toxicity predictions of unidentified chemicals in water by HRMS & ML: how and why?

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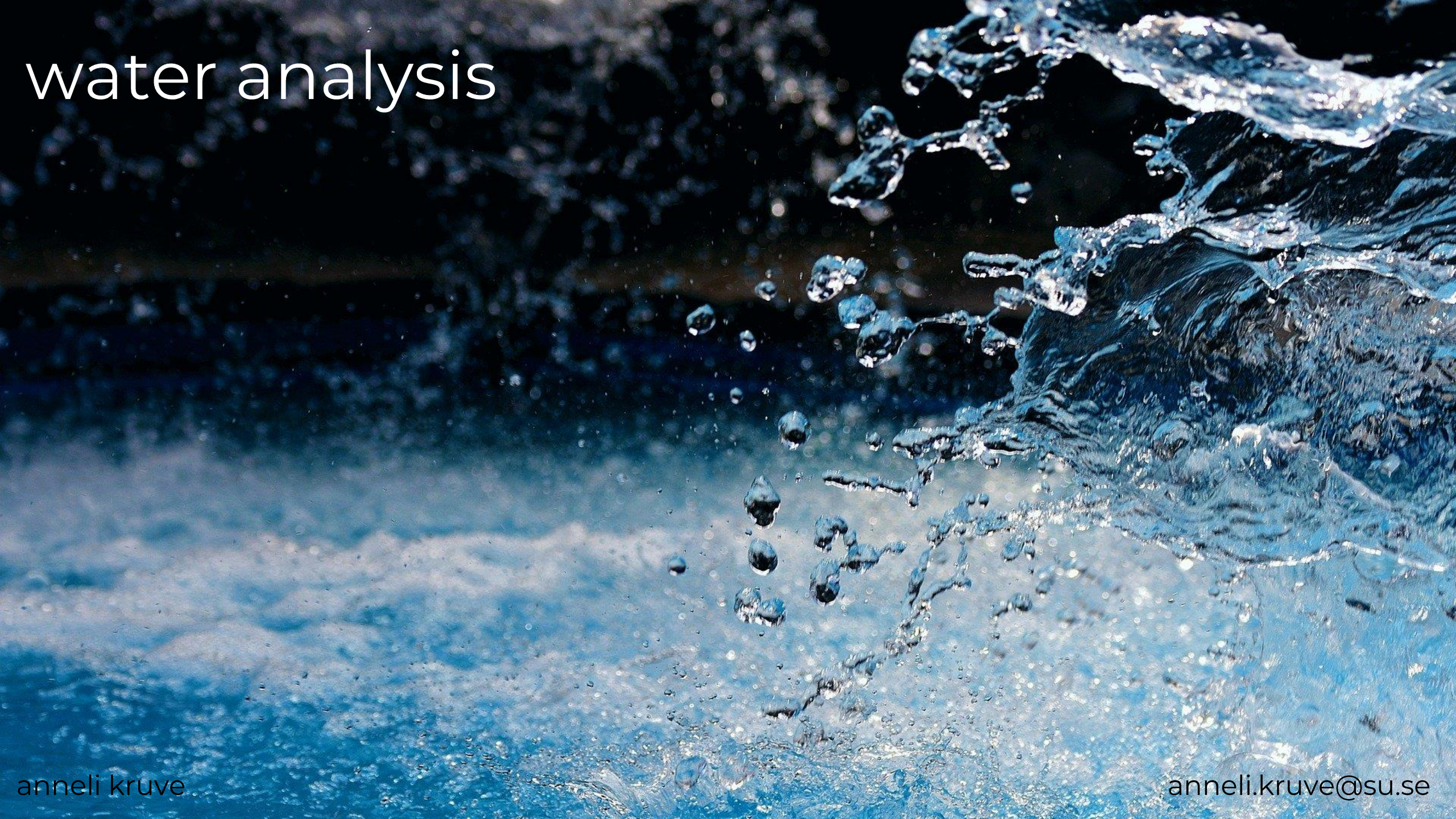
water analysis



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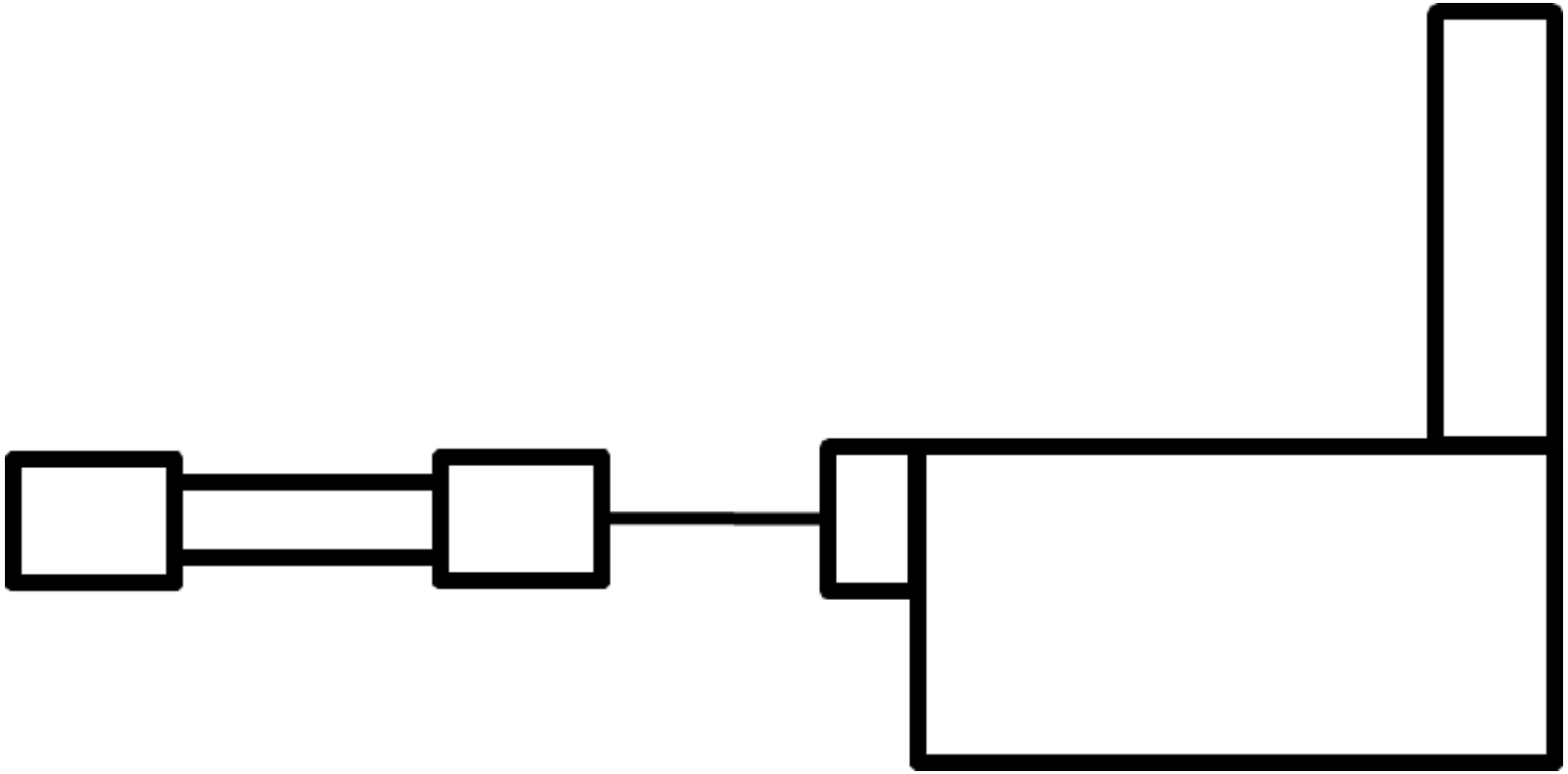
nontarget screening with LC/HRMS



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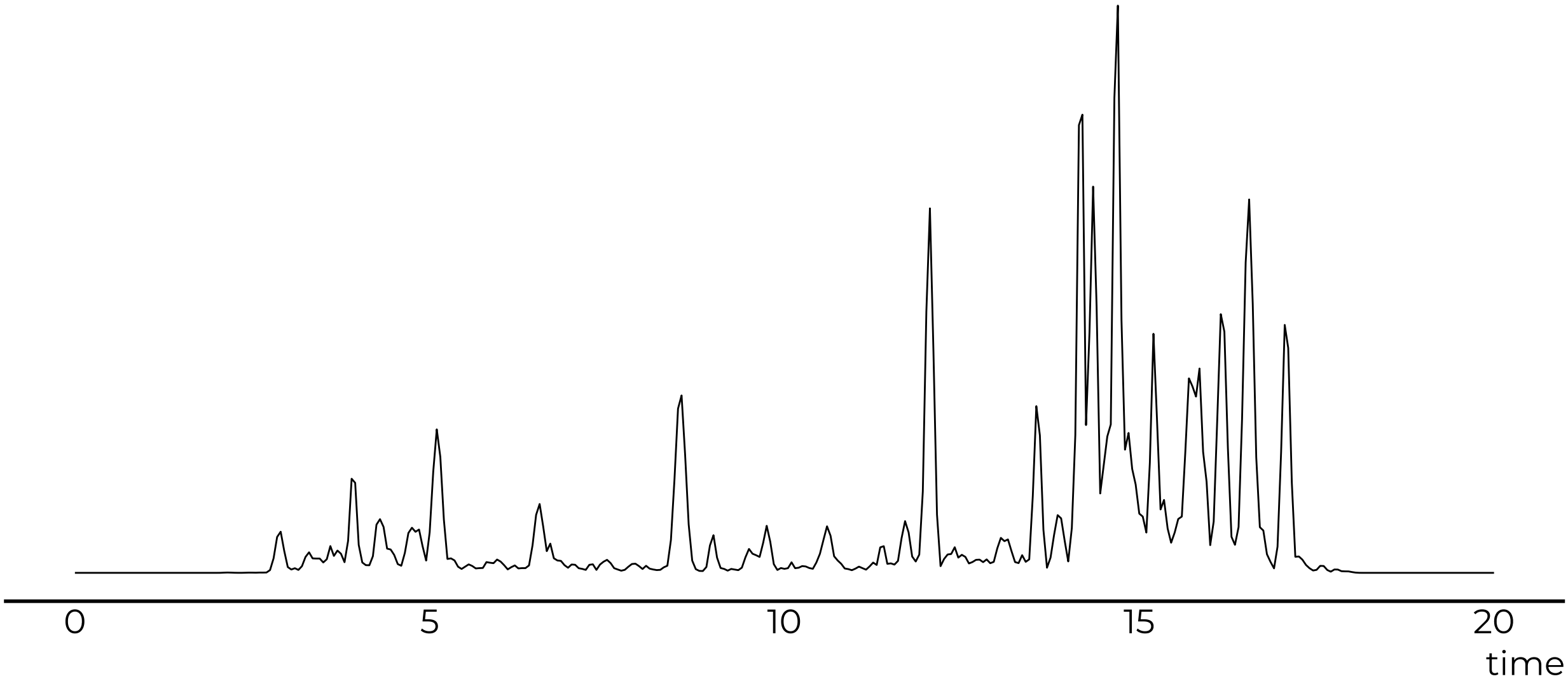
nontarget screening with LC/HRMS



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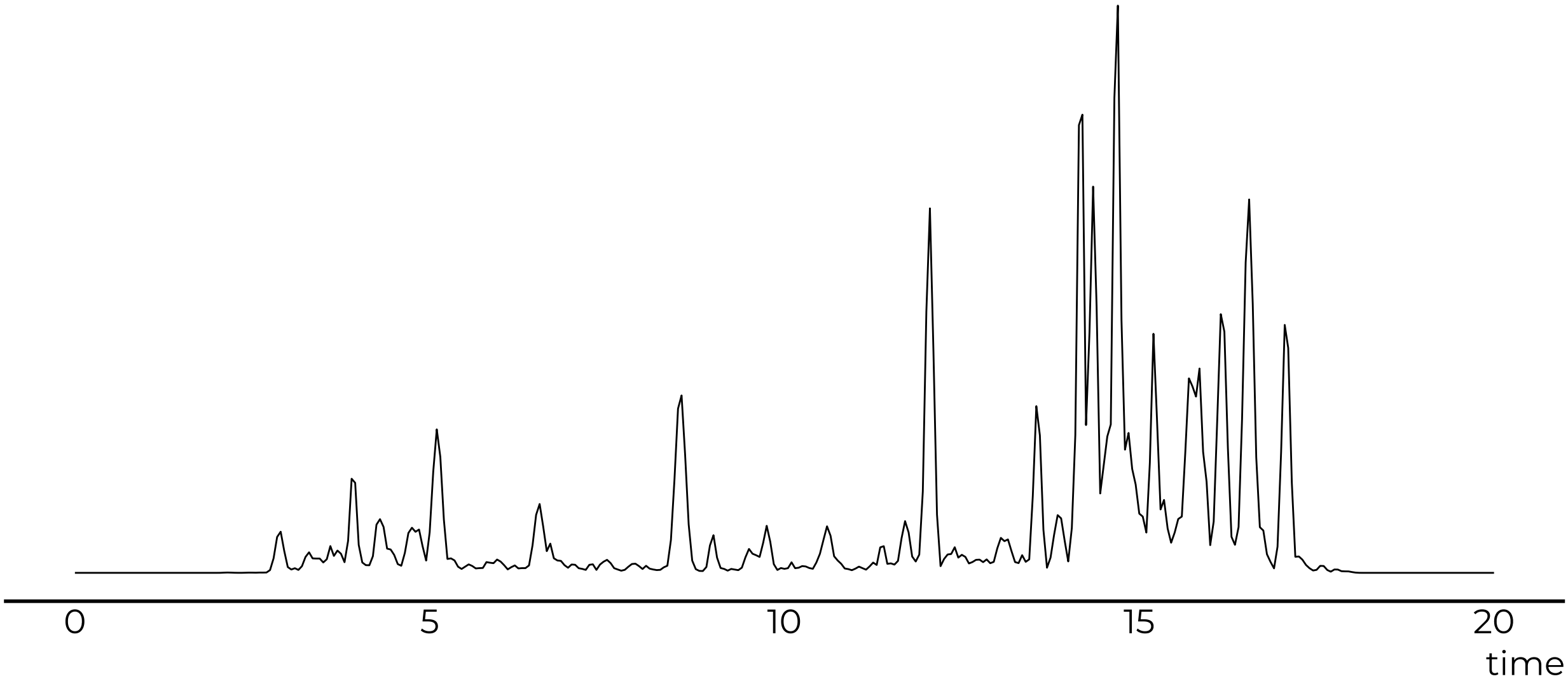
what next?



