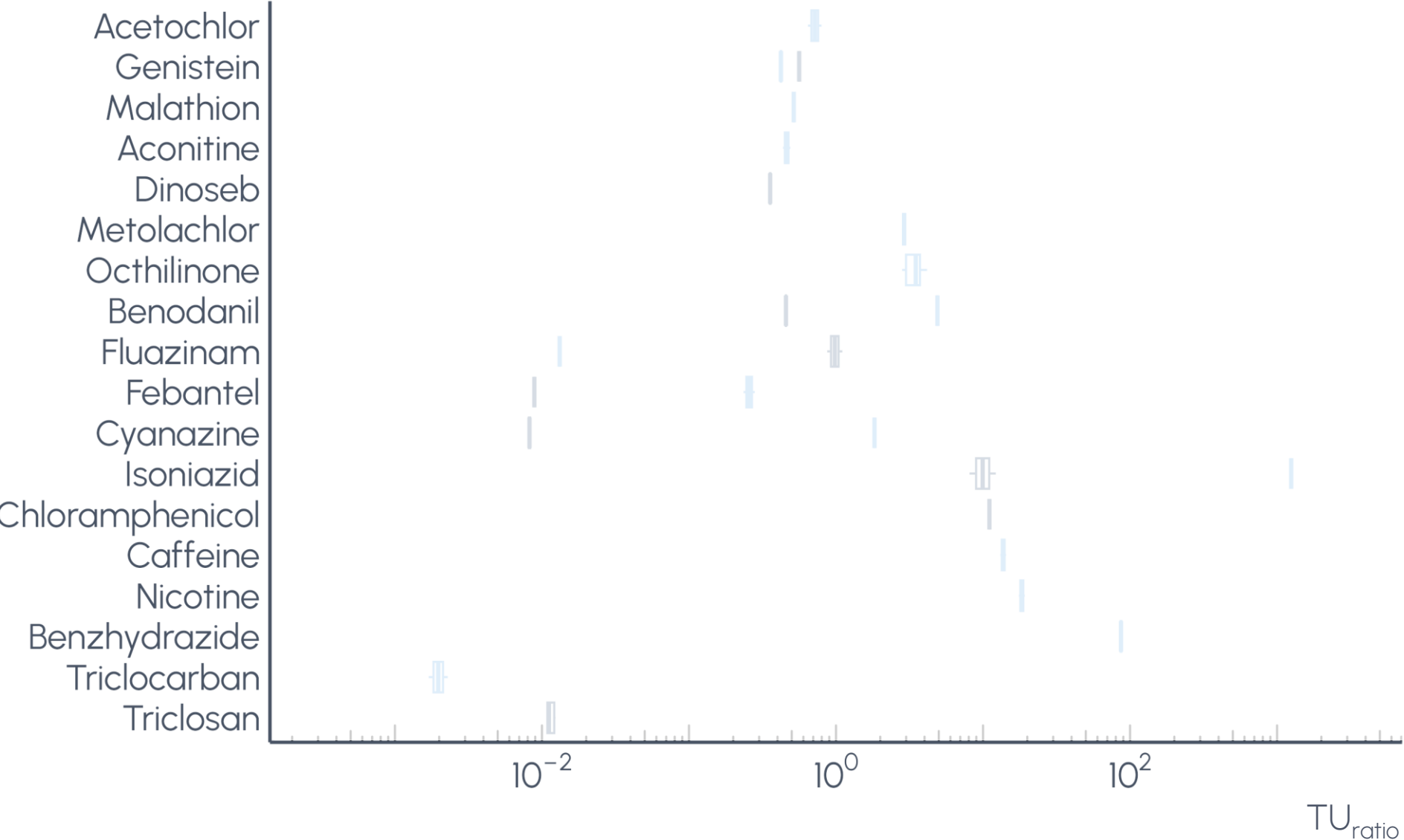
Toxicity can be difficult to model



PERFORMANCE – TU PREDICTED FROM MS²

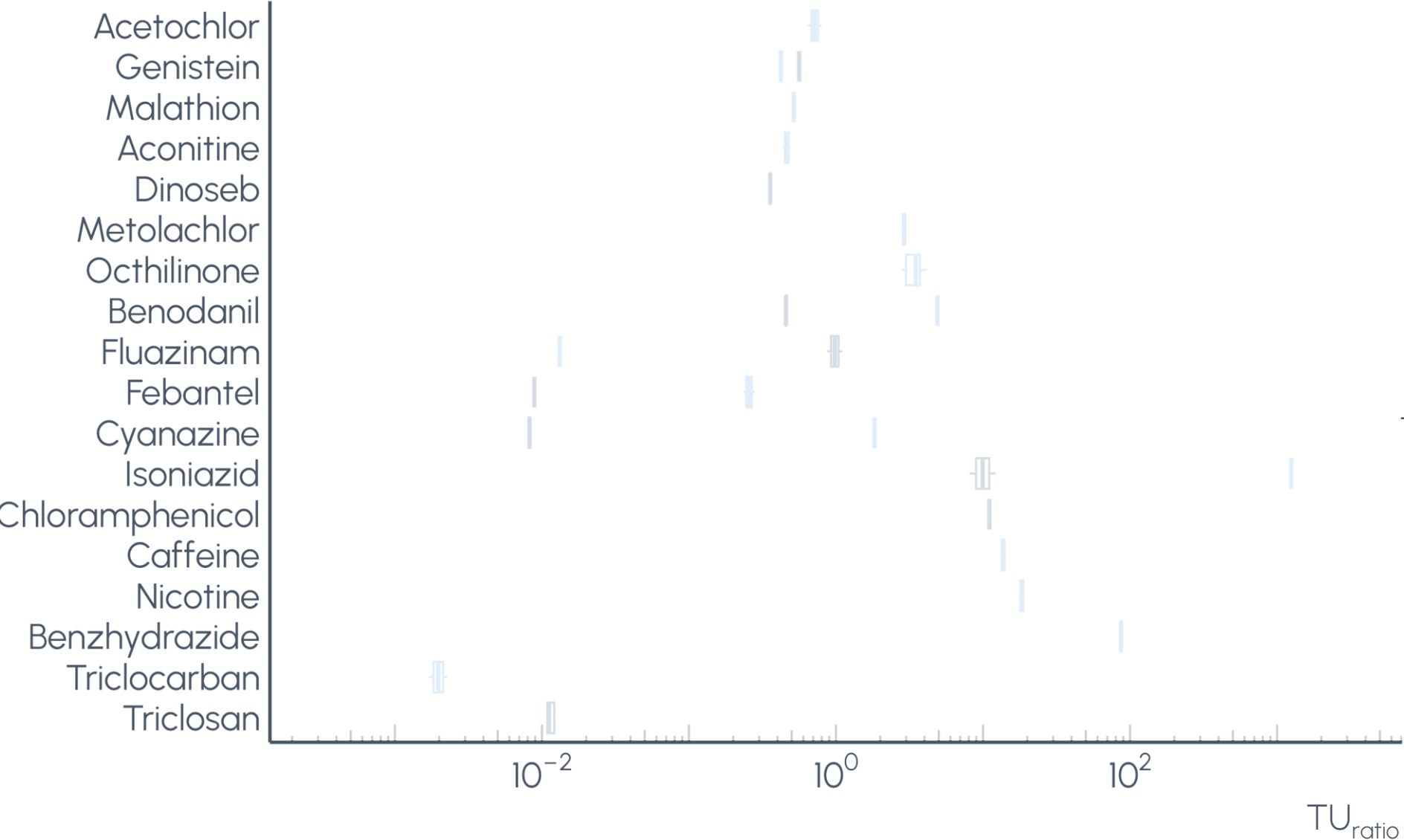
- ESI+
- ESI–

$$TU_{ratio} = \frac{TU_{predicted}}{TU_{theoretical}}$$



