

# Unified pH – What, Why and How?

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Slides: <https://analytical.chem.ut.ee/CCT2023>

# Introduction

- pH is the best known parameter for expressing acidity

Activity of solvated proton

$$\text{pH} = -\log a(\text{H}^+, \text{solvent})$$

- The pH scale in **water** is well established

IUPAC Recommendations 2002:

R. P. Buck et al *Pure Appl. Chem.* 2002, 74, 2169

## Other solvents? Mixed solvents?

- In water pH is established and clear
- In practice very often non-aqueous or mixed solvents

**The situation is much more complicated  
with other solvents/media**

## The standard state

- In every solvent (medium) the **activity of solvated proton** is linked to its **concentration** in *that solvent*
- The **standard state** is 1 M (or 1 m)  $\text{H}^+$  in *that solvent*

The conventional standard state is  
***concentration-based***

- **But:** The same concentration of protons **in different solvents have hugely different ability** to influence processes
  - Catalysis, protonation of bases, etc

# Solvents differ by the ability to solvate H<sup>+</sup>

- By the ability of decreasing the **chemical potential** of H<sup>+</sup>
- Transfer free energies of H<sup>+</sup> from water to solvents:

Solvent	$\Delta_{\text{transfer}} G^\circ$ of H <sup>+</sup> from H <sub>2</sub> O (kJ/mol)
MeNO <sub>2</sub>	95
MeCN	<b>46.4</b>
MeOH	10.4
Water	0.0
DMSO	<b>-19.4</b>
Pyridine	-28

One pH unit corresponds to 5.7 kJ/mol

The **same [H<sup>+</sup>]** leads to difference of **11.5 pH units**

## As a Result ...

- The same pH in different solvents refers to the same  $H^+$  concentration but to **different acidity in terms of chemical potential**
  - It is the chemical potential that matters (protonation of bases, catalysis, acidic hydrolysis, redox potential, ...)
  - **Every solvent (or mixture) has its own pH scale**
  - **Not comparable to other solvents**

**Example:**

**pH 7 in water is neutral,**  
**pH 7 in MeCN is strongly acidic**

In mixtures: somewhere in between

## As another Result ...

- The  $pK_a$  values of the same compound in different solvents **can be very different**
  - And it is the difference between pH and  $pK_a$  that controls ionization (charge state)

### Example:

$pK_a$  of benzoic acid in water is 4.2,  
 $pK_a$  of benzoic acid in MeCN is 21.5

In mixtures: somewhere in between

## Conclusion:

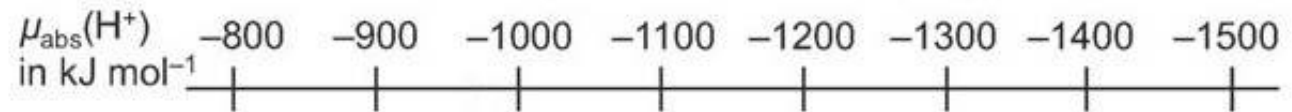
The conventional pH ...

- ... is **non-comparable** between solvents
  - Different solvents → different standard states
  - The same pH in different solvents refers to different acidity
  
- ... is **limited** to few solvents



# Absolute/Universal pH possible? Yes: $\text{pH}_{\text{abs}}$

- $\text{pH}_{\text{abs}}$  values are linked to **absolute chemical potential of  $\text{H}^+$** 
  - „Aligned“ to pH in water:  $\text{pH}_{\text{abs}}^{\text{H}_2\text{O}}$  and pH are equivalent
    - $\text{pH}_{\text{abs}}^{\text{H}_2\text{O}}$  7.0 corresponds to  $\mu_{\text{abs}}(\text{H}^+) -1144 \text{ kJ mol}^{-1}$
- $\text{pH}_{\text{abs}}^{\text{H}_2\text{O}}$  values in any solvent/medium are comparable



$$\text{pH}_{\text{abs}}^{\text{H}_2\text{O}} = \frac{-\mu_{\text{abs}}(\text{H}^+, \text{solv}) + \Delta_{\text{solv}}G^\circ(\text{H}^+, \text{H}_2\text{O})}{RT \ln 10}$$

14 H<sub>2</sub>O

34 DMSO

39 MeCN



# Comparability!

**Example:  $\text{pH}_{\text{abs}}^{\text{H}_2\text{O}}$  7.0**  
**measured in any solvent/medium**  
**has the same acidity as**  
**aqueous solution with pH 7.0**

The original development was (mostly)  
computational

Can  $\text{pH}_{\text{abs}}^{\text{H}_2\text{O}}$  be measured?