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prioritization

toxicity

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prioritization

toxicity

concentration

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prioritization

toxicity

concentration

risk

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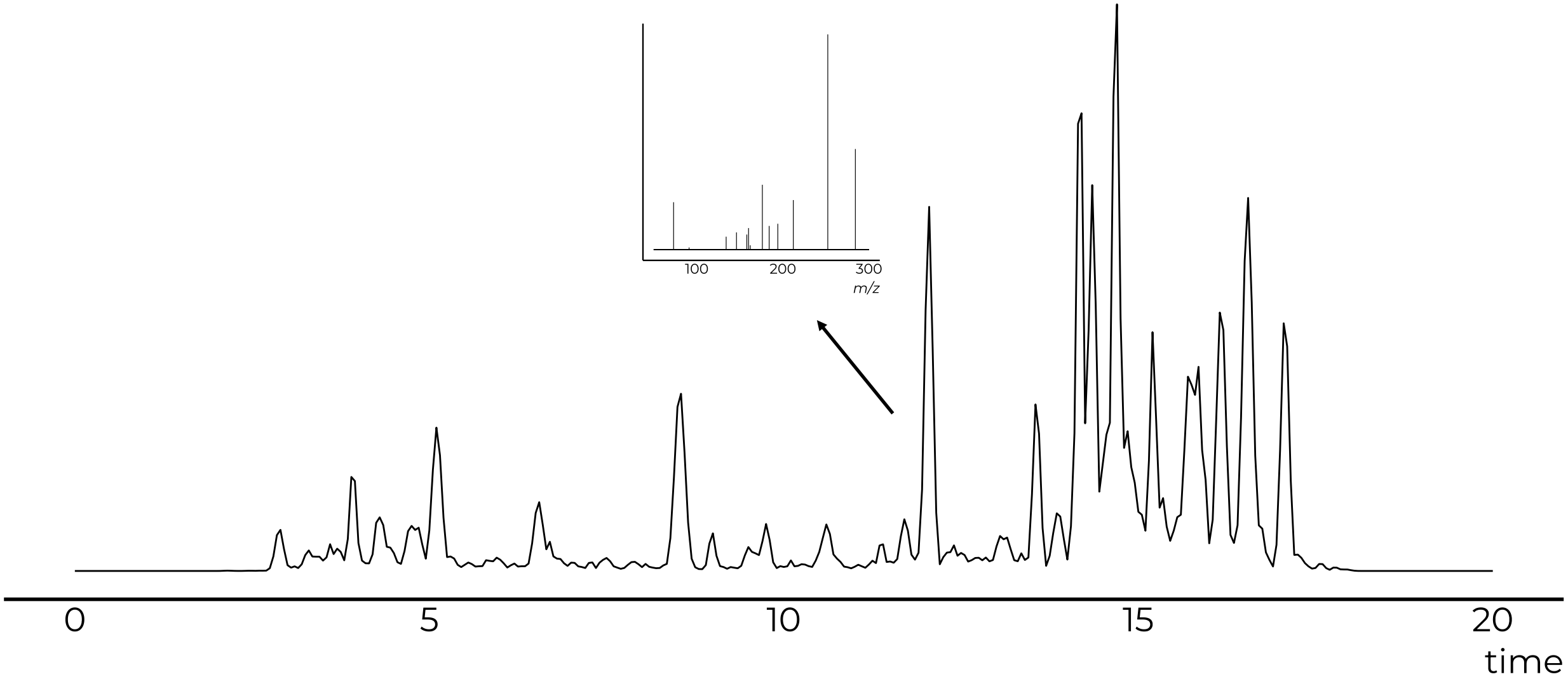
nontarget screening with LC/HRMS



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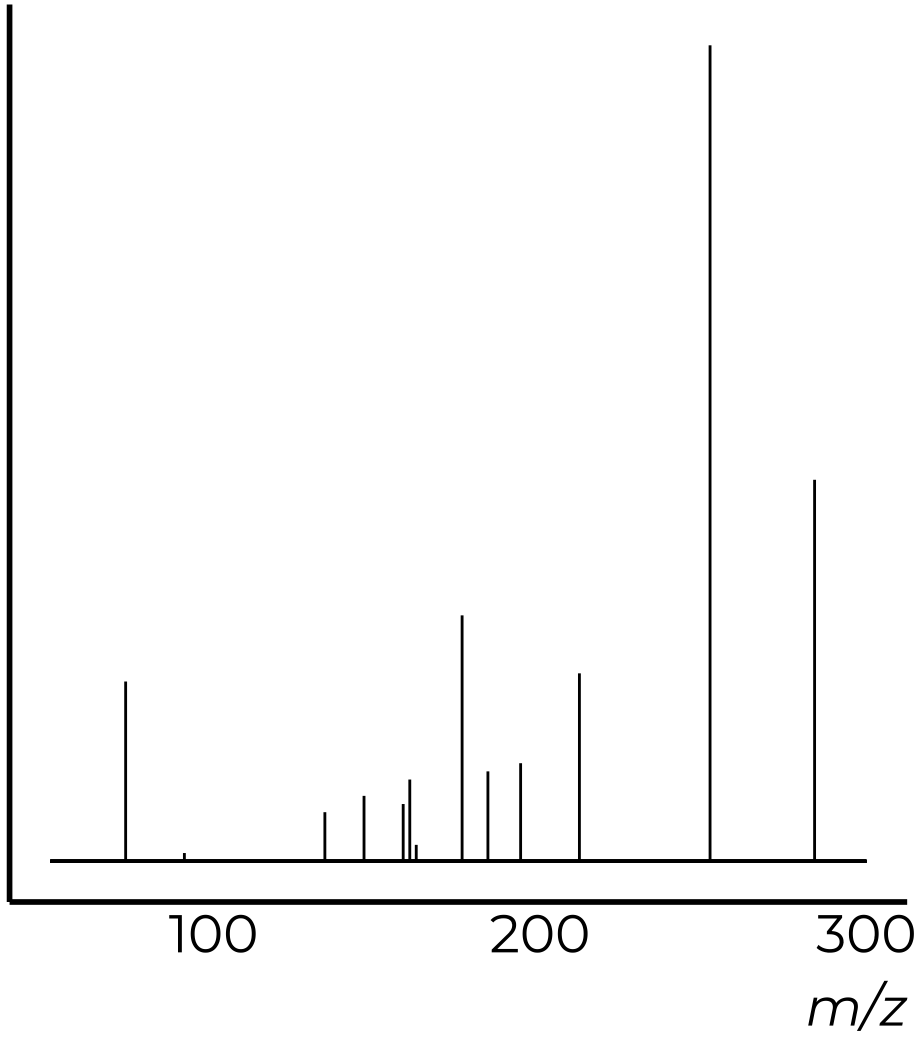
toxicity assessment



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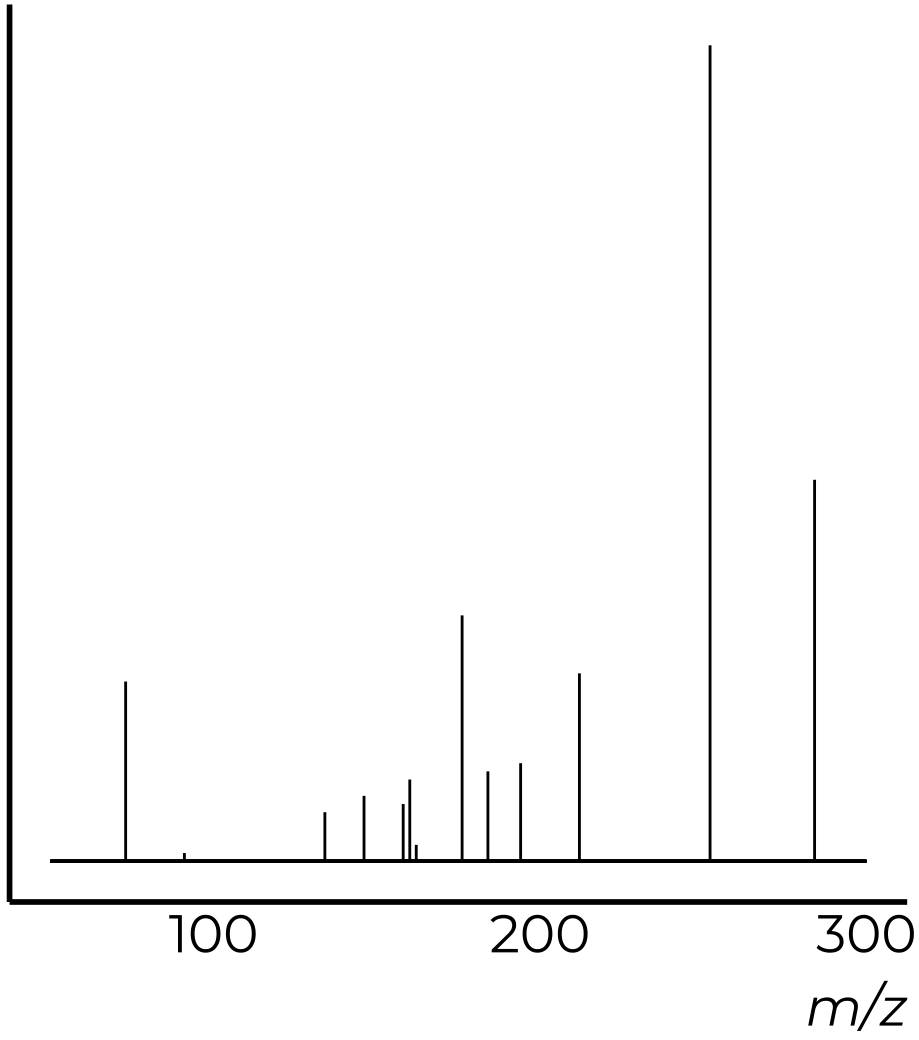
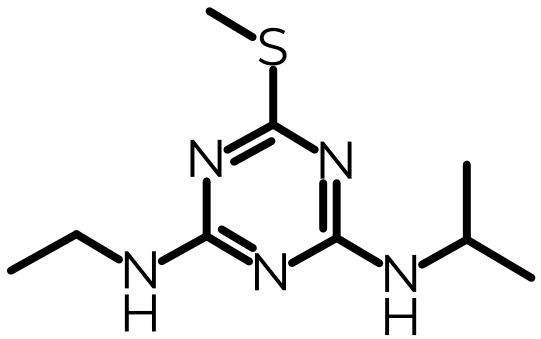
toxicity assessment





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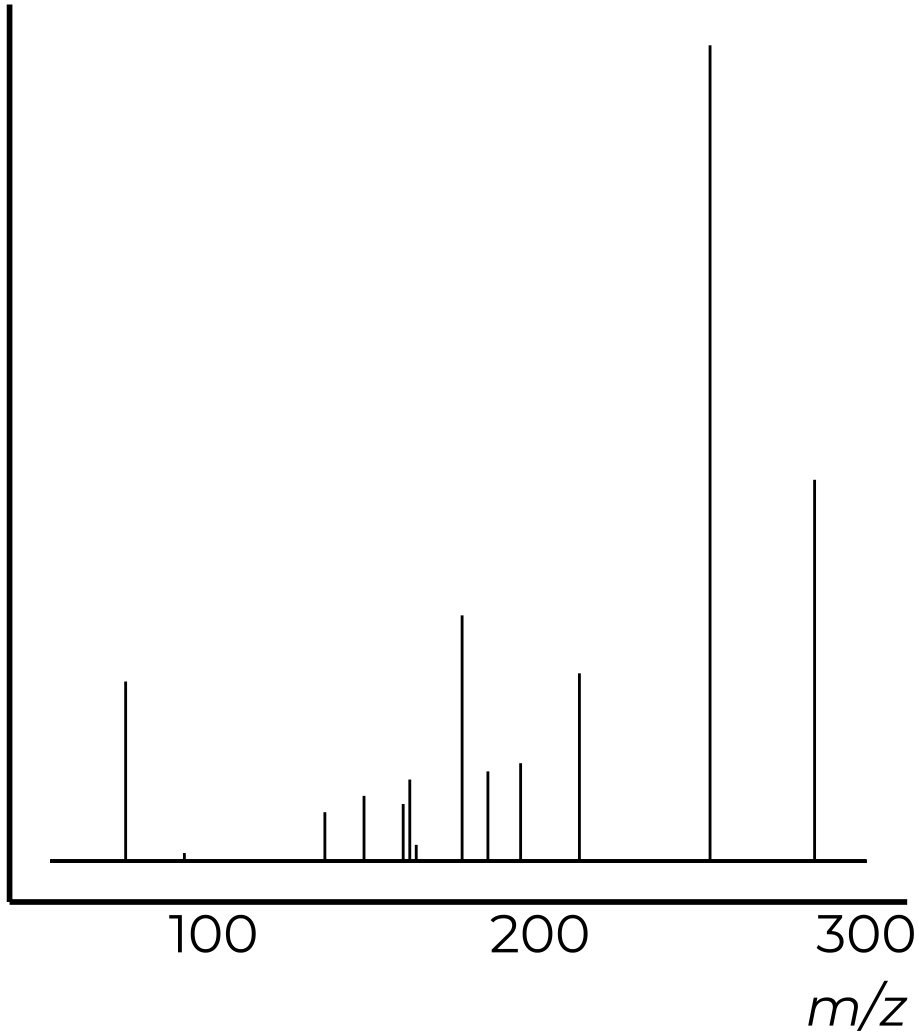
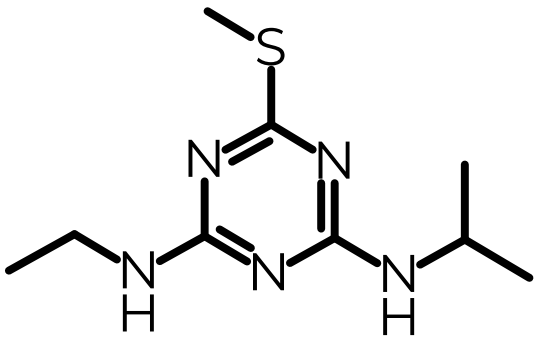
toxicity assessment





LC_{50} = 9.3 mg/L

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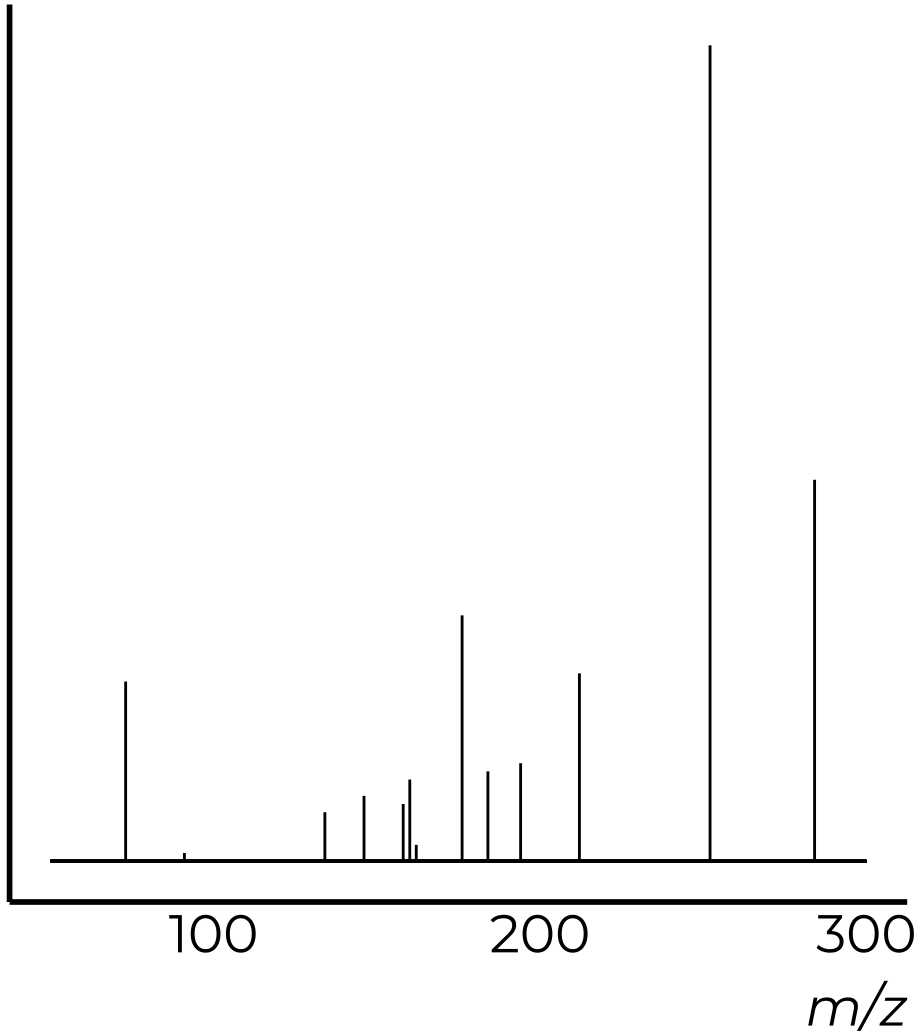
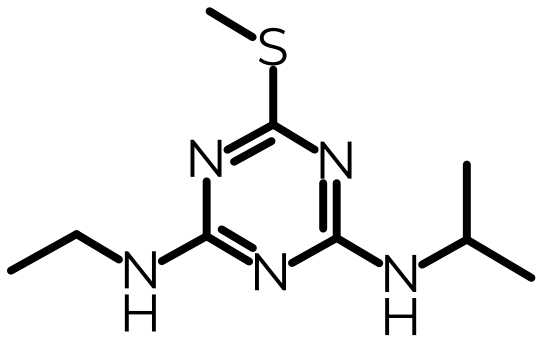
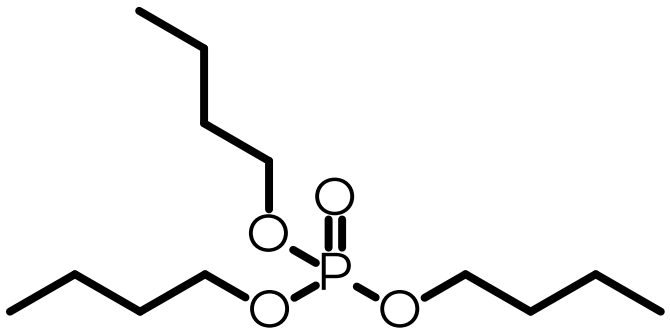
toxicity assessment





