The Ionization Prediction Summit

Utilizing pKa Values for Effective Crop Protection: On Systemicity and Efficacy of Molecules

Bayer Crop Science

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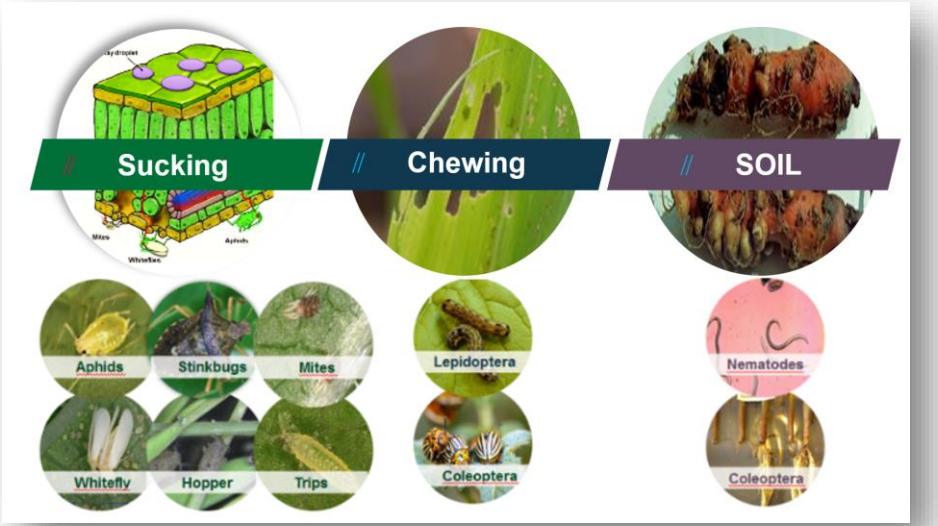
Agenda

- Short introduction crop protection
- Systemicity and efficacy in plants
- Example: Movento
- Summary