PERFORMANCE – TU PREDICTED FROM MS²

- ESI+
- ESI-



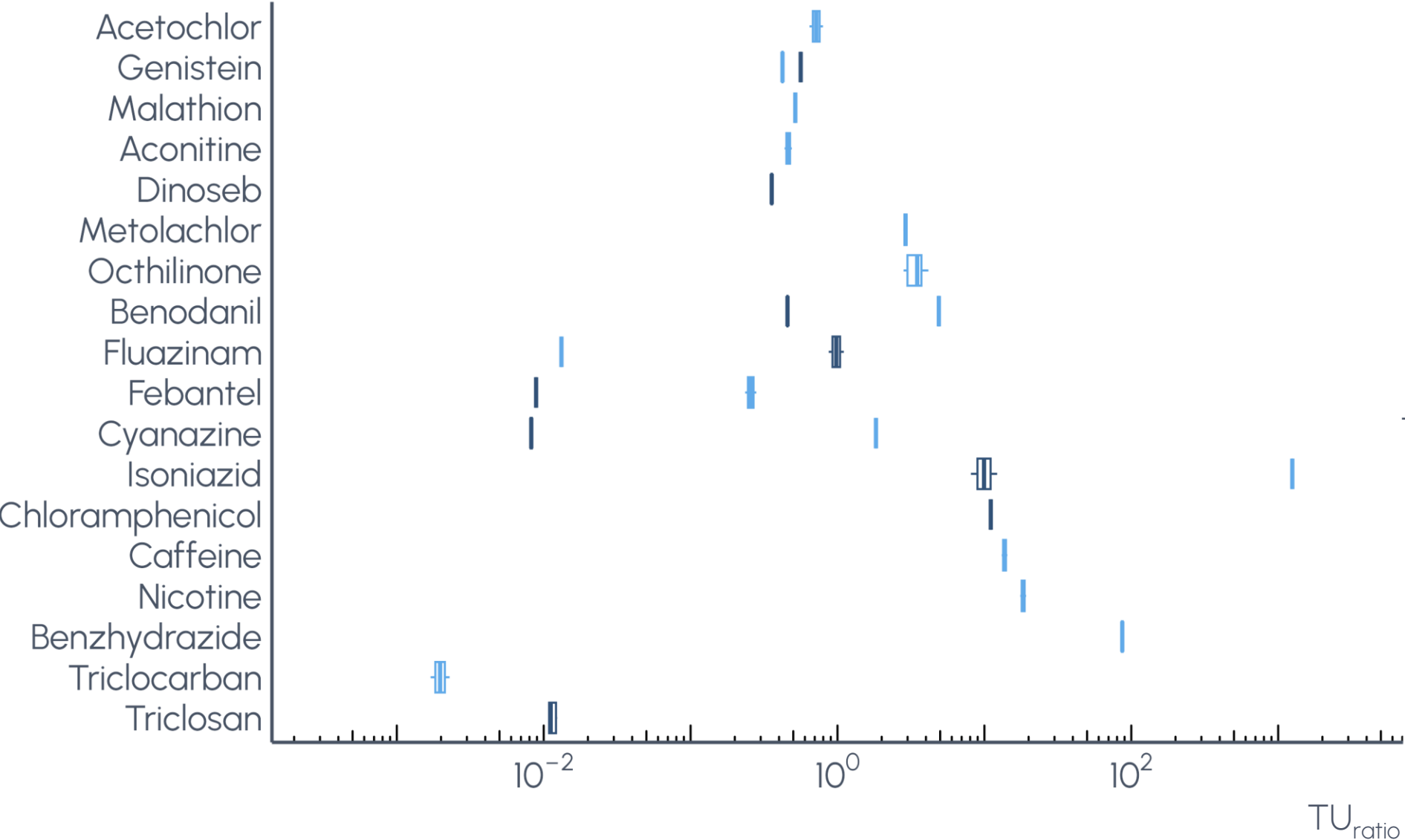
$$TU_{ratio} = \frac{TU_{predicted}}{TU_{theoretical}}$$

$$TU_{predicted} = \frac{conc_{predicted}}{LC_{50\ predicted}}$$