LC_{50} = 9.3 mg/L



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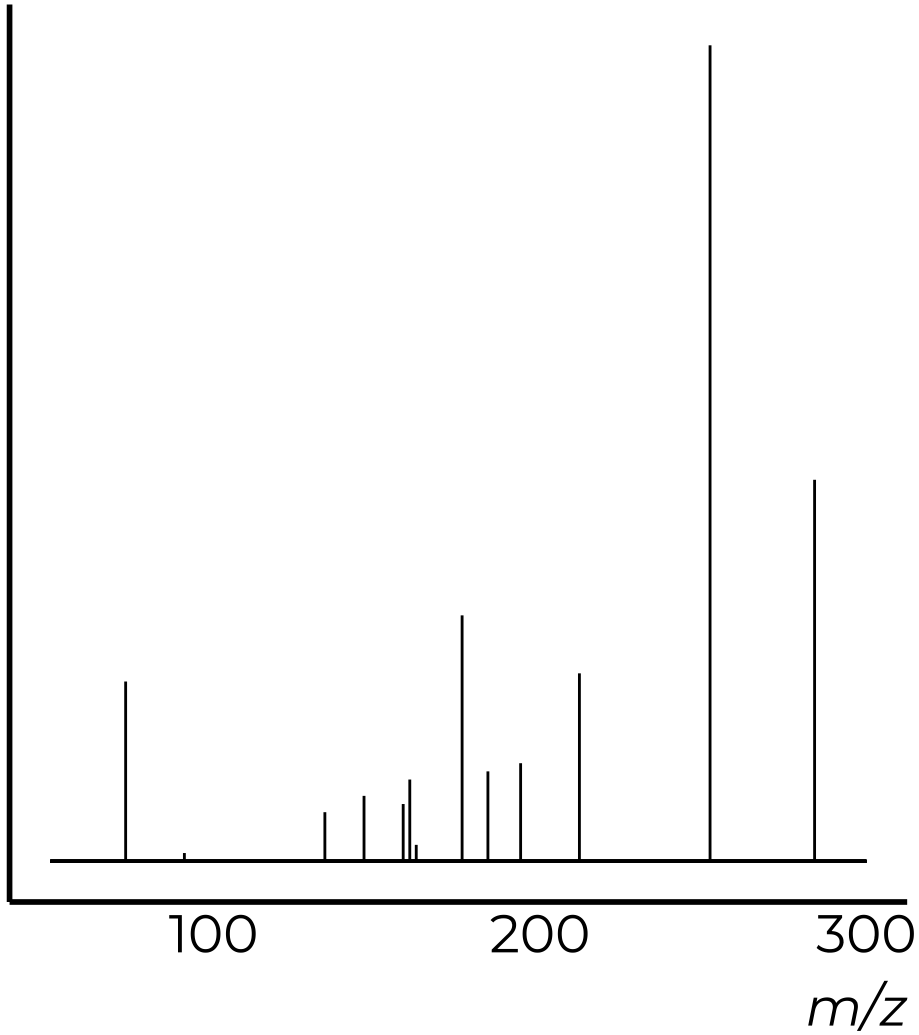
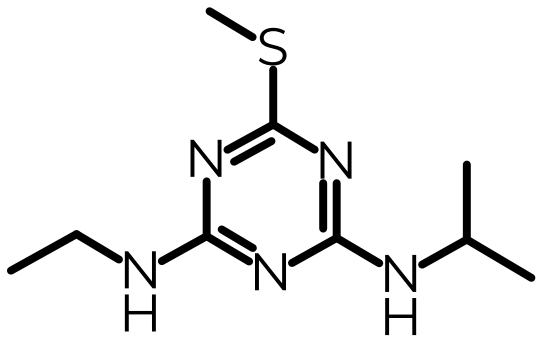
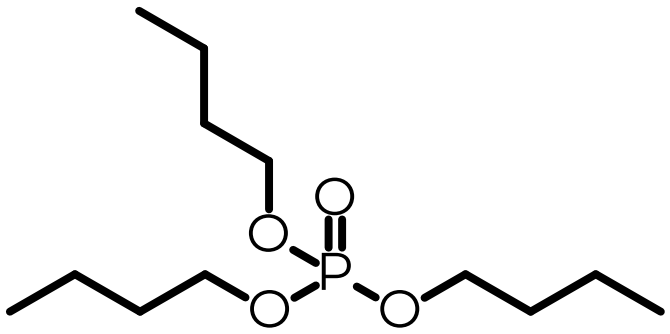
toxicity assessment





LC_{50} = 9.3 mg/L



LC_{50} = ? mg/L

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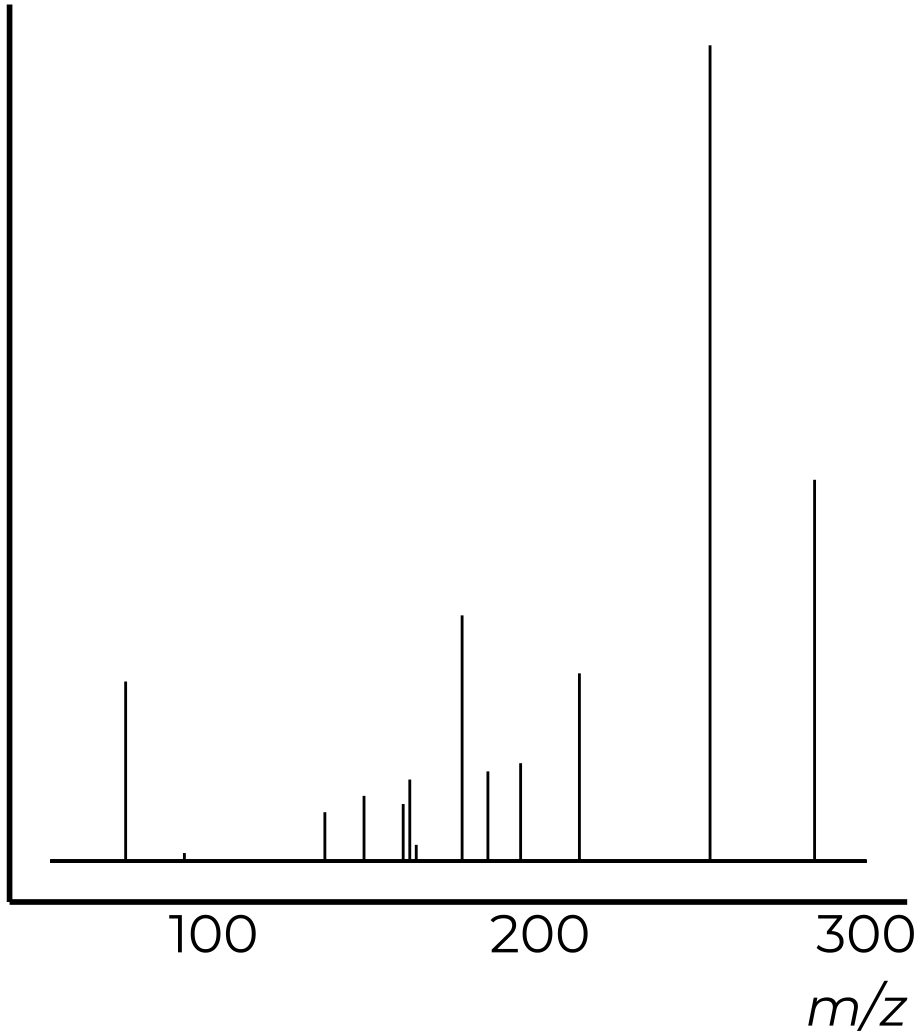
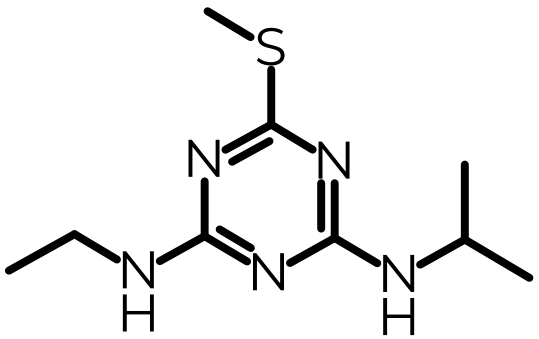
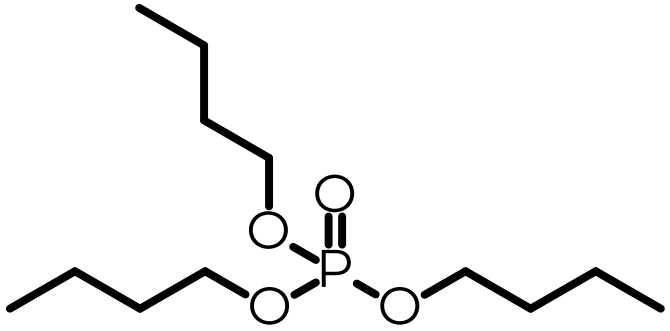
toxicity assessment





LC_{50} = 9.3 mg/L



LC_{50} = ? mg/L

?

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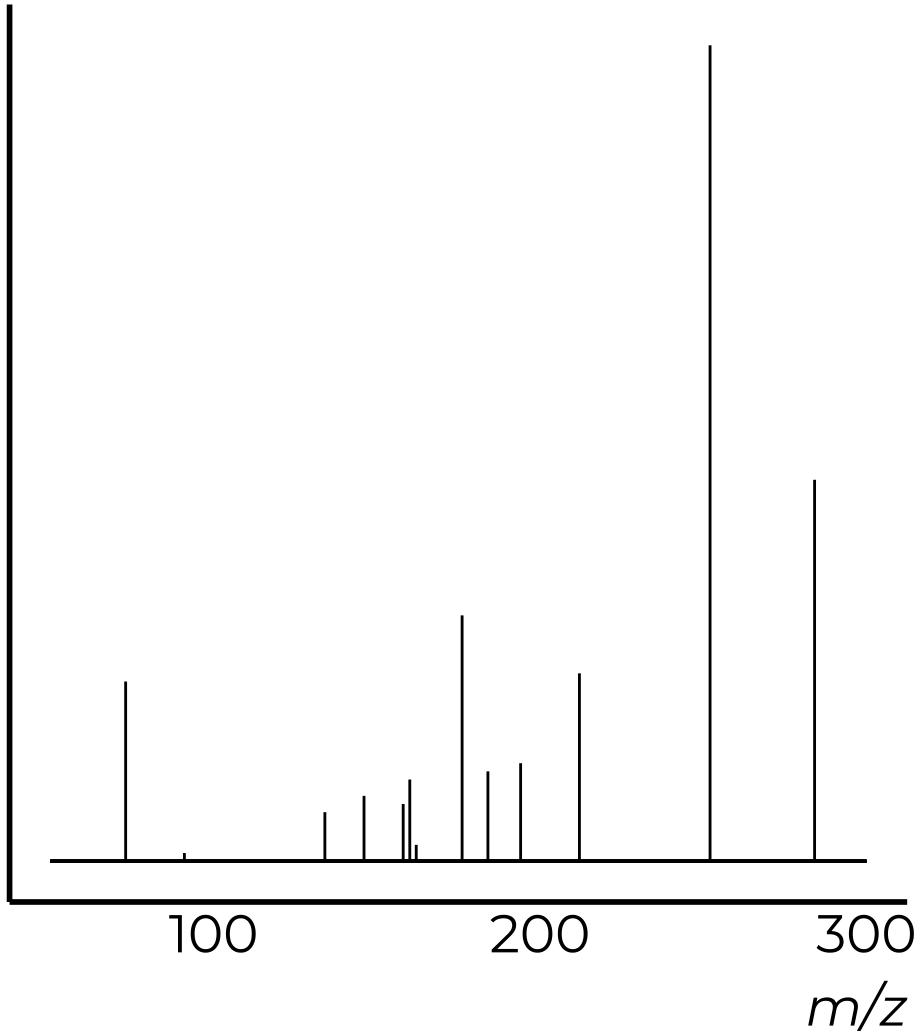
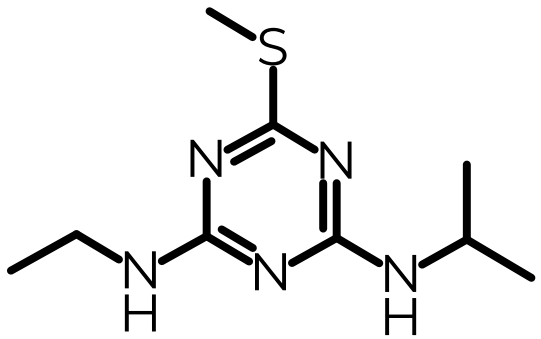
toxicity assessment





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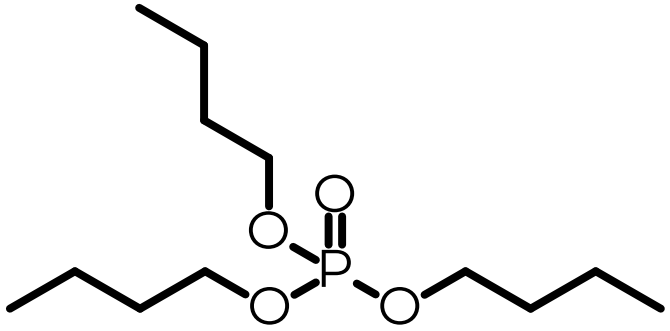

LC_{50} = ? mg/L

LC_{50} = ? mg/L

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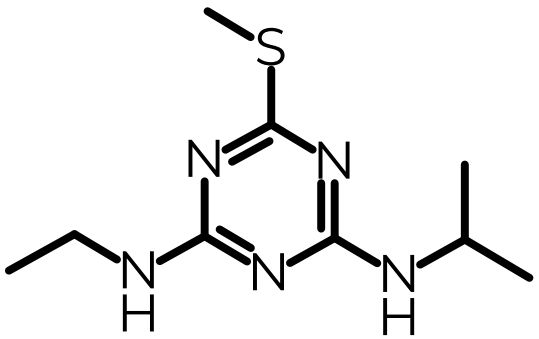
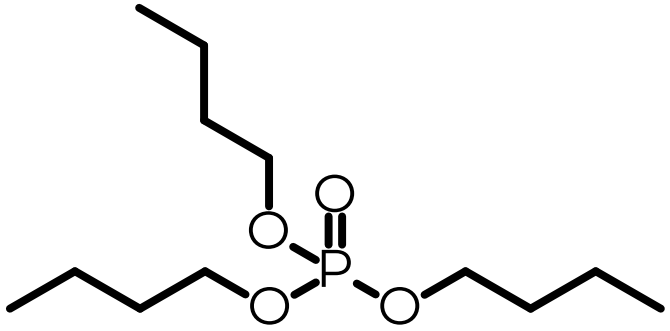
toxicity assessment



LC_{50} = 9.3 mg/L



LC_{50} = ? mg/L

?