Yes!

Using differential potentiometry

A. Suu et al *Anal. Chem.* 2015, 87, 2623-2630

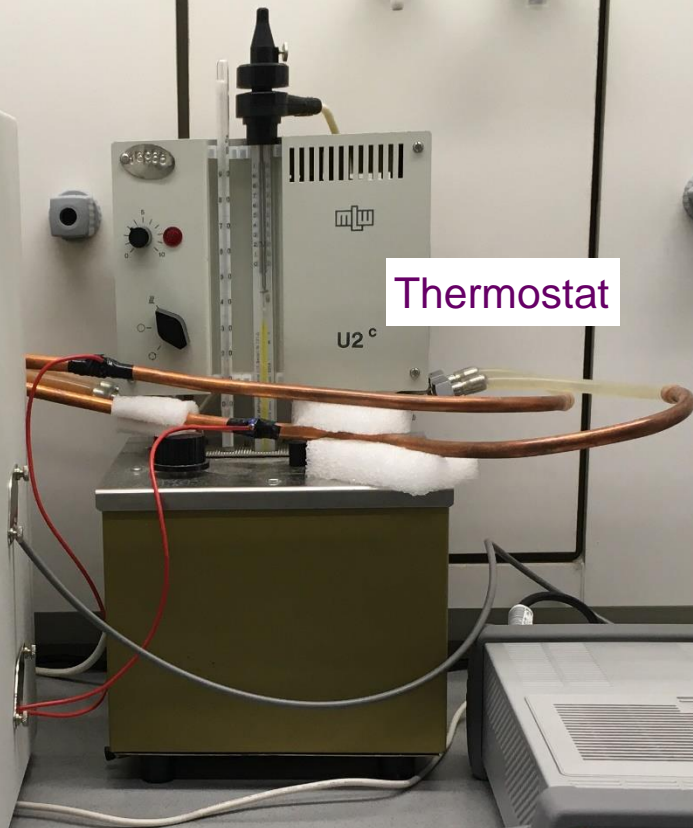
A. Heering et al *Symmetry* 2020, 12, 1150