$$TU_{theoretical} = \frac{conc_{spiked}}{LC_{50\ database}}$$

PERFORMANCE – TU PREDICTED FROM MS²

- ESI+
- ESI-



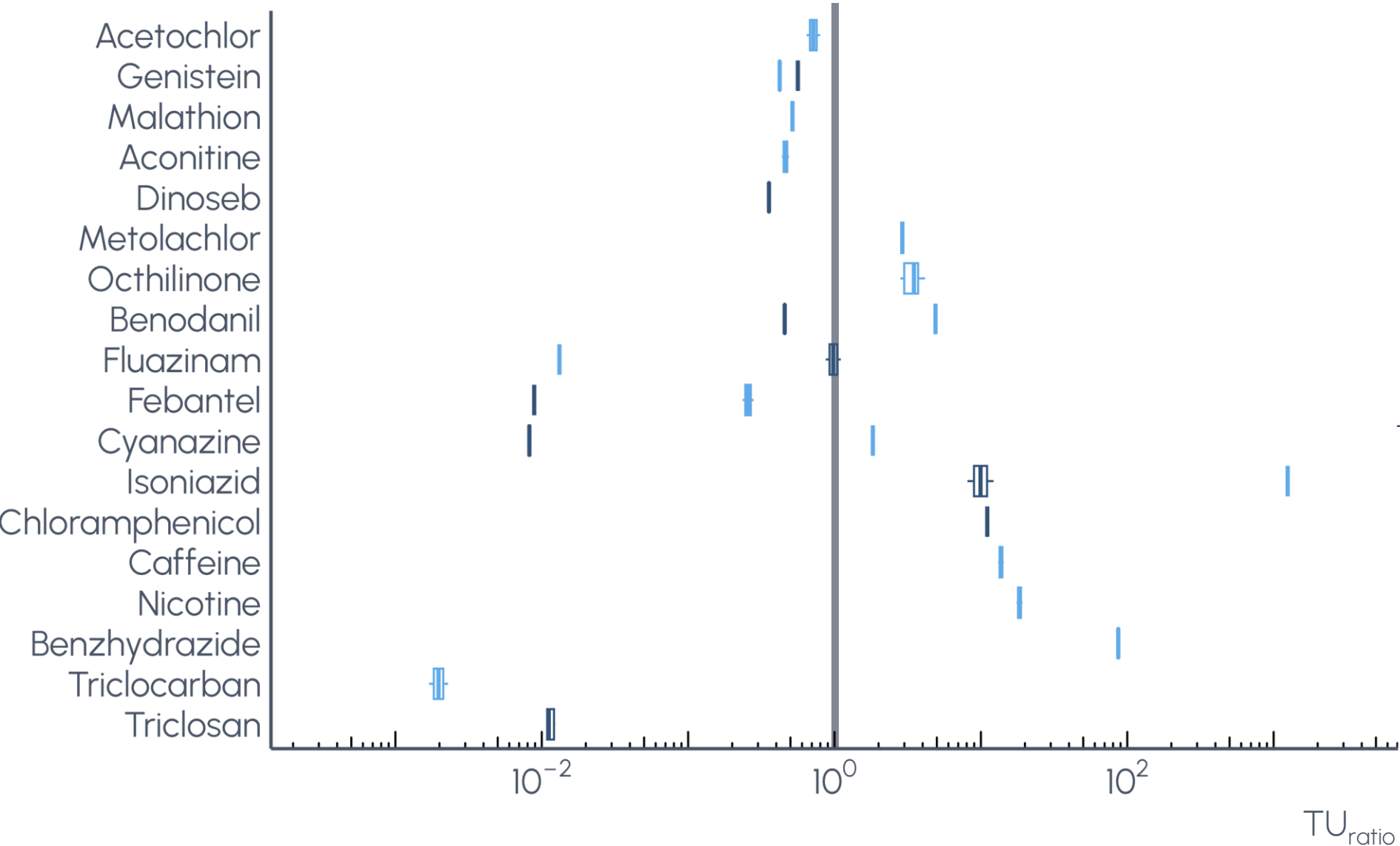
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PERFORMANCE – TU PREDICTED FROM MS²