LC_{50} = ? mg/L

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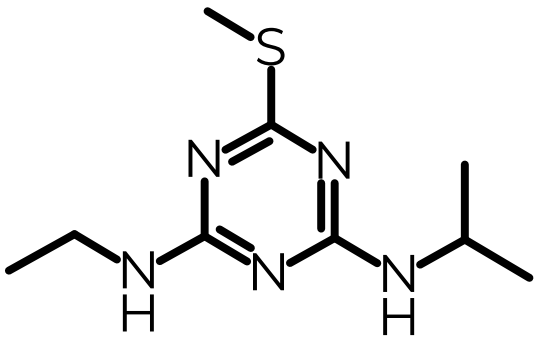
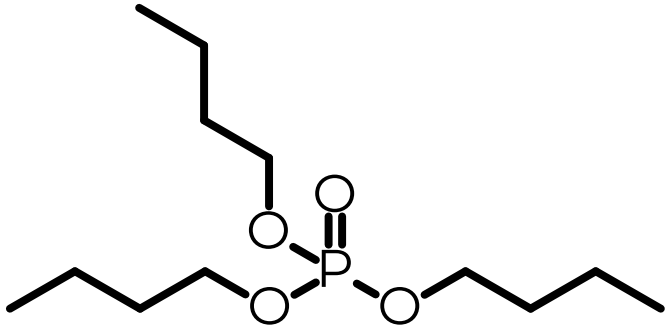
toxicity assessment

<1%



LC_{50} = 9.3 mg/L



LC_{50} = ? mg/L

?

LC_{50} = ? mg/L

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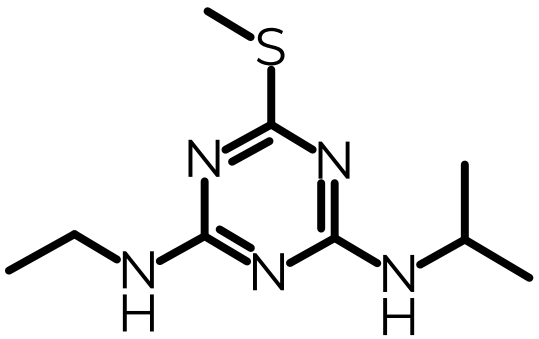
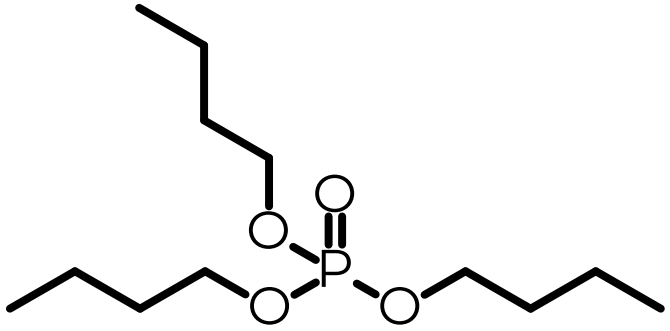
toxicity assessment

<1%



LC_{50} = 9.3 mg/L

<2%



LC_{50} = ? mg/L

?

LC_{50} = ? mg/L

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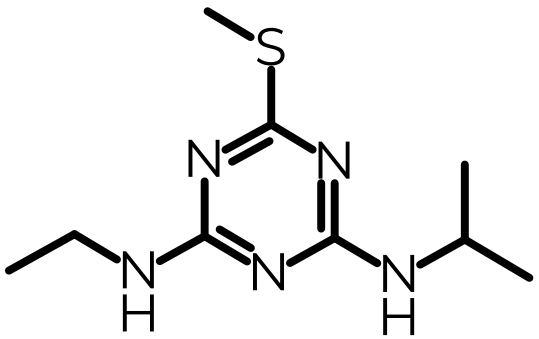
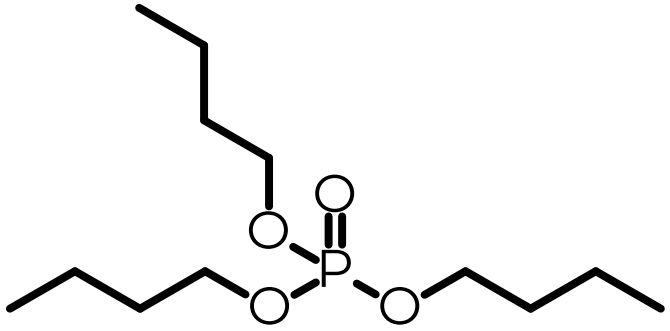
toxicity assessment

<1%



LC_{50} = 9.3 mg/L

<2%



LC_{50} = ? mg/L

~98%

?

LC_{50} = ? mg/L

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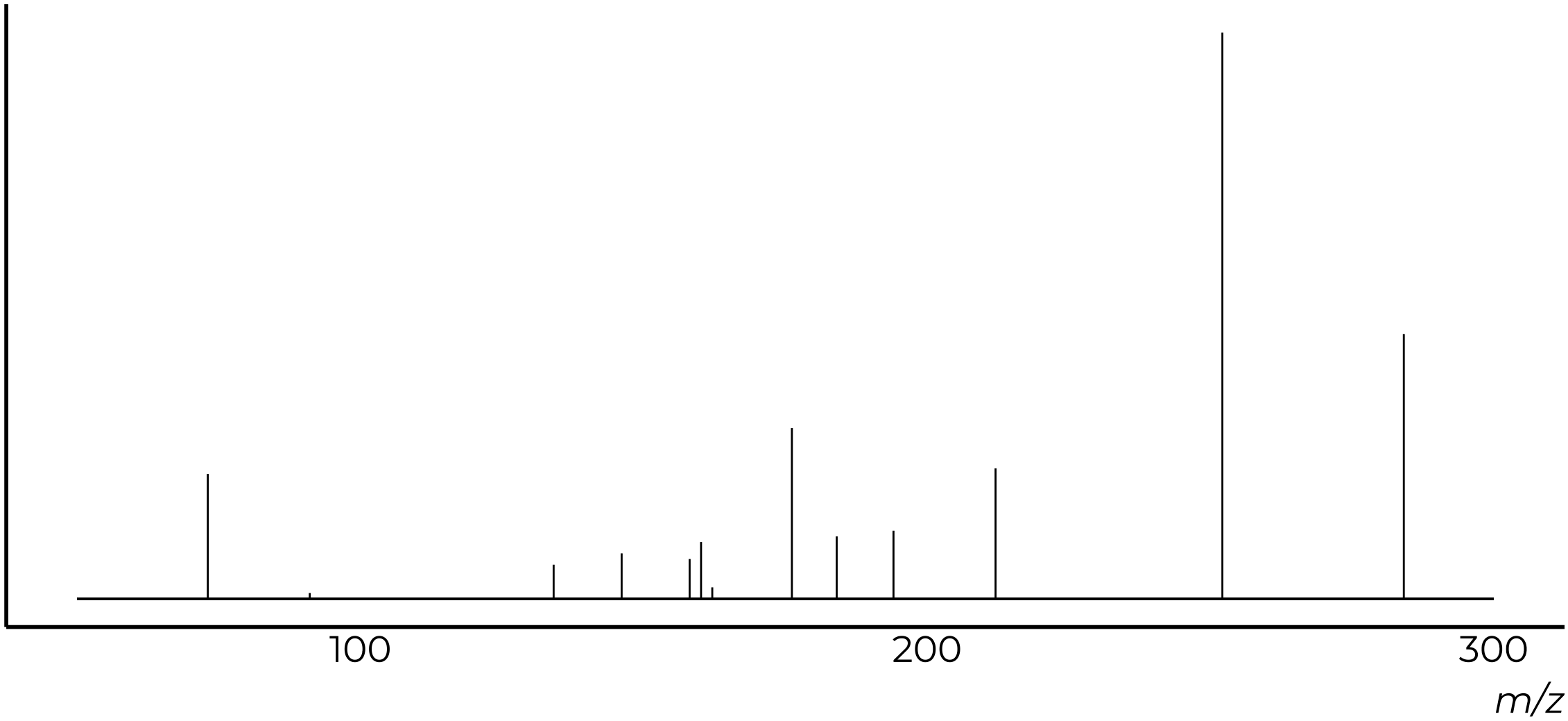
information available

in MS^2 spectra

MS^2 spectra



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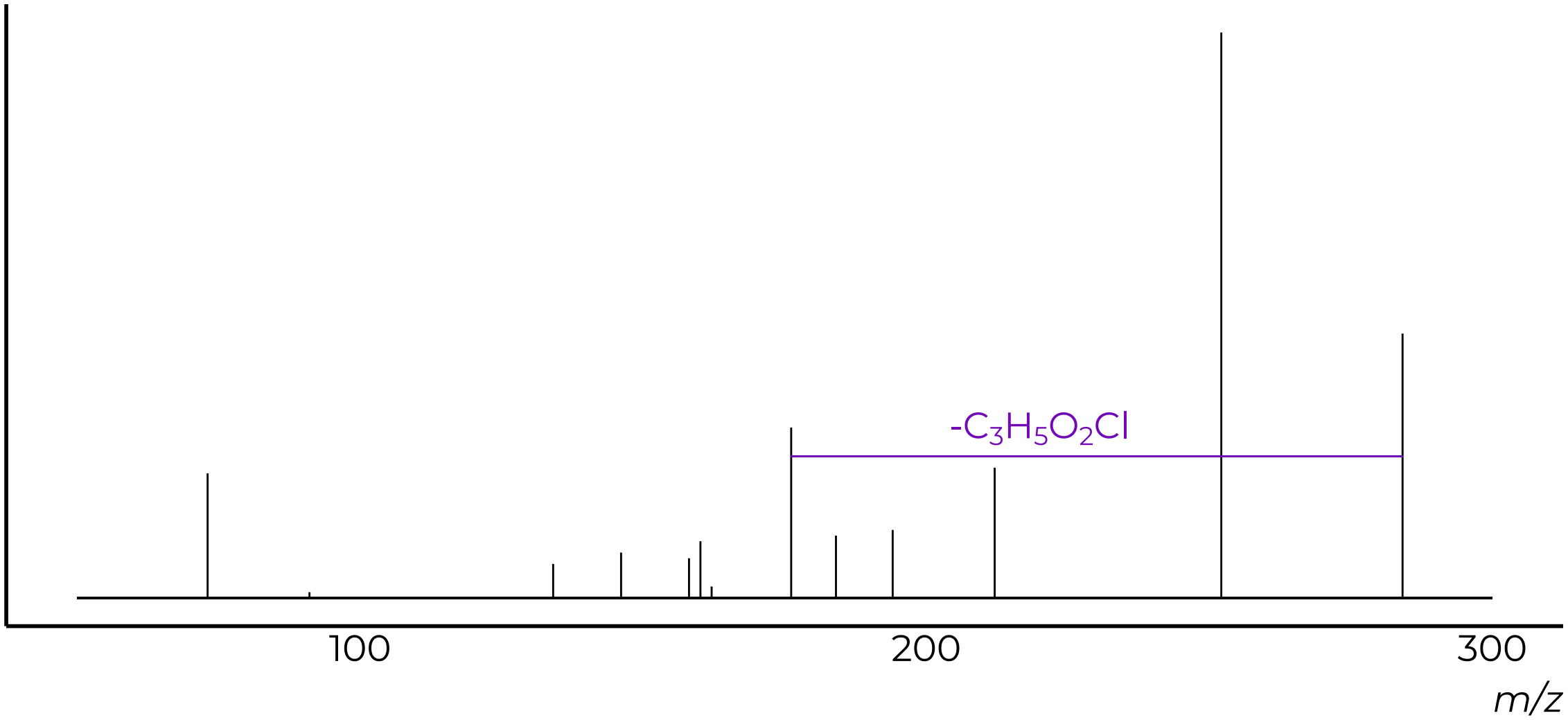
MS^2 spectra



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modelling toxicity

selected endpoint

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selected endpoint

fathead minnow, bluegill and rainbow trout

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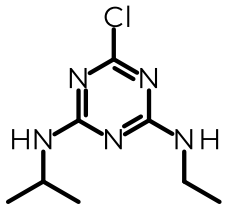
workflow



structure as SMILES

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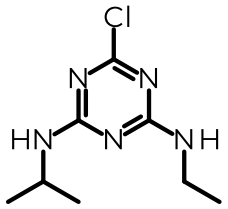
workflow



structure as SMILES

molecular descriptors

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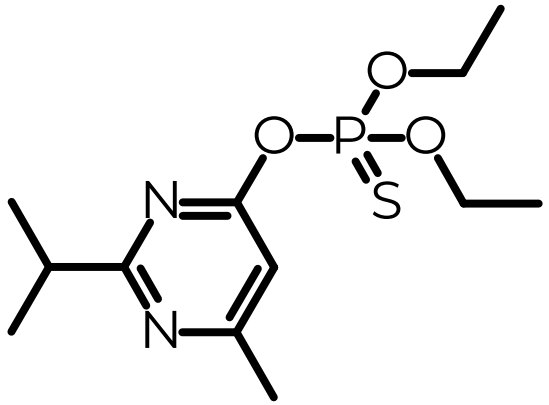
structural fingerprints



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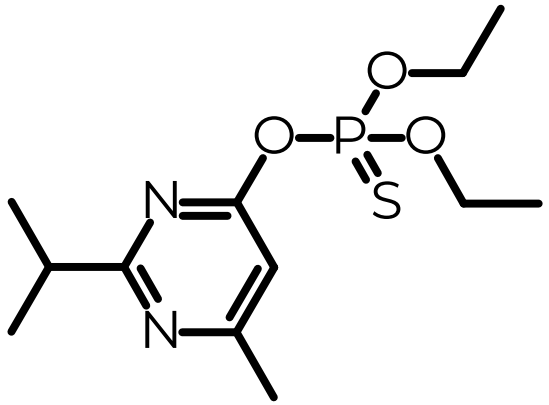
structural fingerprints



R: rcdk

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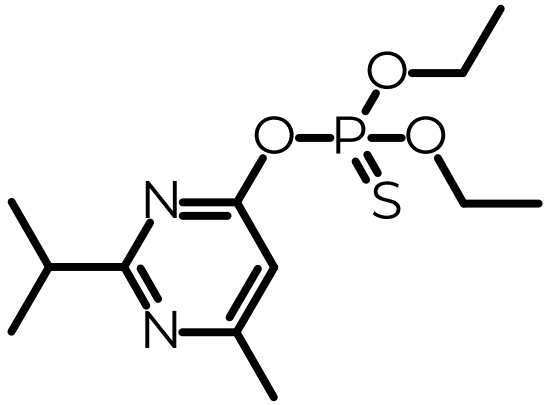
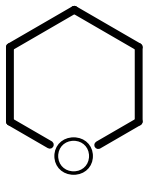
structural fingerprints