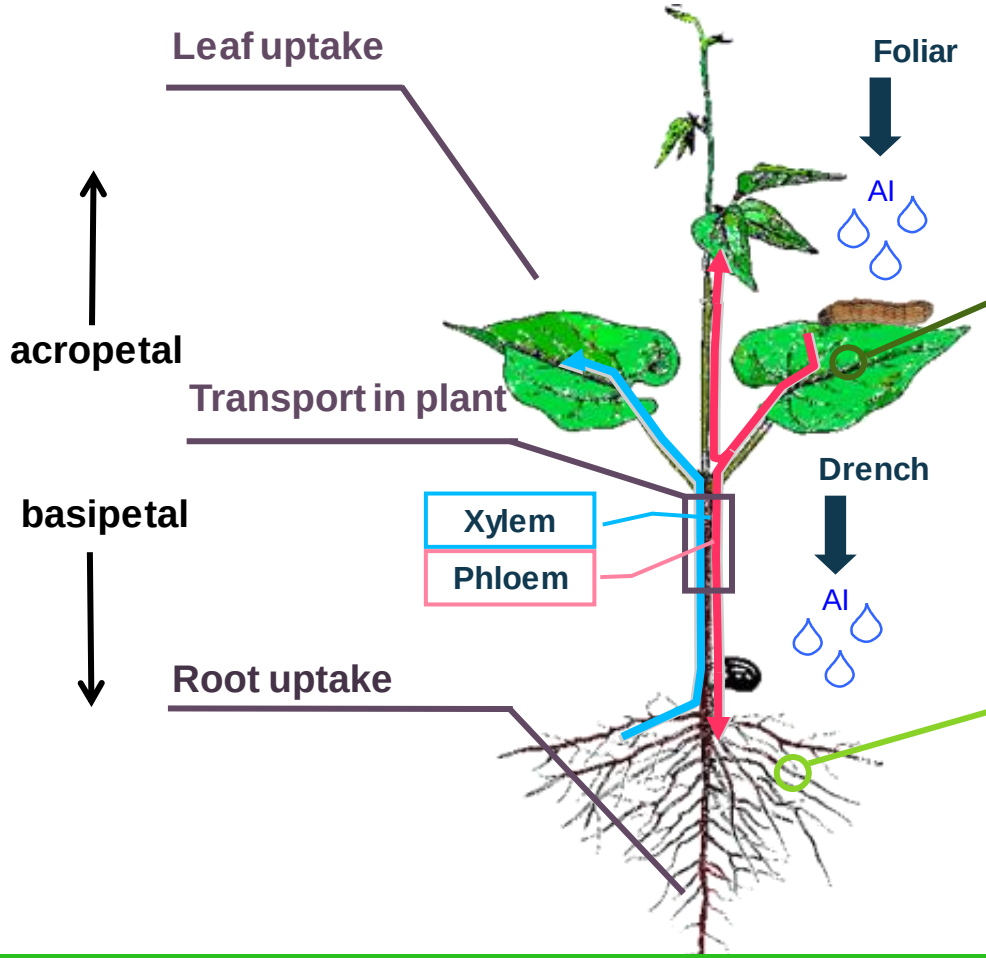
Importance of crop protection

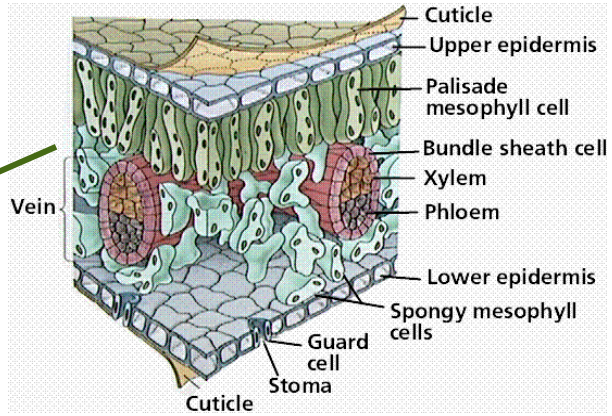
- Significant yield losses from weeds, diseases, and pests necessitate crop protection
- Key pest categories include chewing, sucking, and soil-based pests
- Crop protection molecules must reach target

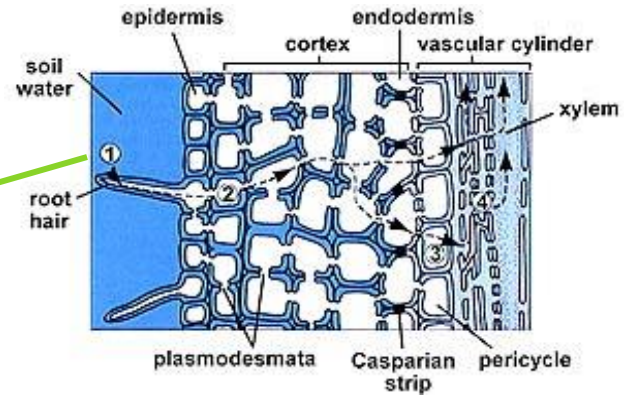


Goal: increase efficacy by increase systemicity - pKa as a major driver

Uptake of agrochemicals in plants







Leaf uptake

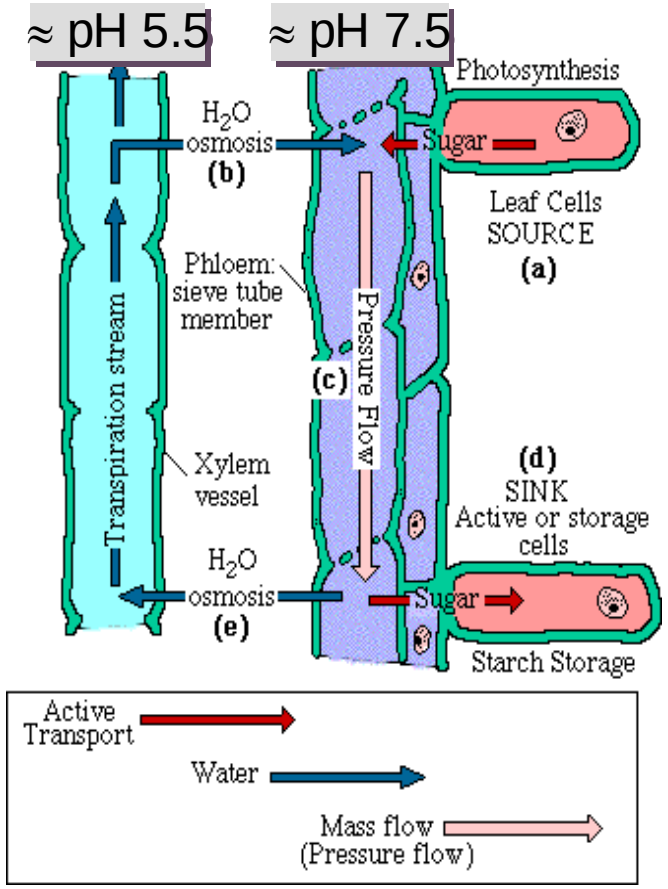
- Permeation through cuticle (similar to polymer membrane)