V. Radtke et al *Pure Appl. Chem.* 2021, 93, 1049

Faraday cage



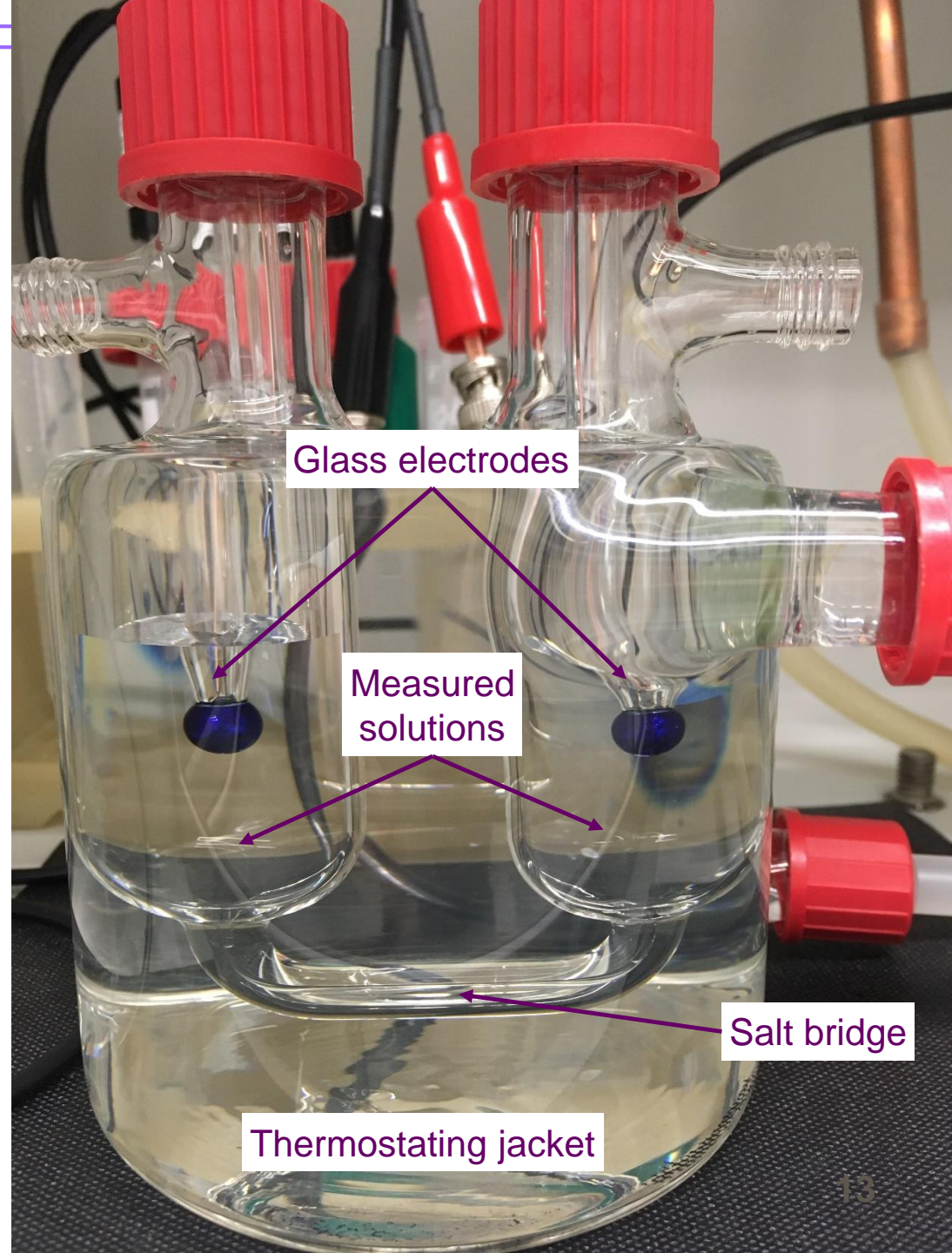
Thermostat



Potentiostat/  
potentiometer



- It is a relative measurement
- $\Delta\text{pH}$  of two solutions is measured
- Anchored to aqueous standard buffers



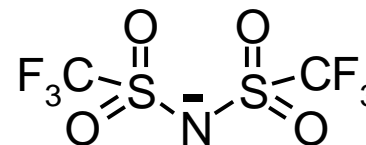
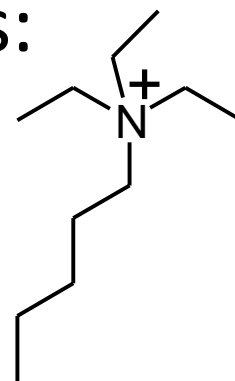