R: rcdk

0	
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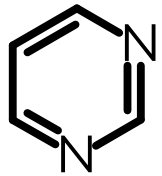
1	

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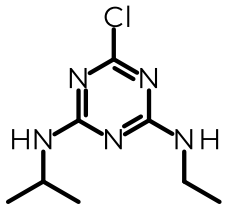
workflow



structure as SMILES

molecular descriptors

machine learning for predicting LC_{50}

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model training

mass (Da)	fp1	...	fp243
317.32000	0	...	0
208.26100	1	...	0
240.21499	1	...	0
300.57998	0	...	0
201.22500	0	...	0

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model training

mass (Da)	fp1	...	fp243
317.32000	0	...	0
208.26100	1	...	0
240.21499	1	...	0
300.57998	0	...	0
201.22500	0	...	0

training set
517
chemicals

test set
130
chemicals

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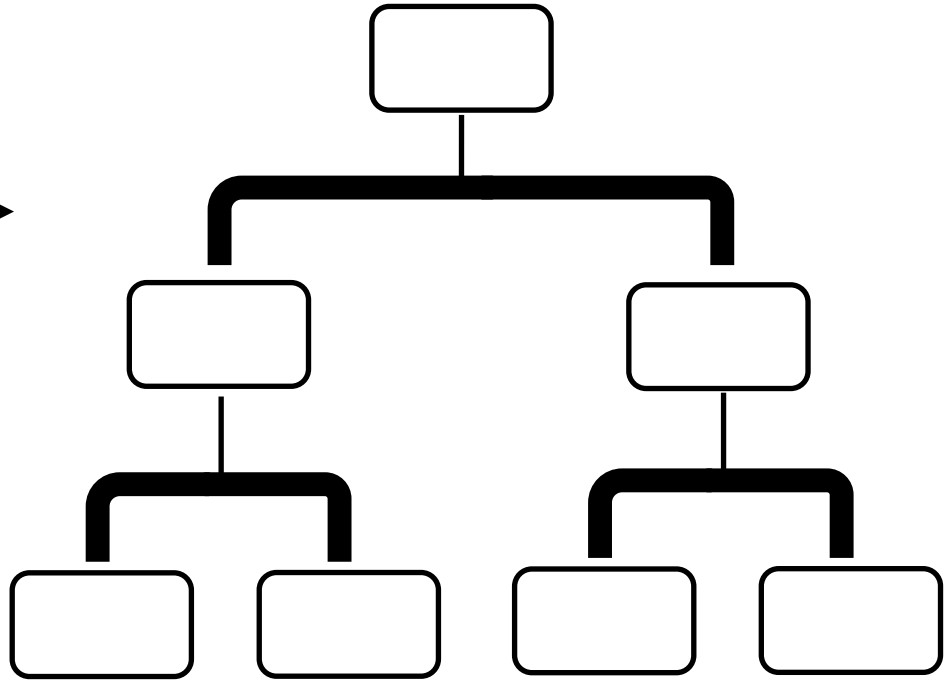
model training

mass (Da)	fp1	...	fp243
317.32000	0	...	0
208.26100	1	...	0
240.21499	1	...	0
300.57998	0	...	0
201.22500	0	...	0

training set
517
chemicals

test set
130
chemicals

gradient
boosting



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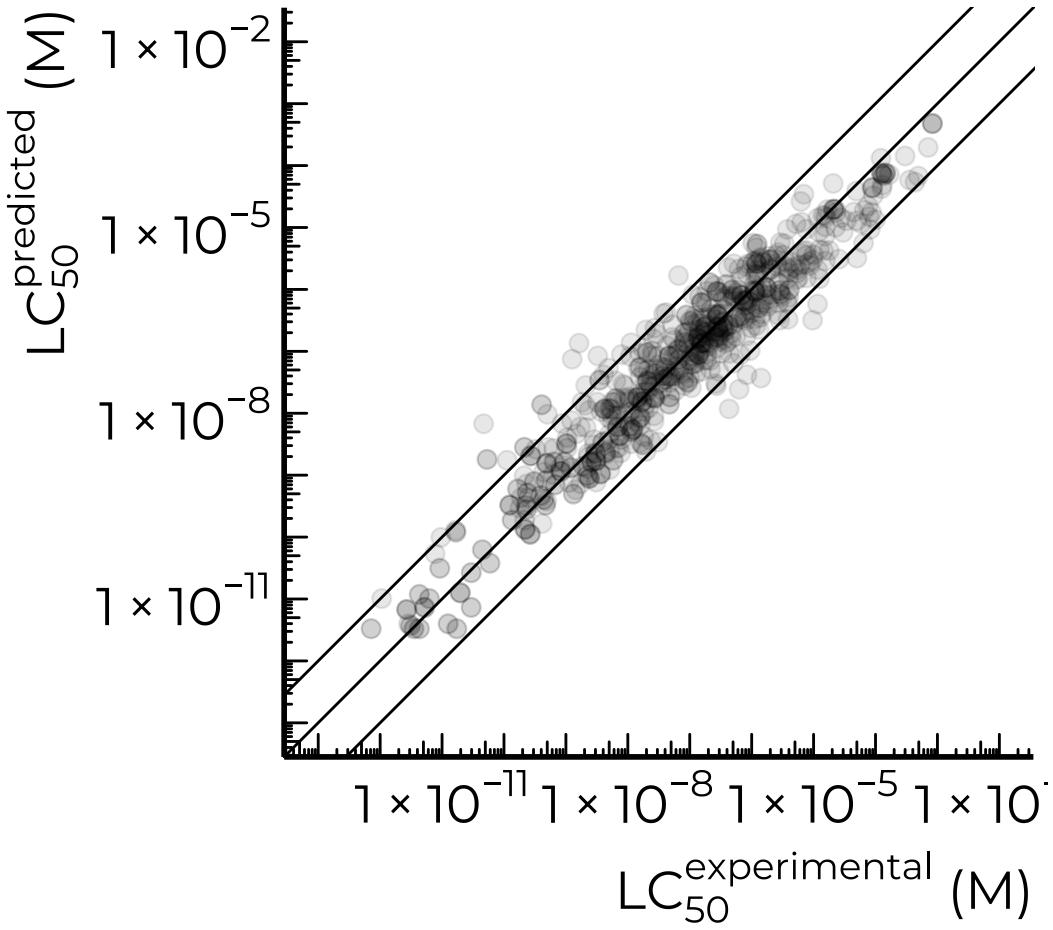
performance

of LC_{50} predictions with molecular fingerprints

LC_{50} predictions

Peets et al. ES&T 2022

fish LC_{50}



training set

RMSE 0.52 log(M)

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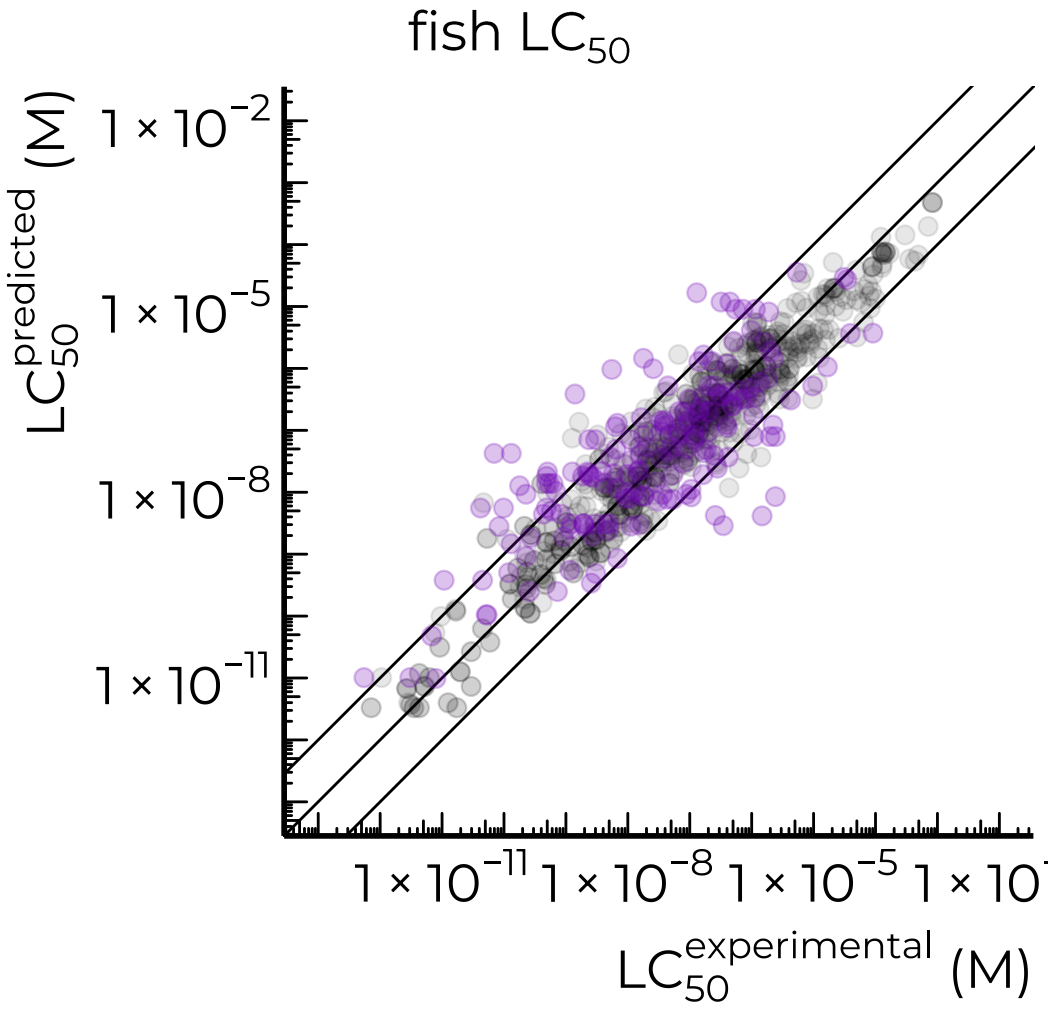
LC_{50} predictions

Peets et al. ES&T 2022



training set

RMSE 0.52 log(M)

test set

RMSE 0.78 log(M)

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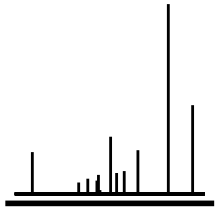
unidentified chemicals

from MS^2 spectra

workflow



MS^2 spectra

molecular fingerprints with SIRIUS+CSI:FingerID

predict LC_{50}

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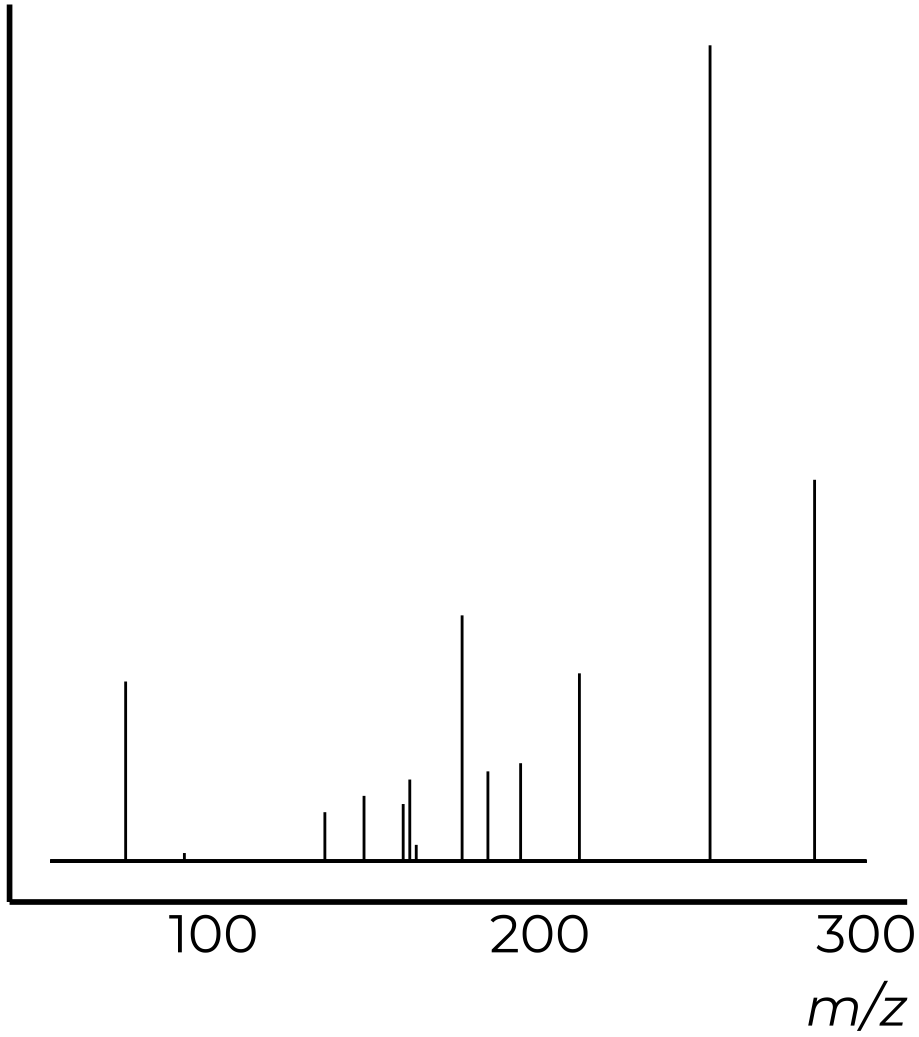
predict for unknown chemicals



?