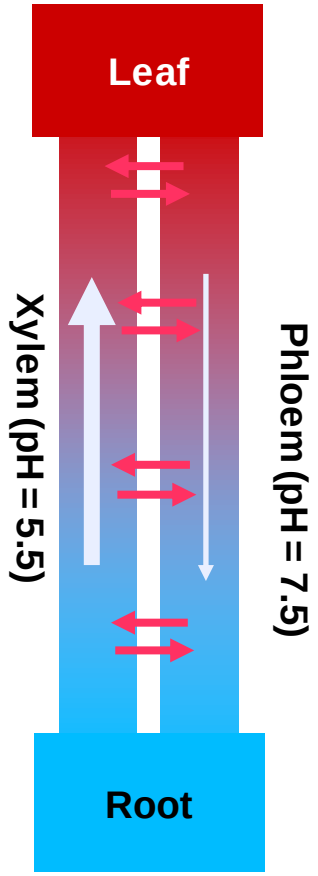
Root uptake

- Permeation through plasma lemma of root cells (phospholipid membrane)

Agrochemicals are taken up and distributed in the plant generally in a passive way along concentration gradients and according to their **physico-chemical** characteristics (watersolubility, lipophilicity and pka)

Phloem-mobility – Mechanism after Foliar Application



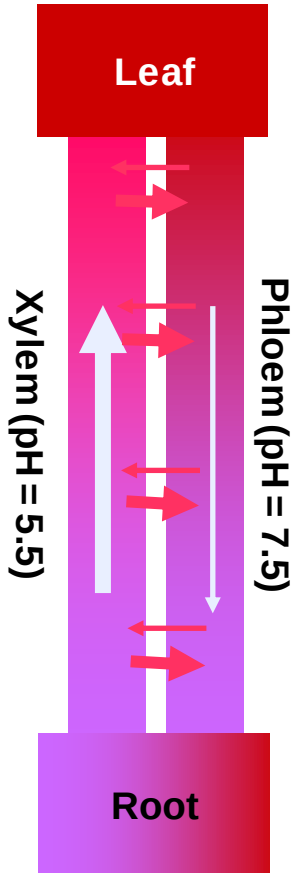


Neutral compounds:

- Equilibration between phloem and xylem
- Equal permeabilities
- Fast xylem transport “wins”
- **No translocation with phloem stream!**

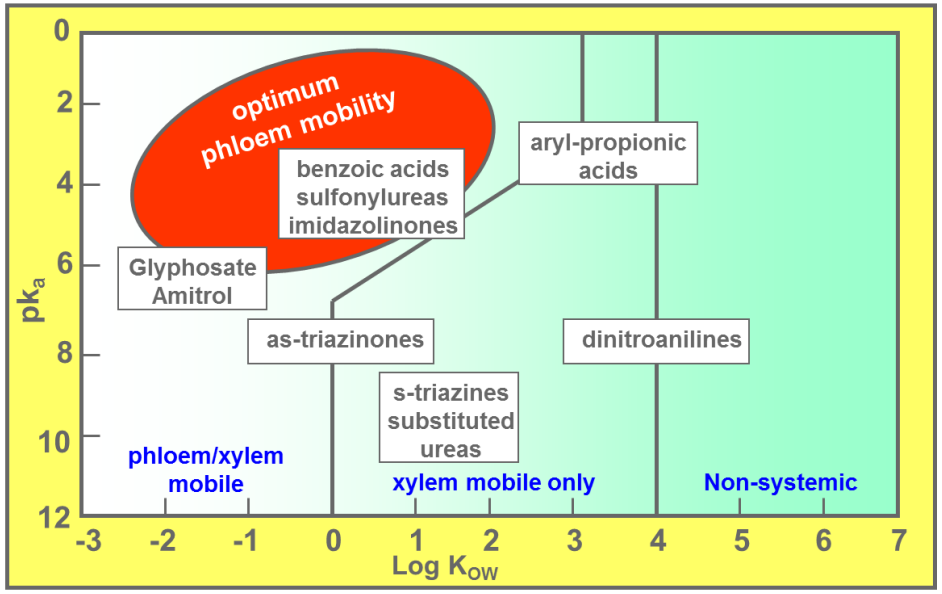
Weak acids:

- Ion trapping in phloem
- Permeabilities different
- Back transport in xylem slow due to low concentrations
- **Translocation with phloem stream possible!**

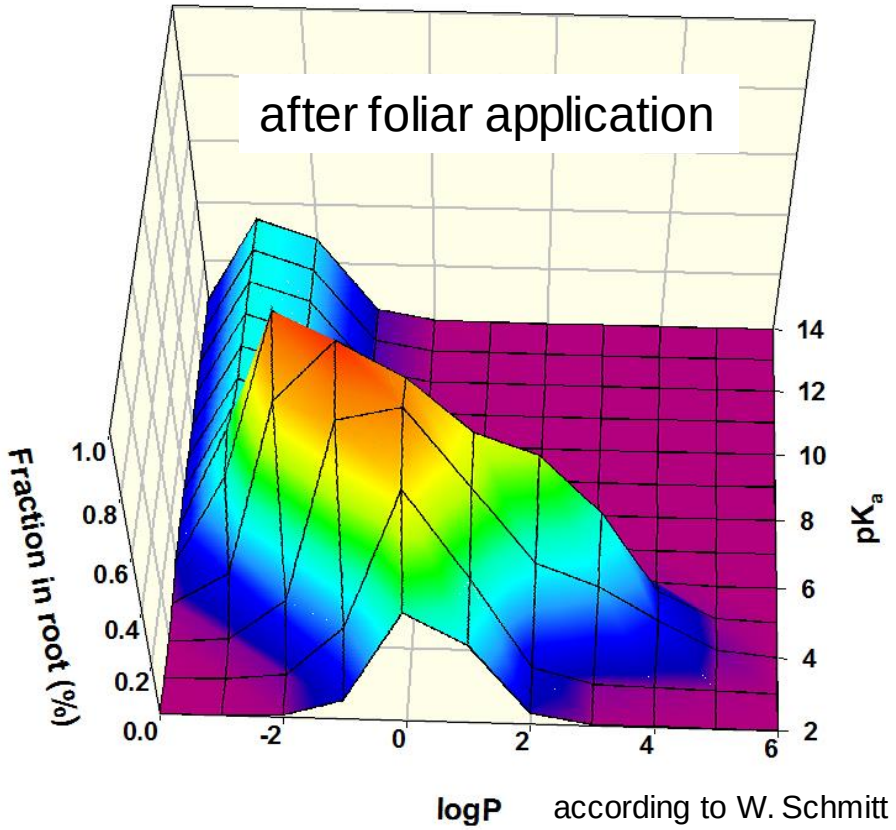


Systemicity of agrochemicals due to pKa and lipophilicity

strong acids



non-ionized



according to W. Schmitt

Bromilow, R., Weed Science, **1990**, 38(3), 305
Kleier, *J. Exp. Botany,* **1996**, (47), 1265