- ESI+
- ESI-



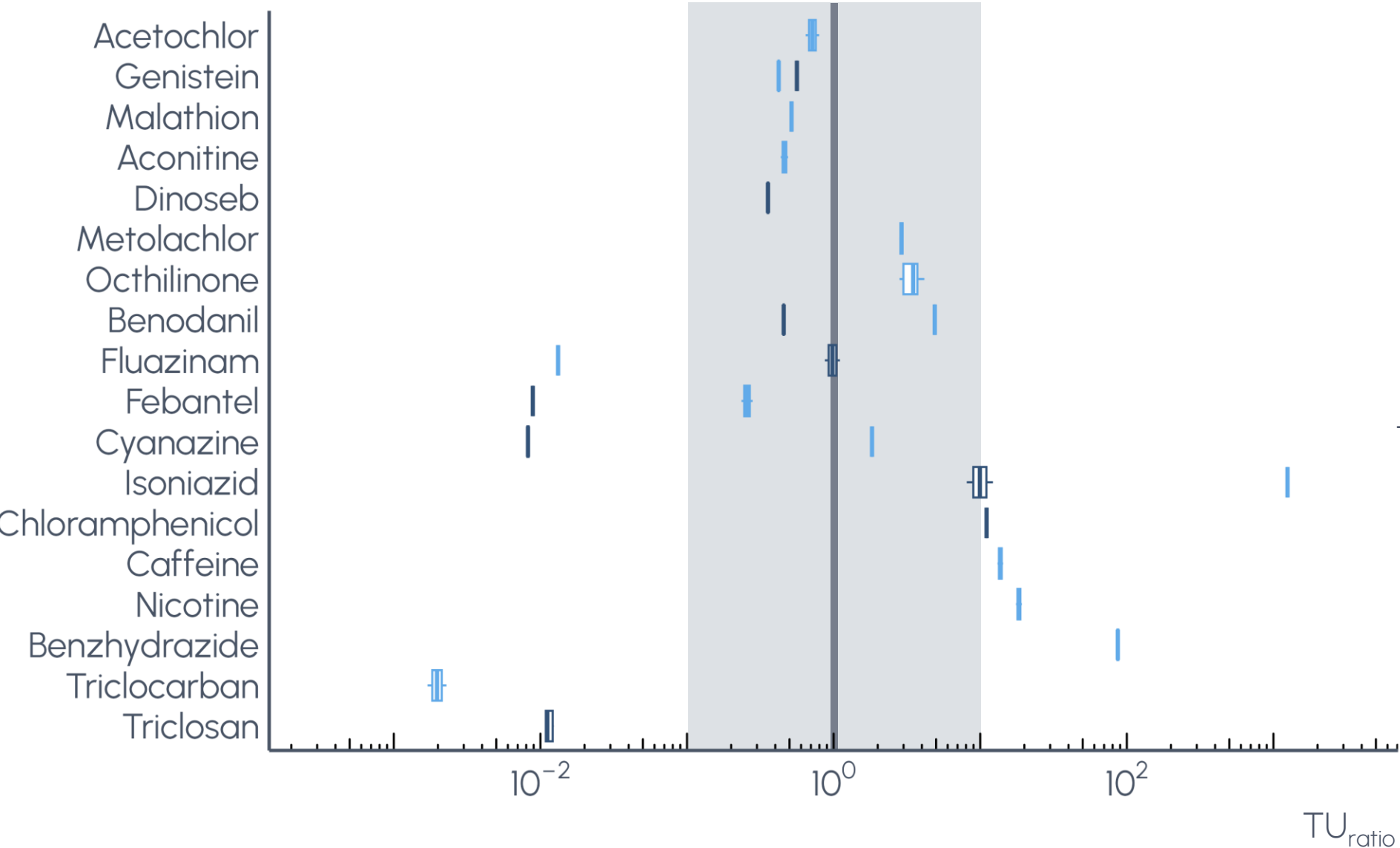
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PERFORMANCE – TU PREDICTED FROM MS²