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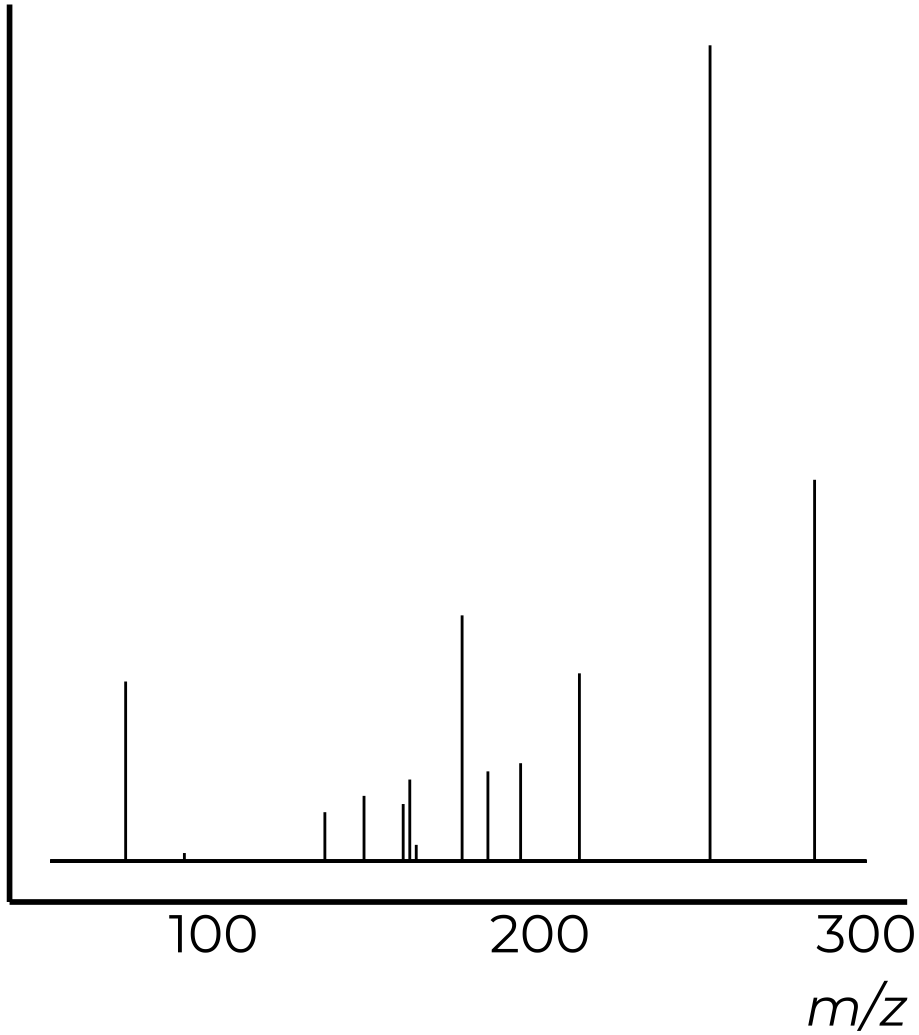
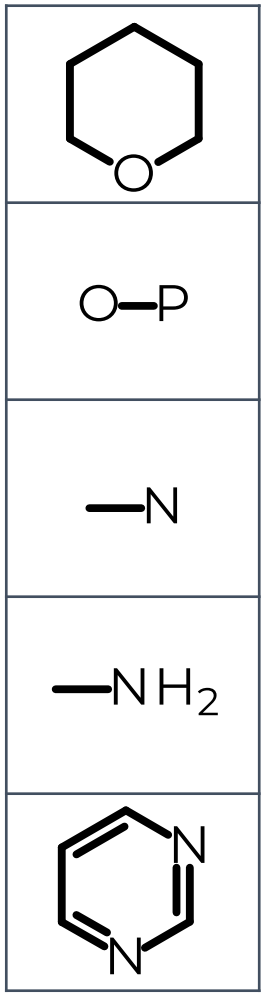
predict for unknown chemicals



SIRIUS+
CSI:FingerID



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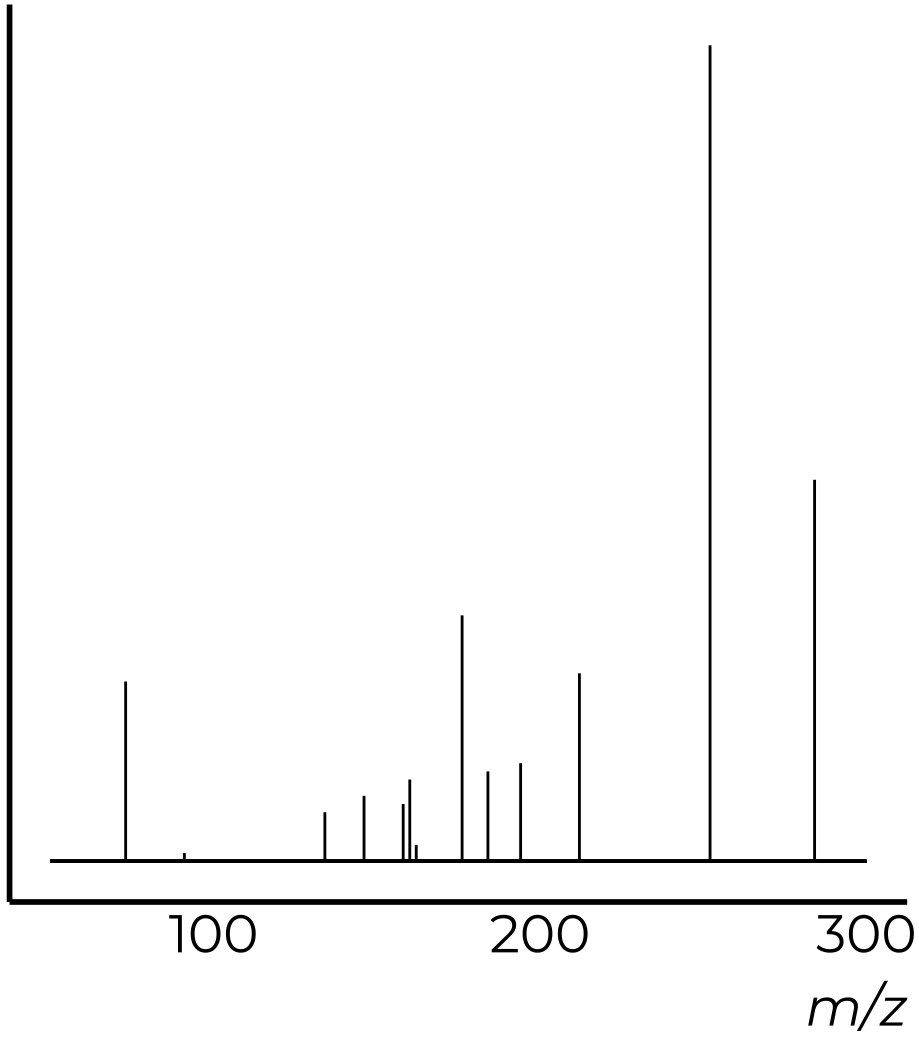
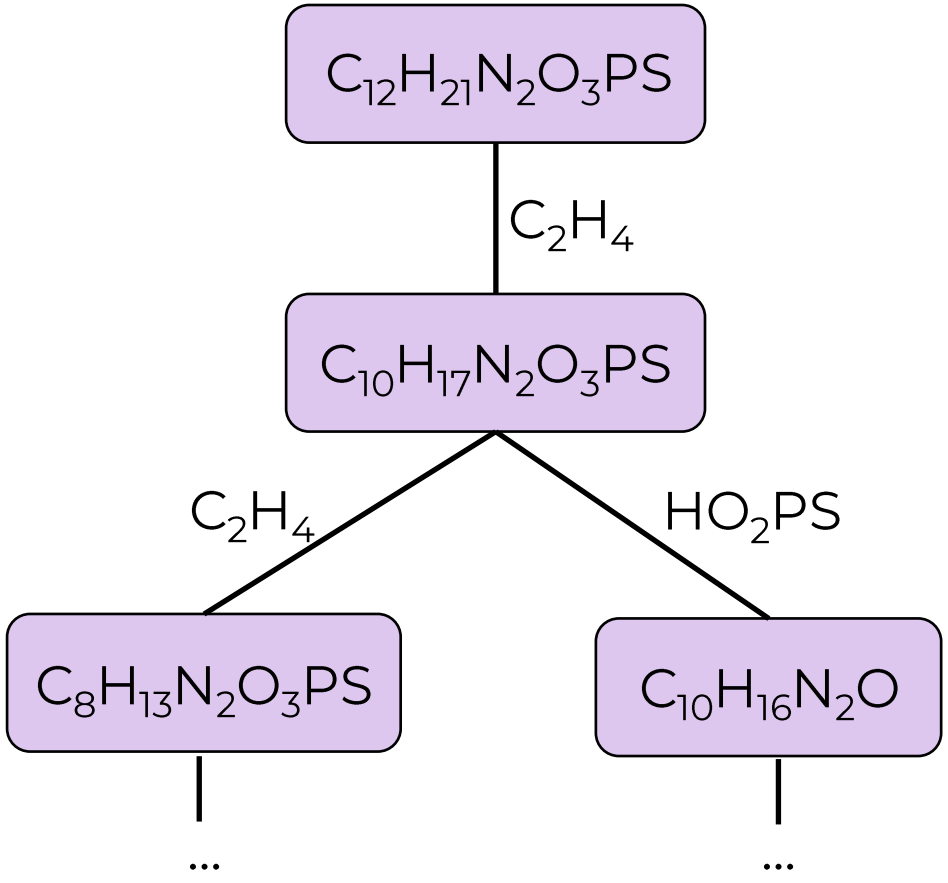
predict for unknown chemicals



SIRIUS+
CSI:FingerID



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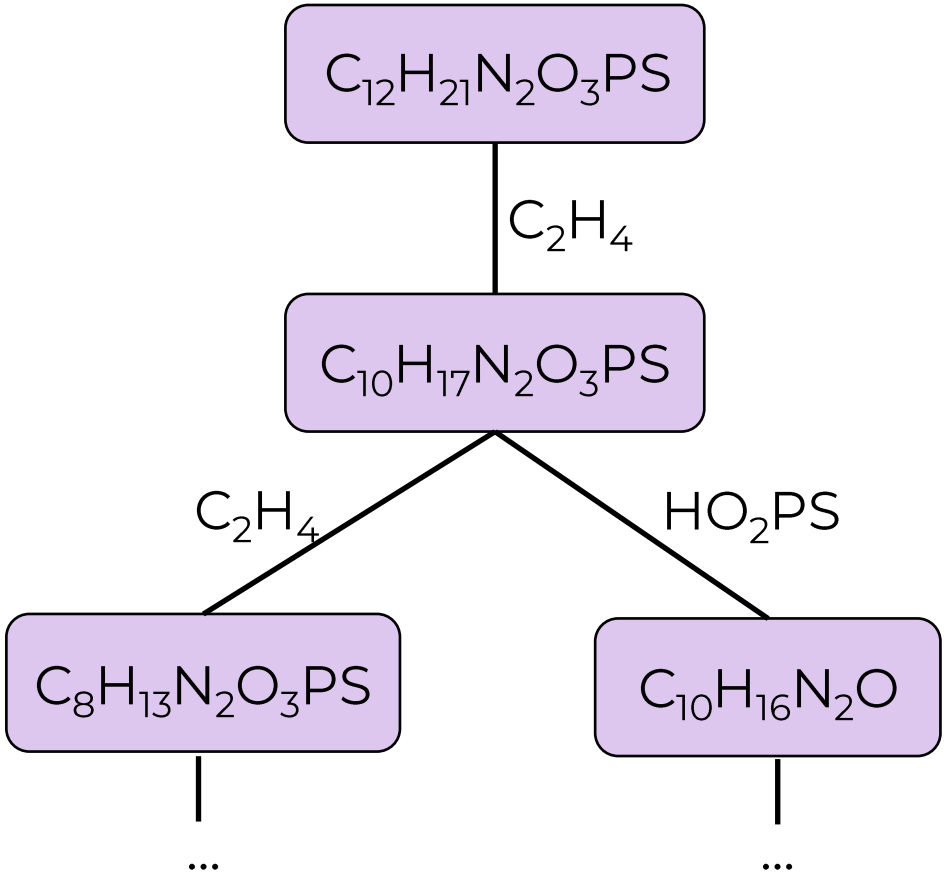
predict for unknown chemicals



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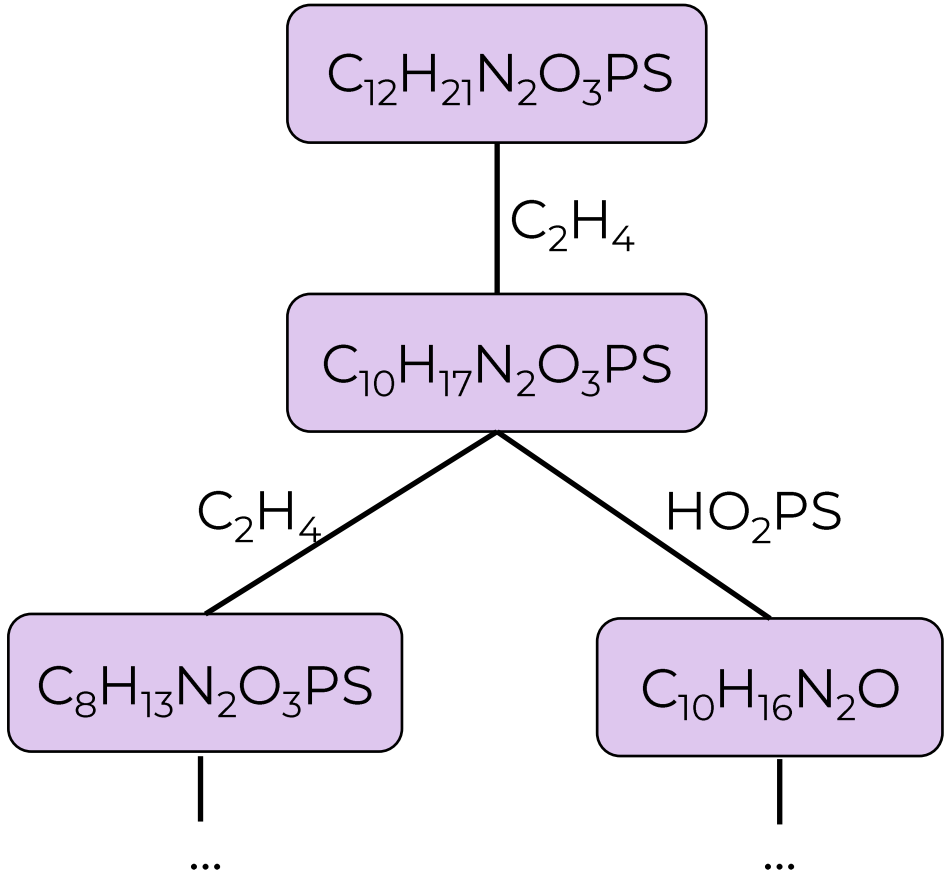
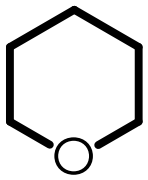
predict for unknown chemicals



0.001	
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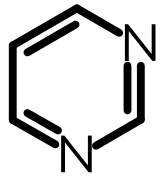
0.988	

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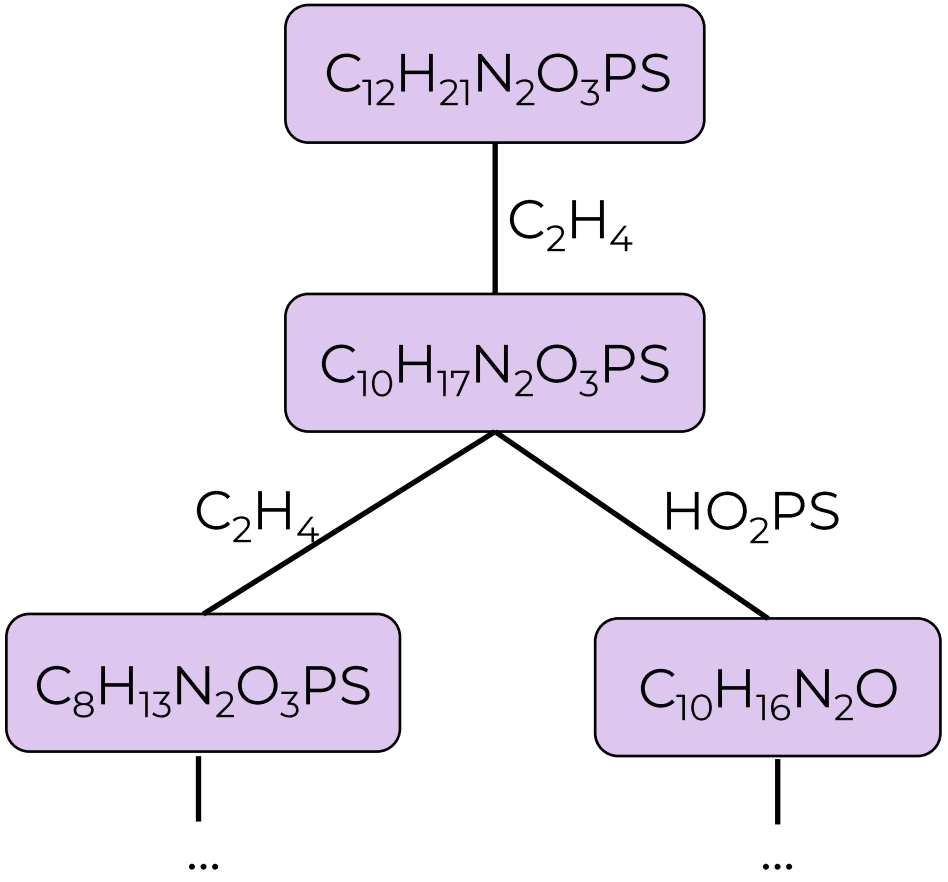
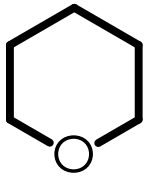
predict for unknown chemicals