## Liquid Junction Potential ...

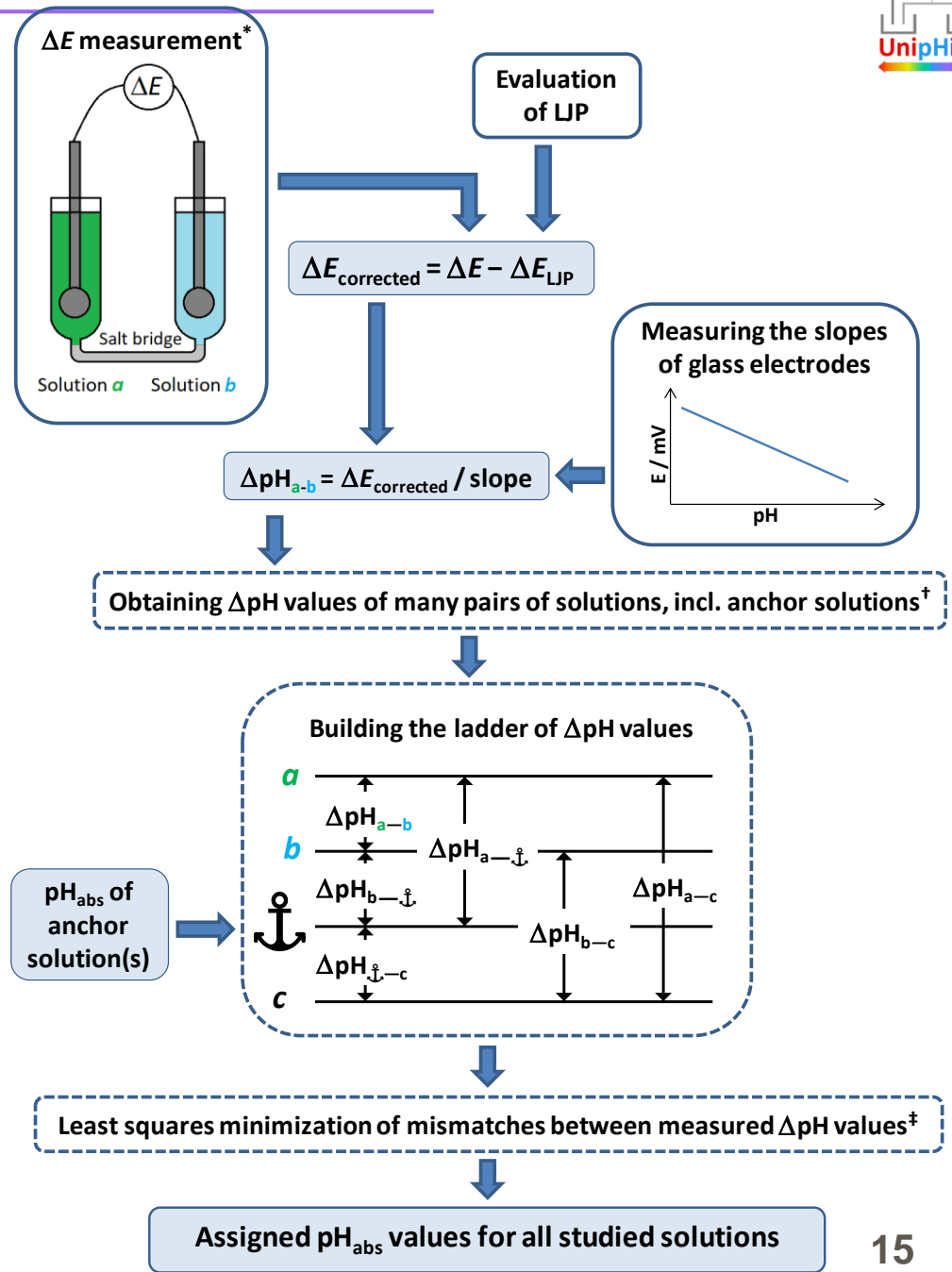
- ... emerges at the interfaces:



- There is an ionic liquid (IL) for salt bridge (SB), which enables **to cancel the LJP**, even between different solvents:

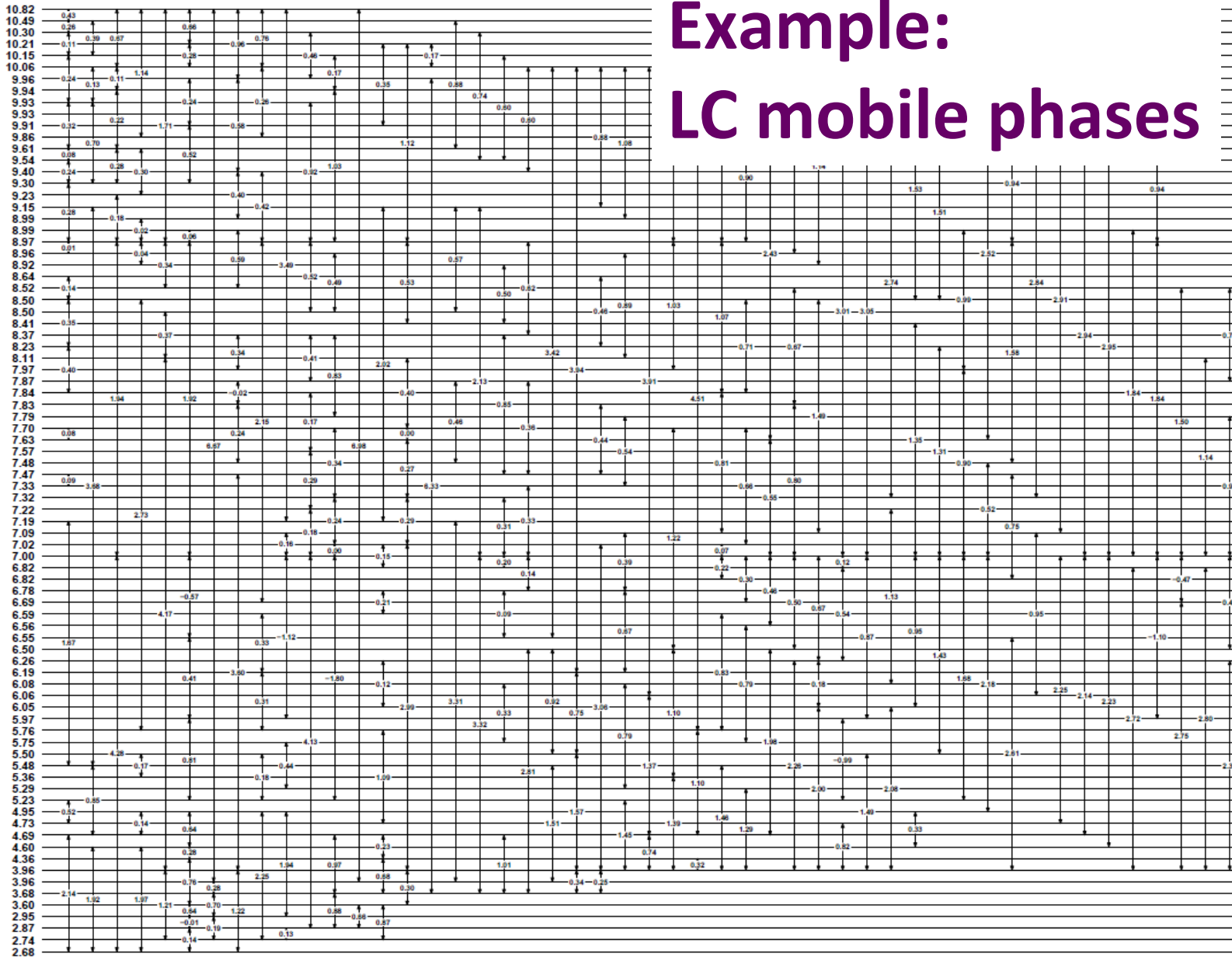


# Principle of measurement



Mobile phase  $pH_{abs}^{H_2O}$

MeCN/ 1 mM NH<sub>3</sub> 80/20 10.82  
MeOH/ pH 10 (TFE) 25/75 10.49  
MeOH/ pH 10 (HFIP) 25/75 10.30  
MeCN/ 1 mM NH<sub>3</sub> 50/50 10.21  
MeOH/ pH 9.5 (HFTB) 25/75 10.15  
Aqueous buffer pH 10.01 10.06  
MeOH/ 1 mM NH<sub>3</sub> 80/20 9.96  
MeOH/ pH 9.5 (PP) 25/75 9.94  
MeOH/ pH 9.5 (acetate) 25/75 9.93  
MeOH/ 1 mM NH<sub>3</sub> 20/80 9.93  
MeOH/ 1 mM NH<sub>3</sub> 50/50 9.91  
MeCN/ 1 mM NH<sub>3</sub> 20/80 9.86  
MeOH/ pH 9 (TFE) 25/75 9.61  
MeOH/ pH 9 (HFIP) 25/75 9.54  
MeOH/ pH 9 (HFTB) 25/75 9.40  
MeOH/ pH 8.5 (HFIP) 25/75 9.30  
MeOH/ pH 8.5 (TFE) 25/75 9.23  
MeCN/ pH 5 (acetate) 80/20 9.15  
MeOH/ pH 8.5 (HFTB) 25/75 8.99  
MeOH/ pH 7.5 (phosphate) 50/50 8.99  
Aqueous buffer pH 9.00 8.97  
MeOH/ pH 9 (acetate) 25/75 8.96  
MeOH/ pH 9 (PP) 25/75 8.92  
MeCN/ pH 5.5 (formate) 80/20 8.64  
MeOH/ pH 7 (HFTB) 80/20 8.52  
MeCN/ pH 5 (formate) 80/20 8.50  
MeOH/ pH 8.5 (acetate) 25/75 8.50  
MeOH/ pH 6.5 (PP) 25/75 8.44  
MeOH + 5 mM HFTB/ pH 7 (HFTB) 80/20 8.37  
MeCN/ pH 4.5 (formate) 80/20 8.23  
MeOH/ pH 5 (acetate) 90/10 8.11  
MeOH/ pH 7.5 (phosphate) 20/80 7.97  
MeOH + 5 mM HFTB/ pH 7 (HFTB) 40/60 7.87  
MeCN/ pH 4 (formate) 80/20 7.84  
MeOH/ pH 7 (HFTB) 40/60 7.83  
MeOH/ pH 7 (HFTB) 25/75 7.79  
MeOH/ pH 5 (acetate) 80/20 7.70  
MeOH/ pH 7 (PP) 25/75 7.63  
MeOH/ pH 5.5 (formate) 80/20 7.57  