- ESI+
- ESI-



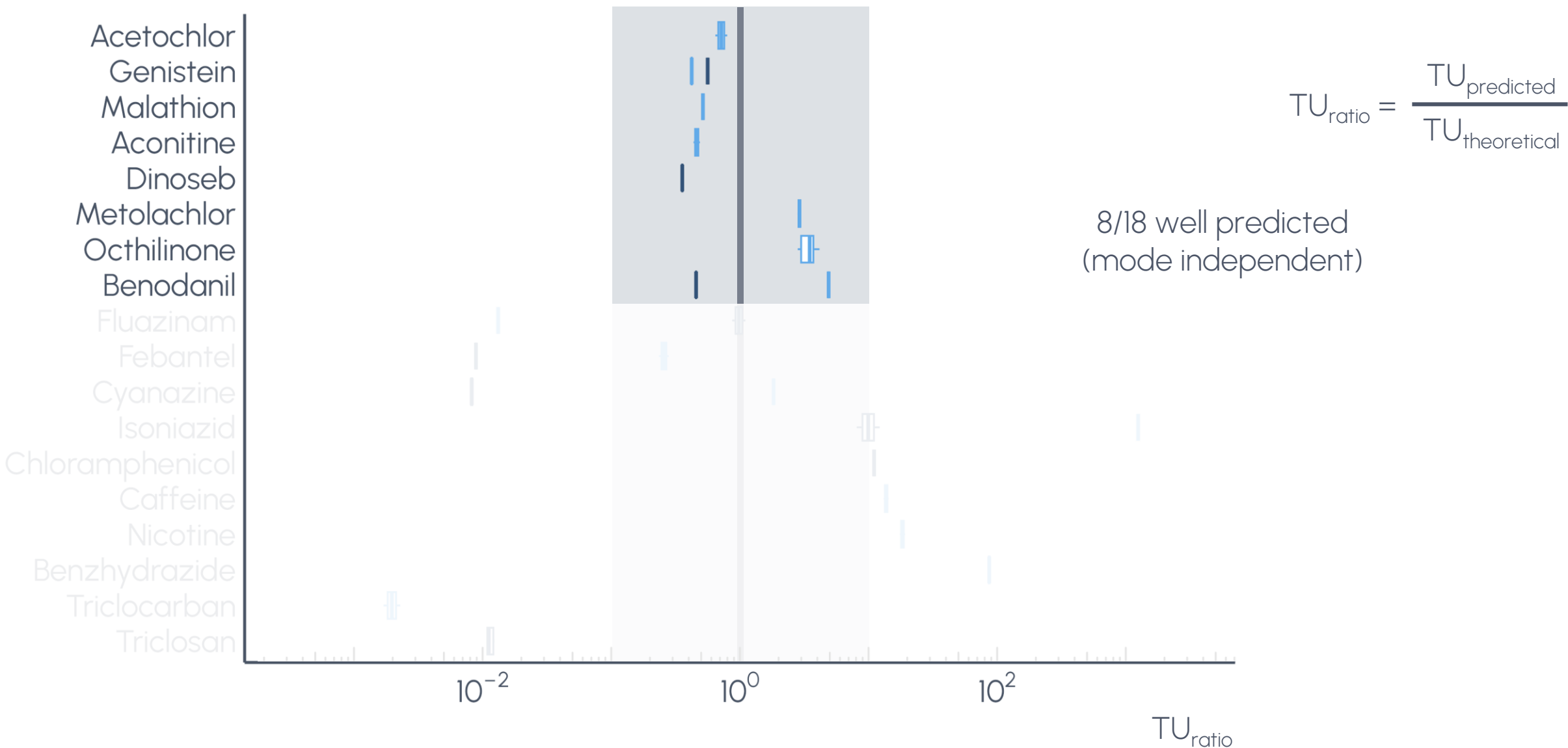
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