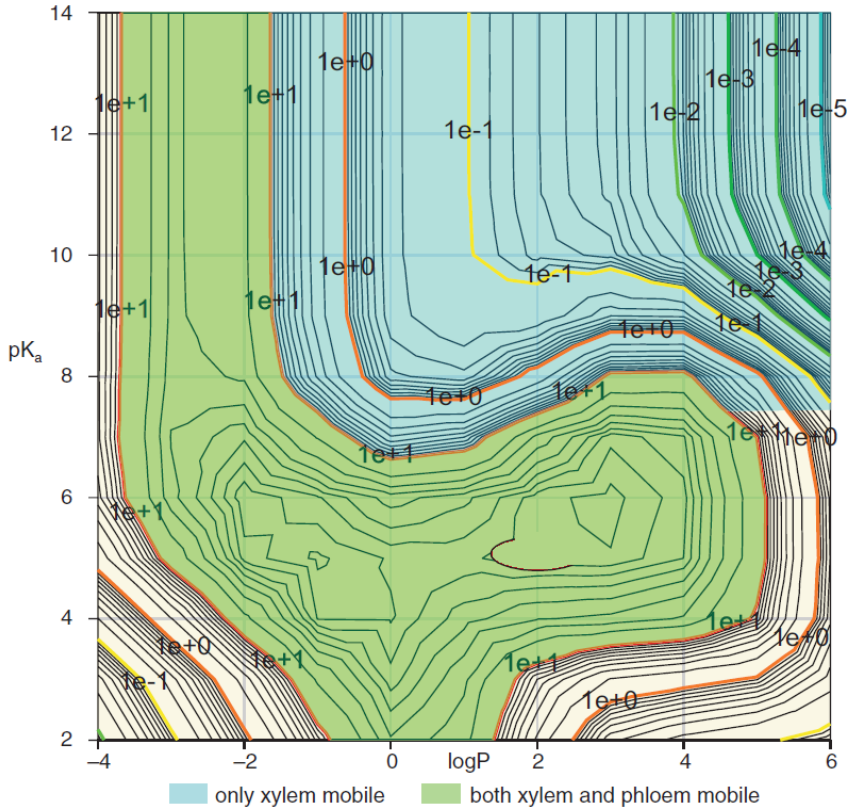
Systemicity of weak acids can be estimated based on pKa and lipophilicity

Example: Mobility of an Insecticide

Experimental Setup

Fig. 3: Phloem mobility bioassay for aphids using Savoy cabbage.

Predicted Physchem Mobility Relationship



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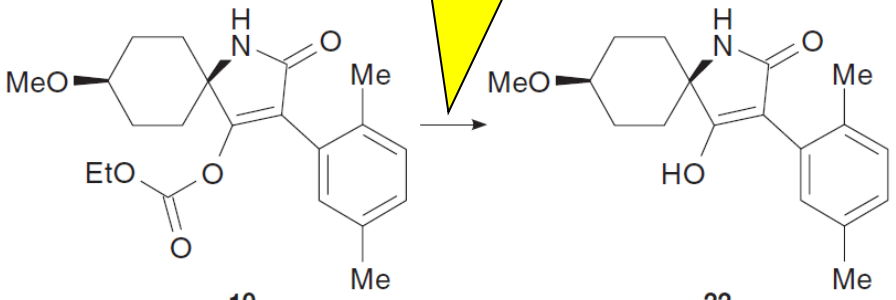
Example: Mobility of an Insecticide