MeOH/ pH 7 (HFTB) 5/95 7.48  
MeOH + 5 mM HFTB/ pH 7 (HFTB) 5/95 7.47  
MeOH/ pH 6 (HFTB) 25/75 7.33  
MeOH/ pH 7 (acetate) 25/75 7.32  
MeOH/ pH 5 (formate) 80/20 7.22  
MeCN/ pH 4.5 (acetate) 50/50 7.19  
MeCN/ pH 5.5 (formate) 50/50 7.09  
MeOH/ pH 6 (PP) 25/75 7.02  
Aqueous buffer pH 7.00 7.00  
MeOH/ pH 6 (acetate) 25/75 6.82  
MeOH/ pH 5 (HFTB) 25/75 6.82  
MeCN/ pH 5.5 (formate) 40/60 6.78  
MeCN/ pH 4 (formate) 75/25 6.69  
MeCN/ pH 5 (formate) 50/50 6.59  
MeOH/ pH 5.5 (formate) 50/50 6.56  
MeCN/ pH 4 (formate) 70/30 6.55  
MeOH/ pH 5 (acetate) 50/50 6.50  
MeOH/ pH 5 (PP) 25/75 6.26  
MeCN/ pH 5 (formate) 40/60 6.19  
MeOH/ pH 5 (formate) 50/50 6.08  
MeCN/ pH 4.5 (formate) 50/50 6.06  
MeOH/ pH 5 (acetate) 25/75 6.05  
MeCN/ pH 4 (formate) 60/40 5.97  
MeCN/ pH 4.5 (formate) 40/60 5.76  
MeOH/ pH 5.5 (formate) 20/80 5.75  
MeOH/ pH 5 (acetate) 20/80 5.50  
MeCN/ 0.1% HCOOH 80/20 5.48  
MeOH/ pH 5 (acetate) 10/90 5.36  
MeOH/ pH 5 (formate) 20/80 5.29  
MeCN/ pH 4 (formate) 40/60 5.23  
MeOH/ 0.1% HCOOH 90/10 4.95  
MeCN/ pH 4 (formate) 25/75 4.73  
MeOH/ 0.1% HCOOH 80/20 4.69  
0.1% HCOOH MeOH/ 0.1% HCOOH 90/10 4.60  
0.1% HCOOH MeOH/ 0.1% HCOOH 80/20 4.36  
Aqueous buffer pH 4.01 3.98  
MeCN/ 0.1% HCOOH 50/50 3.96  
MeOH/ 0.1% HCOOH 50/50 3.68  
0.1% HCOOH MeOH/ 0.1% HCOOH 50/50 3.60  
MeOH/ 0.1% HCOOH 20/80 2.95  
0.1% HCOOH MeOH/ 0.1% HCOOH 20/80 2.87  
MeOH/ 0.1% HCOOH 10/90 2.74  
0.1% HCOOH MeOH/ 0.1% HCOOH 10/90 2.68