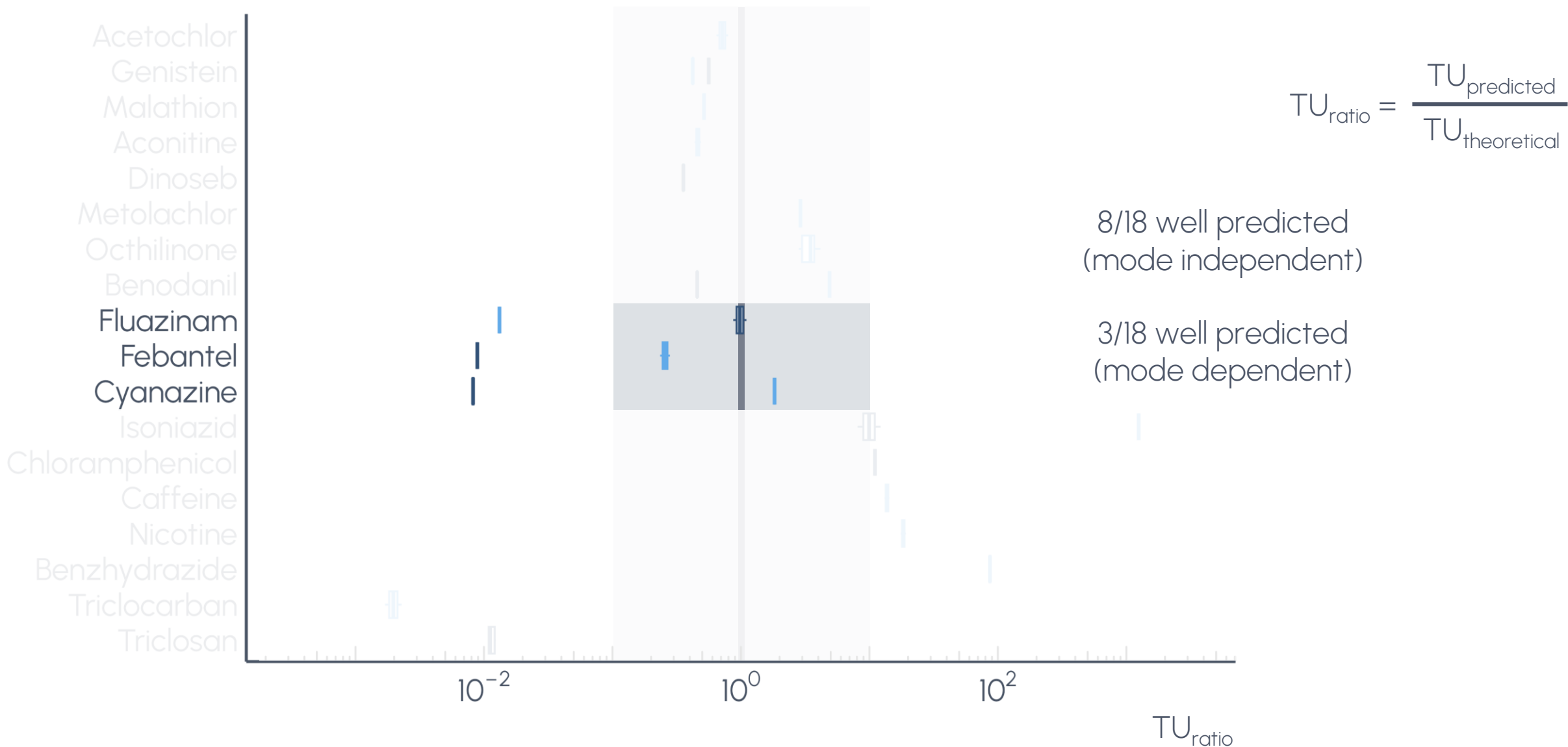
PERFORMANCE – TU PREDICTED FROM MS²