Spirotetramat

in planta / in vivo de-esterification

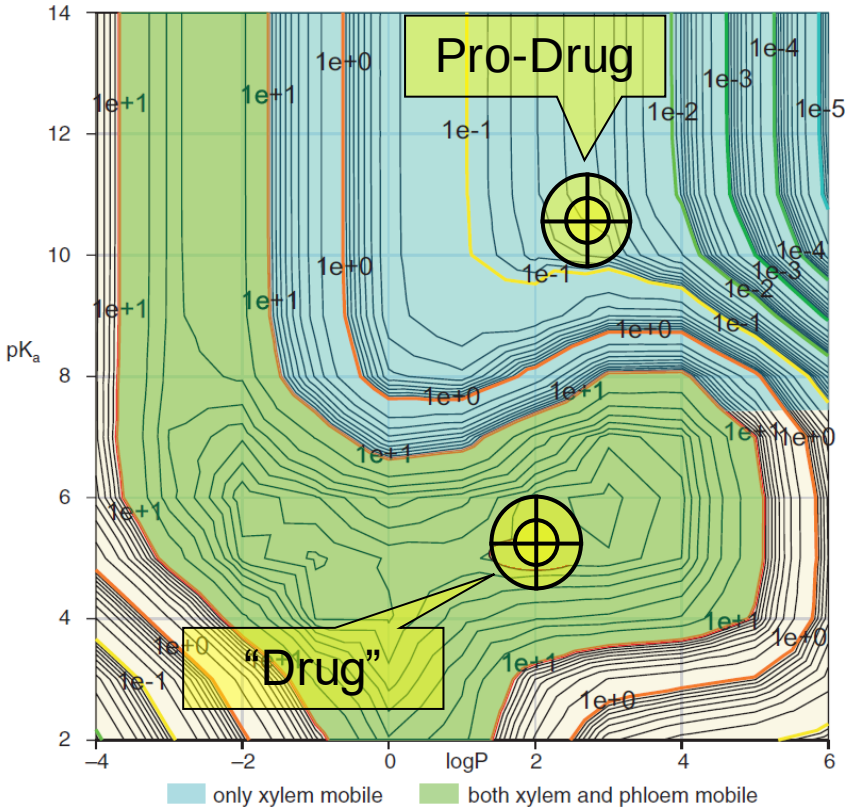


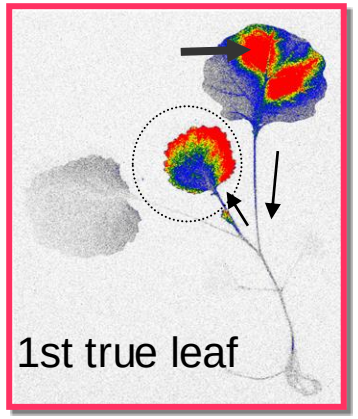
$logP_{ow}$	pH 4	2.51	pH 5	2
	pH 7	2.51	pH 7	0.3
	pH 9	2.50	pH 8	−1.3
pK_a		10.7		5.2

“Pro-drug”:
Penetrates into leaf but cannot reach another leaf

“Drug”:
is transported into other leaves via Phloem (but would not have penetrated into leaf)

Predicted Physchem Mobility Relationship





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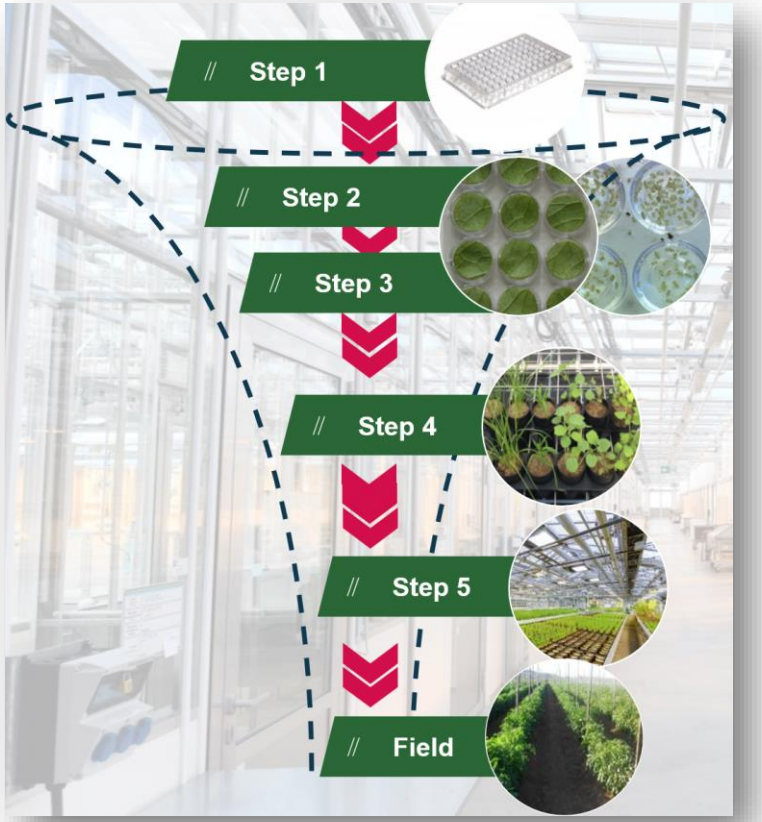
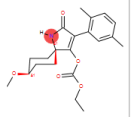
pKa important factor in research screening cascade of molecules

Summing it up

- Elevated experimental costs necessitate robust predictive models
- Employing Simulations Plus software for over a decade to predict pKa values
- pKa predictions are incorporated into our research platforms and utilized regularly
- In 2023, we migrated data of over 4000 crop science compounds to Simulations Plus, which significantly enhanced the model's performance on our hold-out set after retraining



	Predict pKa 1			
	Predicted pKa	SimPlus Success	Predominant charge state at pH 7.40	Lowest acidic pKa (strongest acid - dark red)
1		1	neutral [100.0%]	11.60

Thank you!