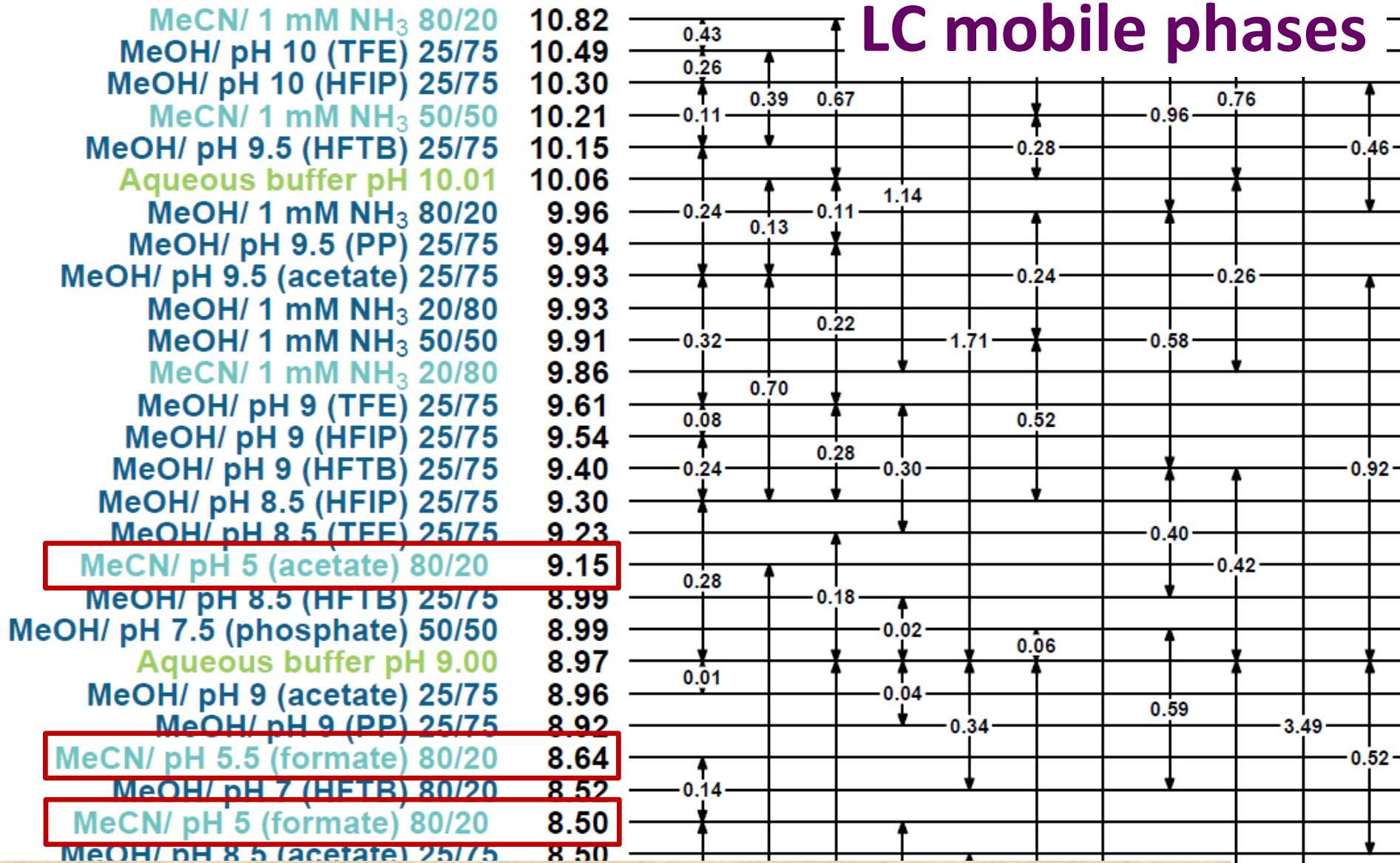


# Example: LC mobile phases



Mobile phase  $\text{pH}_{\text{abs}}^{\text{H}_2\text{O}}$

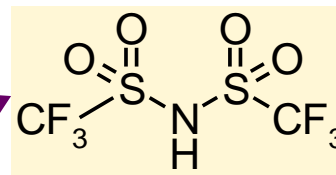
# Example: LC mobile phases



# Example: Extreme acidities in low-polarity solvents (in 1,2-dichloroethane)

- $\epsilon = 10$
- Anchor point:
- Solution of  $\text{Tf}_2\text{NH}$   
 $\text{pH}_{\text{abs}}^{\text{H}_2\text{O}} = -9.7$   
(Computational)