- ESI+
- ESI–



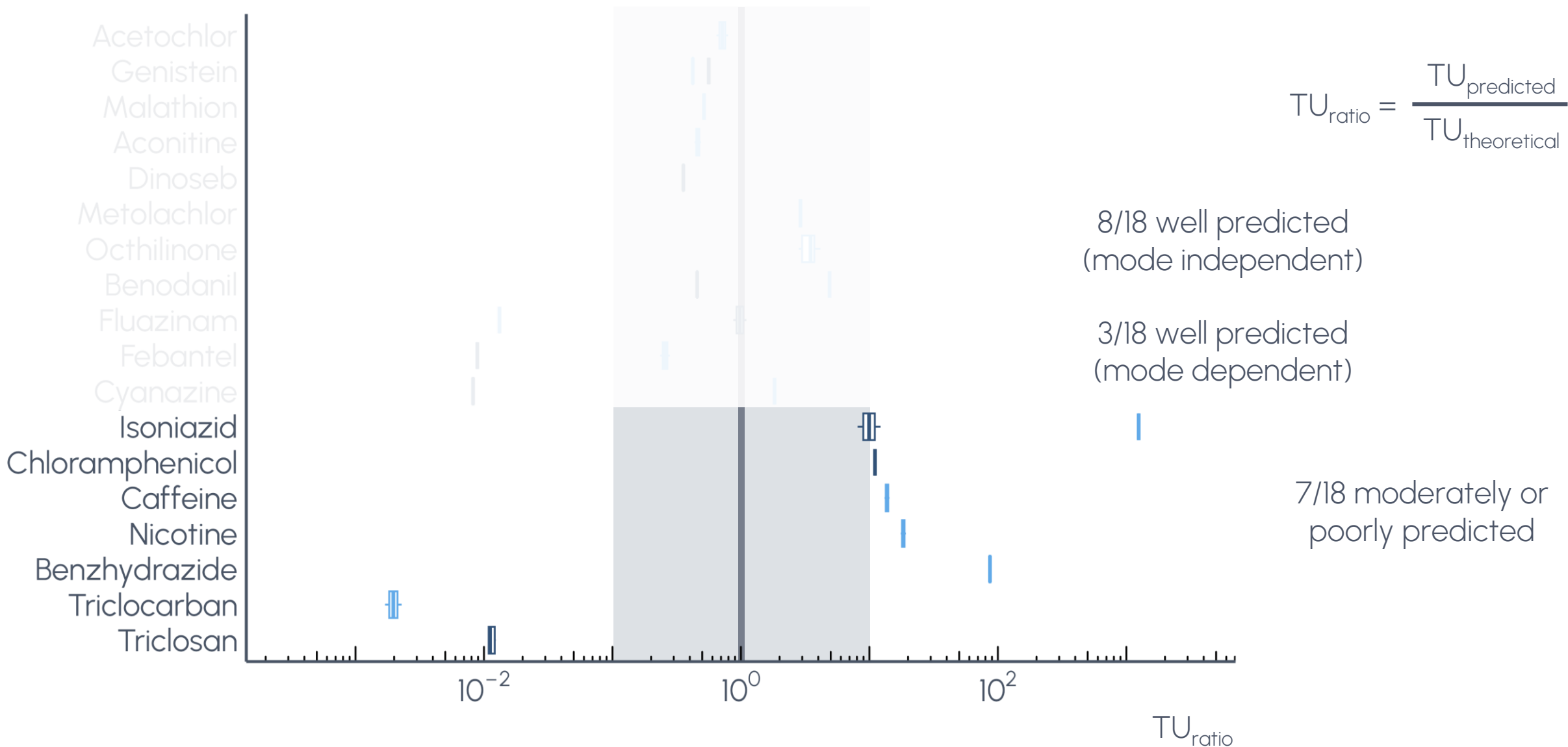
PERFORMANCE – TU PREDICTED FROM MS²

- ESI+
- ESI–



PERFORMANCE – TU PREDICTED FROM MS²

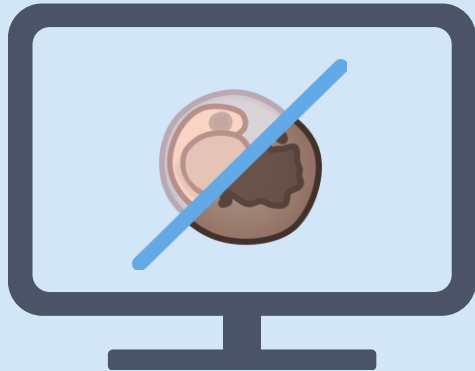
ESI+
ESI-



CONCLUSIONS AND FUTURE PROSPECTS

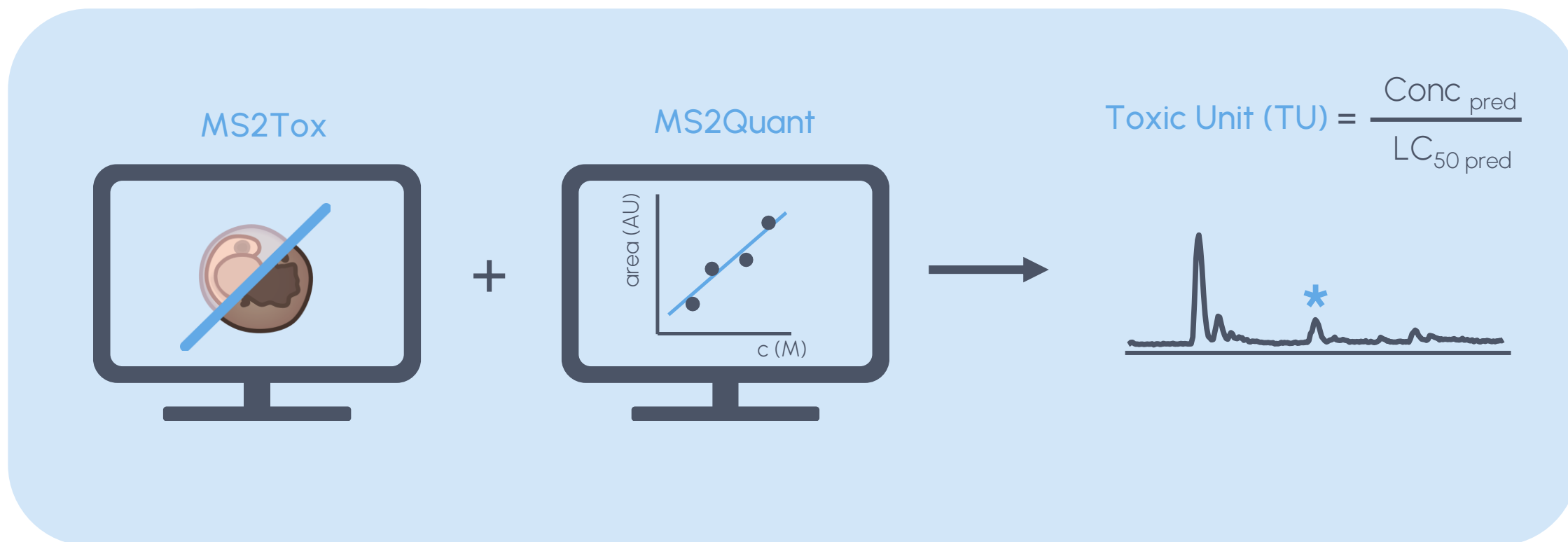
Fish Embryo
Toxicity model

MS2Tox



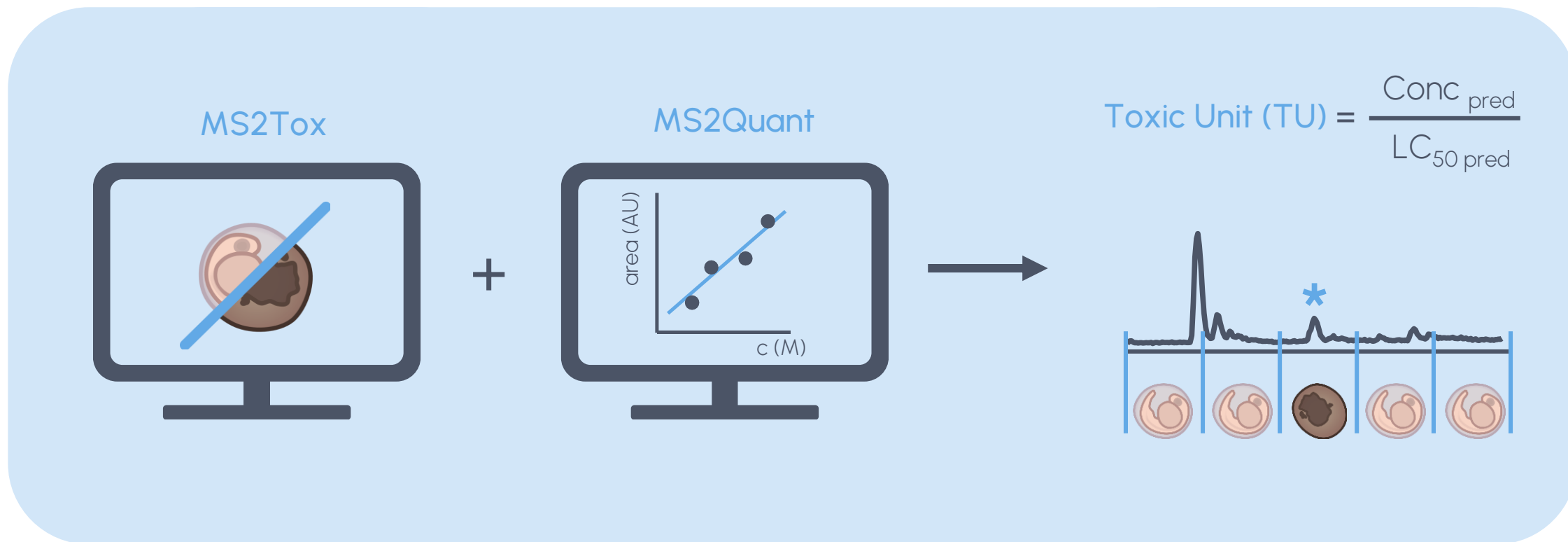
CONCLUSIONS AND FUTURE PROSPECTS

Prioritization



CONCLUSIONS AND FUTURE PROSPECTS

Effect-directed
analysis





Anneli Kruve, Frederic Béen, Lisa Baumann, Ingrida Bagdonaitė, Maria Margalef Jornet, Magnus Breitholtz, Jonathan Martin, Matthew MacLeod

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SUCCeSS - Stockholm University Center for Circular and Sustainable Systems

FORMAS RapMixTox #2021-01511

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