0	
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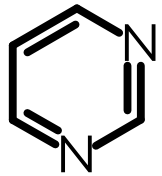
1	

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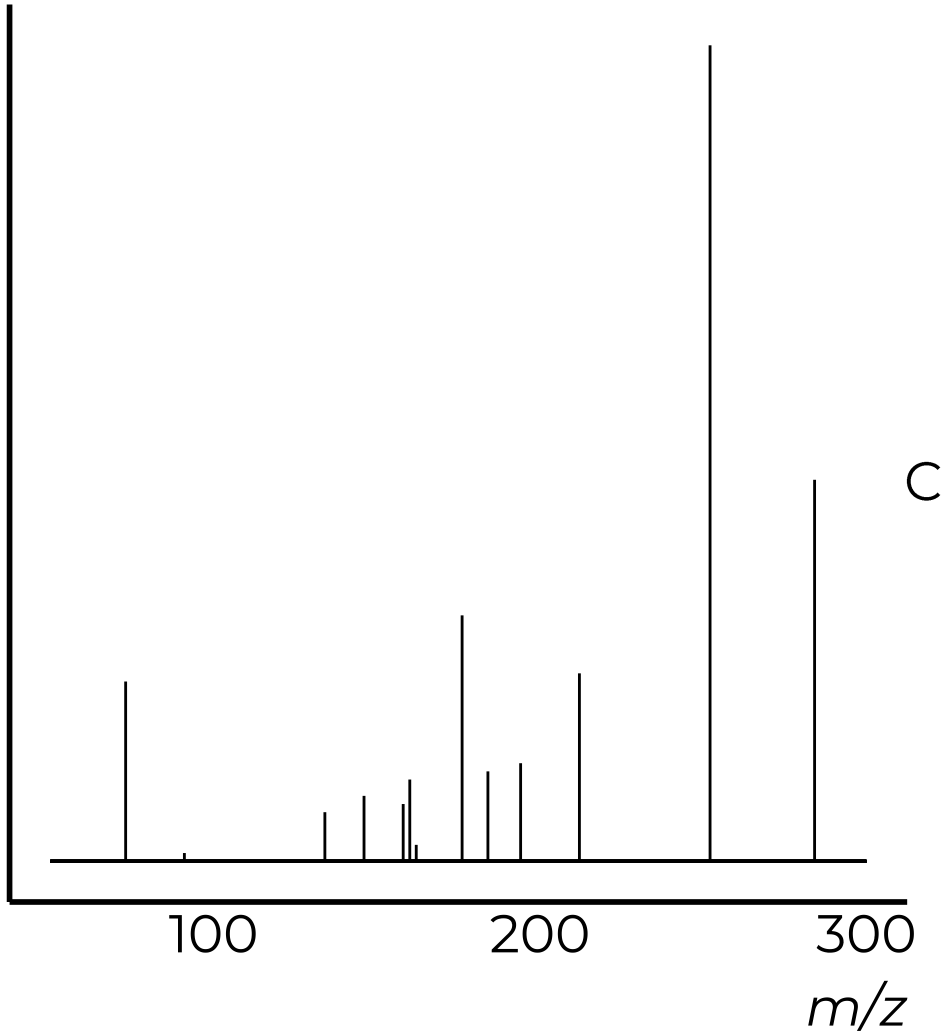
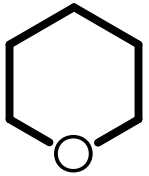


SIRIUS+
CSI:FingerID

0	
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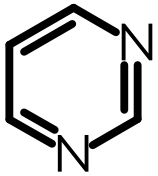
1	

gradient
boosting

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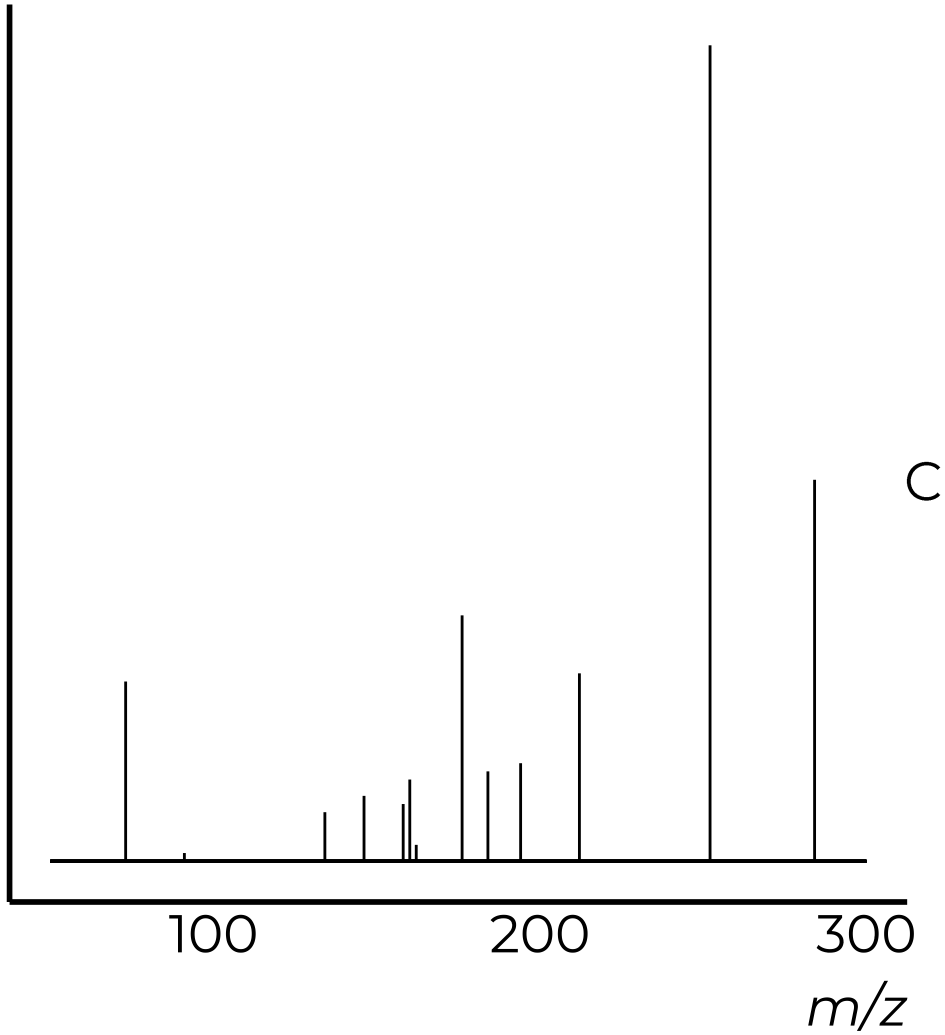
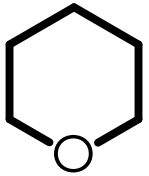
predict for unknown chemicals



SIRIUS+
CSI:FingerID

0	
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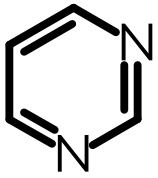
1	

gradient
boosting

LC_{50} =
-2.2 log(mM)

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LC_{50} predictions

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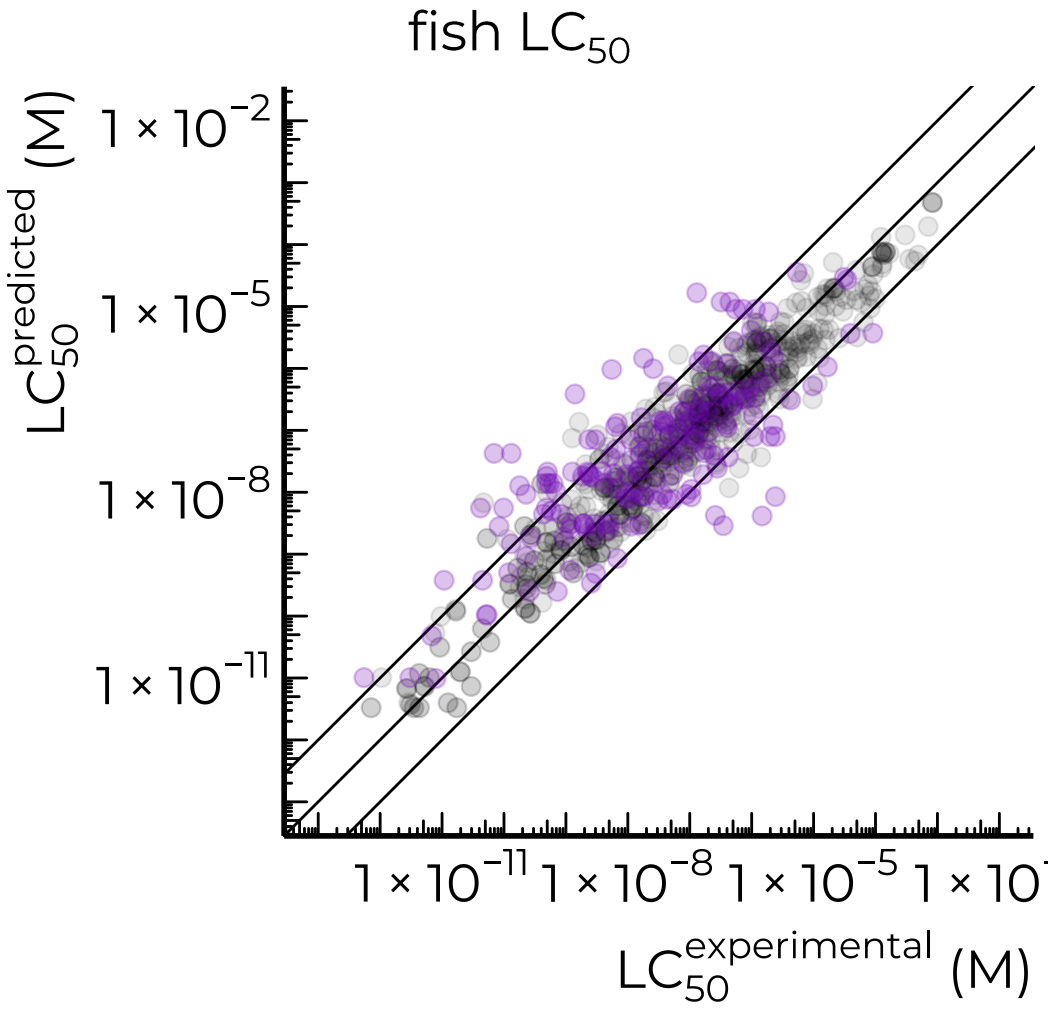
LC_{50} predictions

Peets et al. ES&T 2022



test set on structures

RMSE 0.78 log(M)

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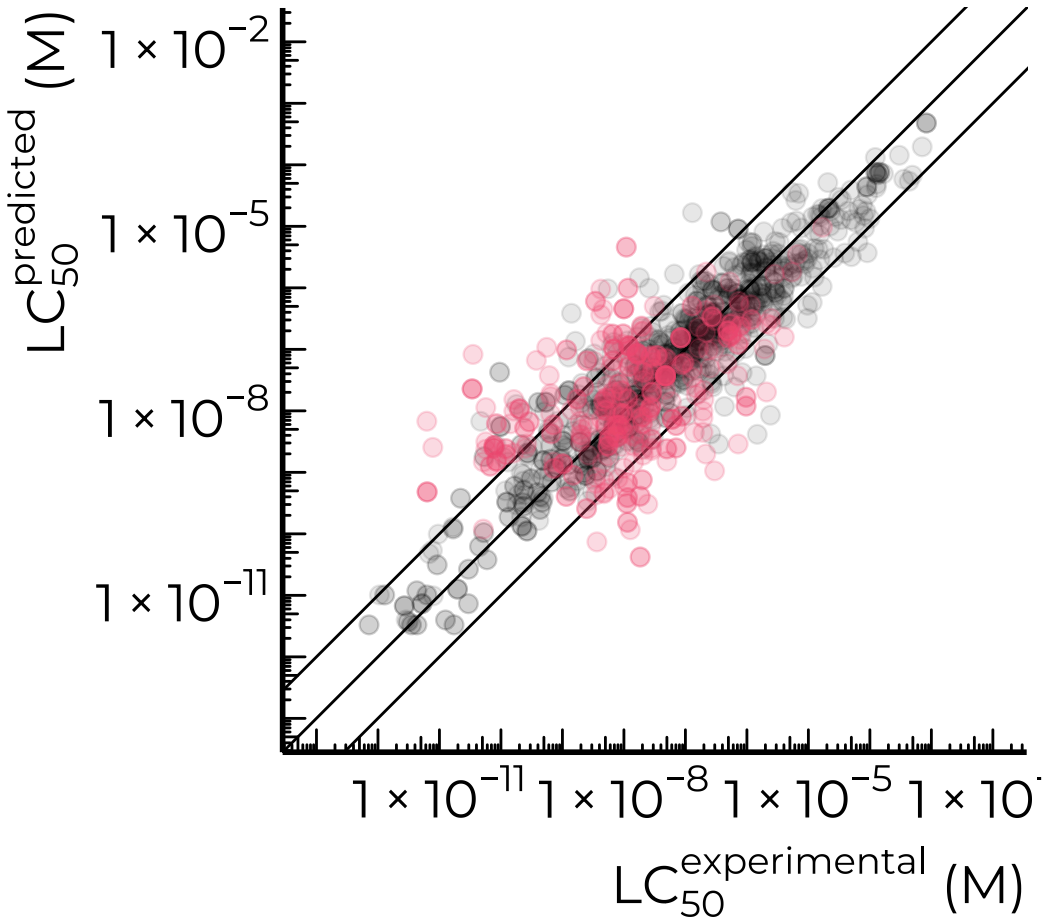
LC_{50} predictions

Peets et al. ES&T 2022

fish LC_{50}



test set on structures

RMSE 0.78 log(M)

validation on MassBank

$RMSE_{model}$ 0.88 log(M)

$SD_{experimental}$ 0.44 log(mM)