	$\text{p}K_{\text{ip,r}}$	$\text{p}K_{\text{a,r}}$	$\text{p}K_{\text{a,DCE}}$	$\text{pH}_{\text{abs}}^{\text{H}_2\text{O}}$
$\text{TfOH}$	-11.4	-11.3	33.7	-9.0
$\text{C}_6\text{H}_5\text{SO}(=\text{NTf})\text{NHTf}$	-11.5	-11.7	33.3	-9.4
$\text{TfCH}(\text{CN})_2$	-11.6	-11.5	33.5	-9.2
$\text{Br-TCNP}$	-11.8	-11.8	33.2	-9.5
$[\text{C}(\text{CN})_2=\text{C}(\text{CN})]_2\text{NH}$	-11.8	-12.0	33.0	-9.7
$3,5\text{-(CF}_3)_5\text{-C}_6\text{H}_3\text{-TCNP}$	-11.8	-12.0	33.0	-9.7
$\text{Tf}_2\text{NH}^f$	-11.9	-12.0	33.0	-9.7
$4\text{-Cl-C}_6\text{H}_4\text{SO}(=\text{NTf})\text{NHTf}$	-12.1	-12.3	32.7	-10.0
$\text{Cl-TCNP}$	-12.1	-12.1	32.9	-9.8
$(\text{C}_3\text{F}_7\text{SO}_2)_2\text{NH}$	-12.1	-12.3	32.7	-10.0
$(\text{C}_4\text{F}_9\text{SO}_2)_2\text{NH}$	-12.2	-12.4	32.6	-10.1
$\text{CN-CH}_2\text{-TCNP}$	-12.3	-12.4	32.6	-10.1
$(\text{C}_2\text{F}_5\text{SO}_2)_2\text{NH}$	-12.3	-12.4	32.6	-10.1
$\text{CF}_3\text{-TCNP}$	-12.7	-12.8	32.2	-10.5
$\text{HClO}_4$	-13.0	-12.8	32.2	-10.5
$\text{CF}_2(\text{CF}_2\text{SO}_2)_2\text{NH}$	-13.1	-13.1	31.9	-10.8
$4\text{-NO}_2\text{-C}_6\text{H}_4\text{SO}(=\text{NTf})\text{NHTf}$	-13.1	-13.3	31.7	-11.0
$\text{HB}(\text{CN})_4$	-13.3	-13.3	31.7	-11.0
$(\text{FSO}_2)_3\text{CH}$	-13.6	-13.6	31.4	-11.3
$\text{Tf}_2\text{CH}(\text{CN})$	-14.9	-15.0	30.0	-12.7
2,3,4,5-tetracyanocyclopentadiene	-15.1	-15.1	29.9	-12.8
$\text{CN-TCNP}$	-15.3	-15.3	29.7	-13.0



# Work underway and future directions

- **Liquid chromatography**

- Predicting and interpreting retention

A. Heering, M. Lahe, M. Vilbaste, J. P. Samin, J. Saame *In preparation.*

- **Low-polarity media**

- Negligible concentration of solvated H<sup>+</sup>, very low conductivity

J. P. Samin, J. Saame, A. Heering, *In preparation.*

E. Paenurk et al *Chem. Sci.* 2017, 8, 6964

- **Acidity in biphasic systems**

- Low-polarity medium at equilibrium with water  
e.g. cell membranes, chemical sensors, extraction

A. Leesment et al, *Anal. Chem.* 2022, 94, 4059

- **Acid catalysis, electrocatalysis**

- Interplay between catalysis and acidity of the medium

G. Maksimov, M. Lõkov et al, *In preparation.*  
Y. Matsubara *ACS Energy Lett.* 2017, 2, 1886

- **Simpler measurement method**

- Routine pH meter and double junction reference electrode

- **Surfaces and confined spaces**

- Heterogeneous catalysis, pH inside pores, molecular cages, ...

# Thank you for your attention!

## Thanks to all contributors!

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