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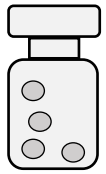
pinpointing toxic chemicals

case study on wastewater



wastewater samples

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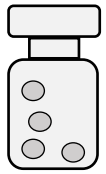
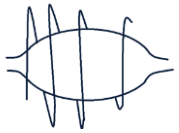
case study on wastewater



wastewater samples



LC/HRMS analysis

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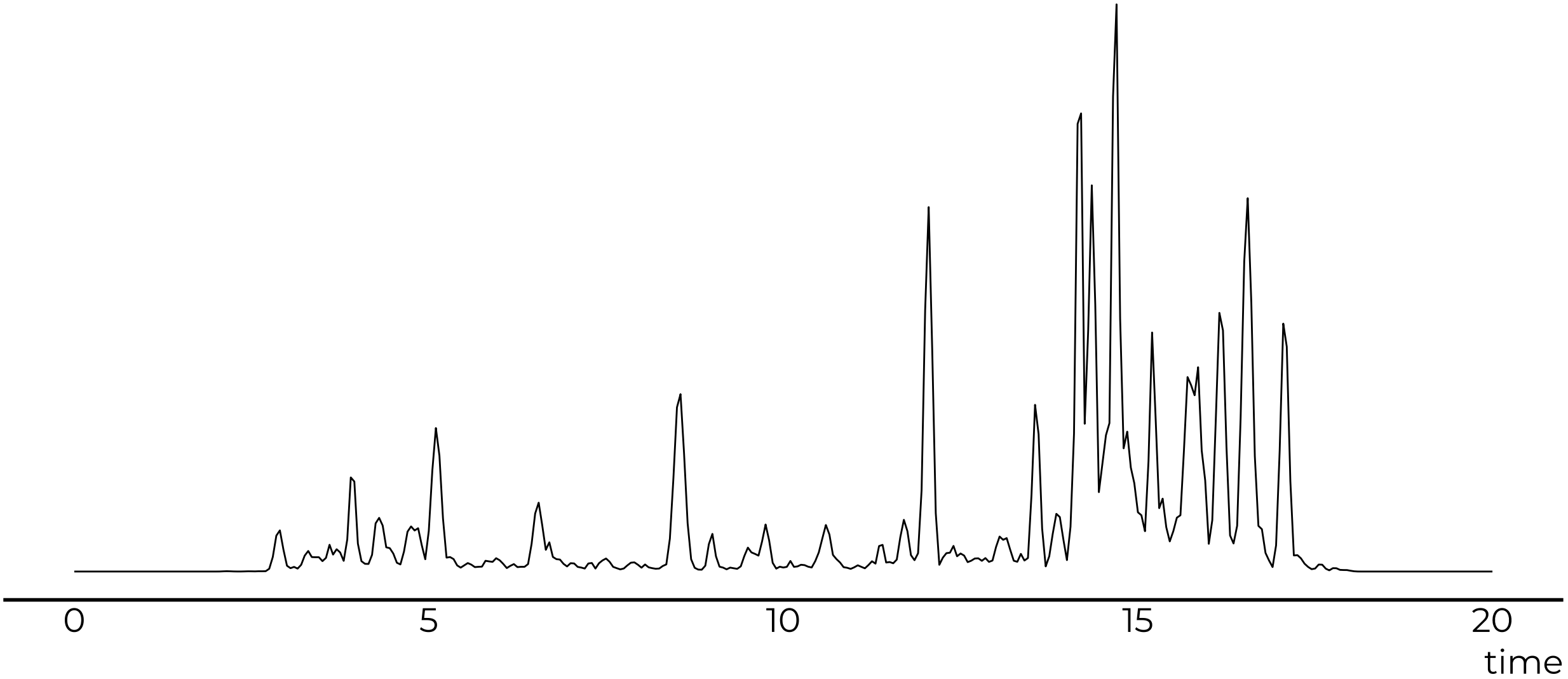
case study on wastewater



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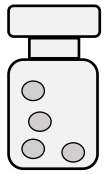
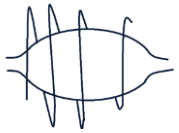
case study on wastewater



wastewater samples



LC/HRMS analysis

MS-DIAL peak picking

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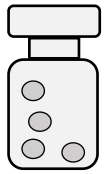
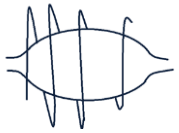
case study on wastewater



wastewater samples



LC/HRMS analysis

MS-DIAL peak picking

SIRIUS+CSI:FingerID

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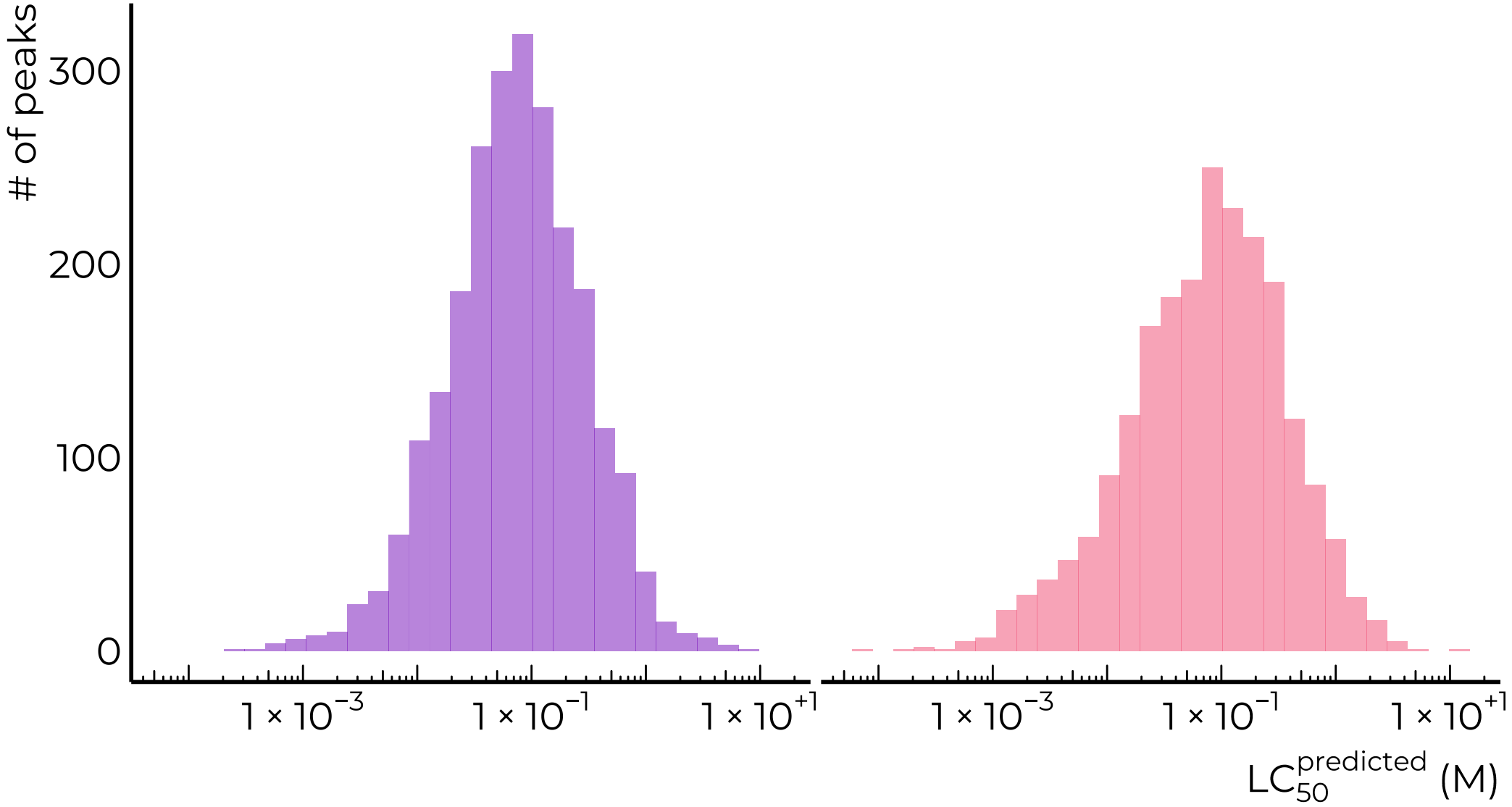
LC_{50} distribution



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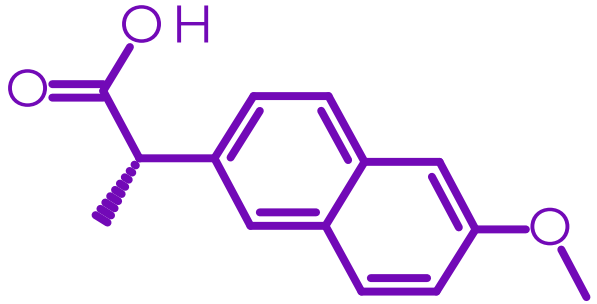
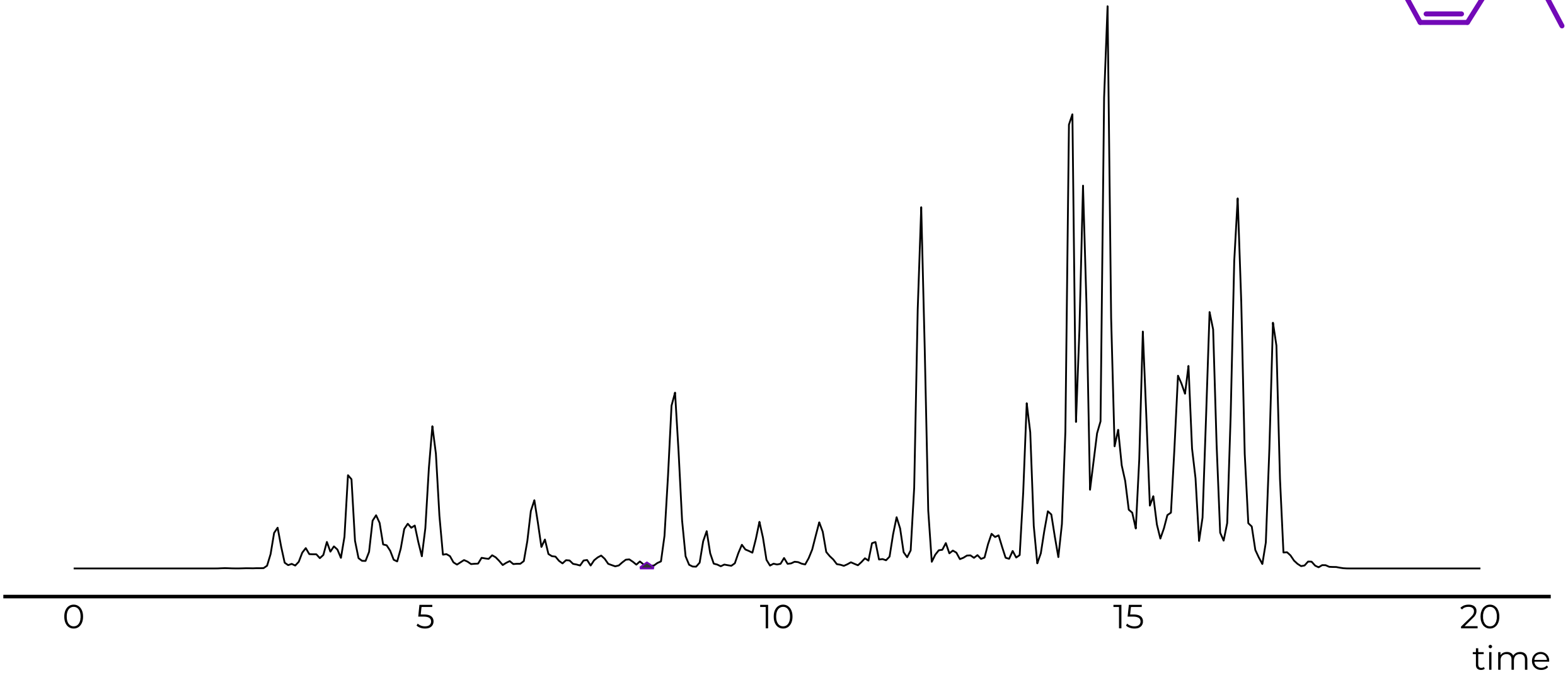
naproxen





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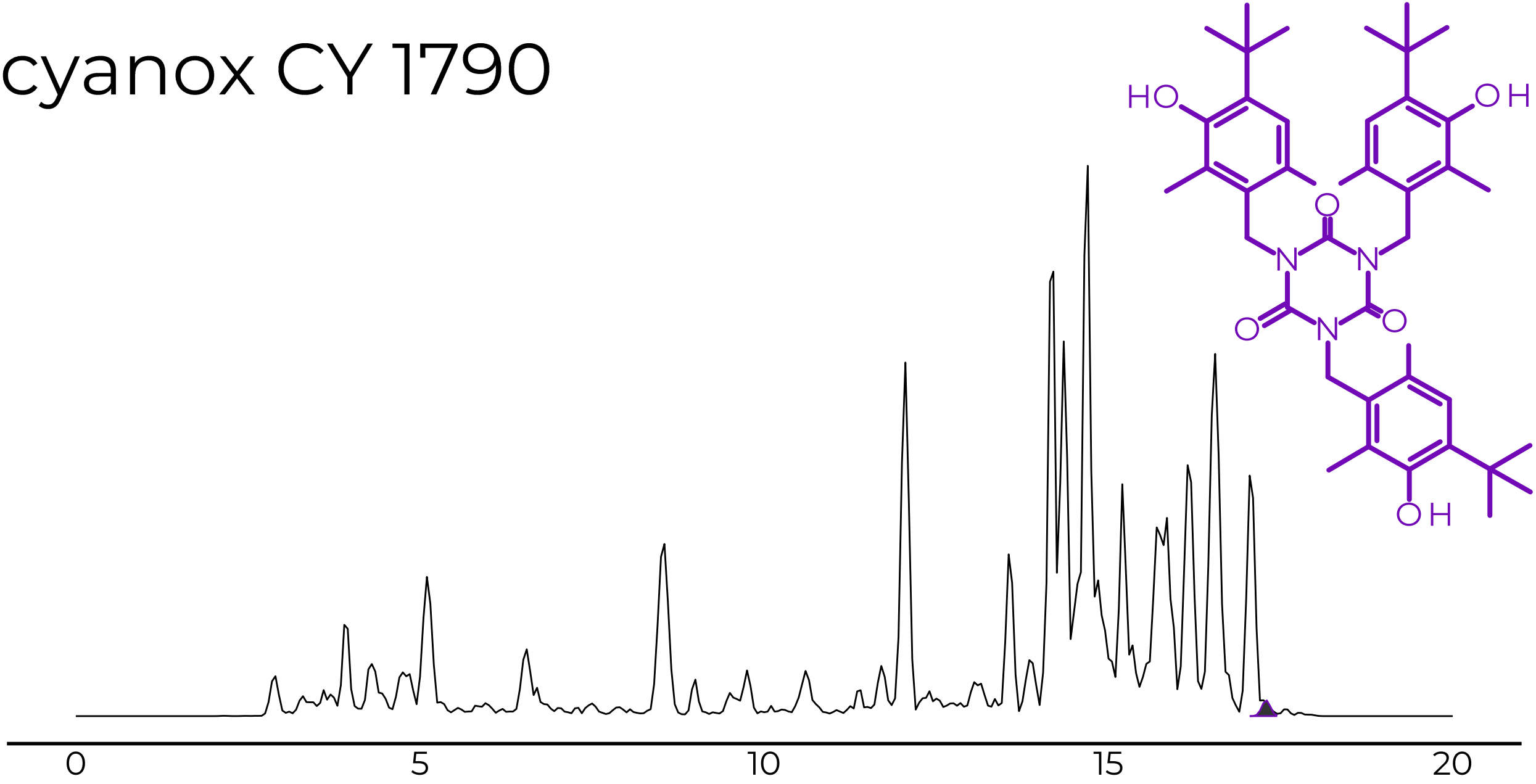
cyanox CY 1790



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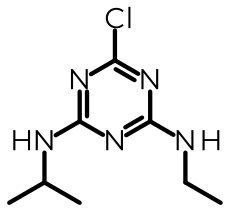
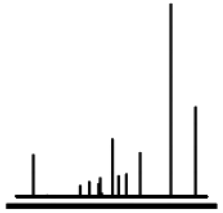
summary

prioritization in NTS

toxicity



structure



MS^2 spectrum

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