



FRIEDRICH-SCHILLER-  
UNIVERSITÄT  
JENA

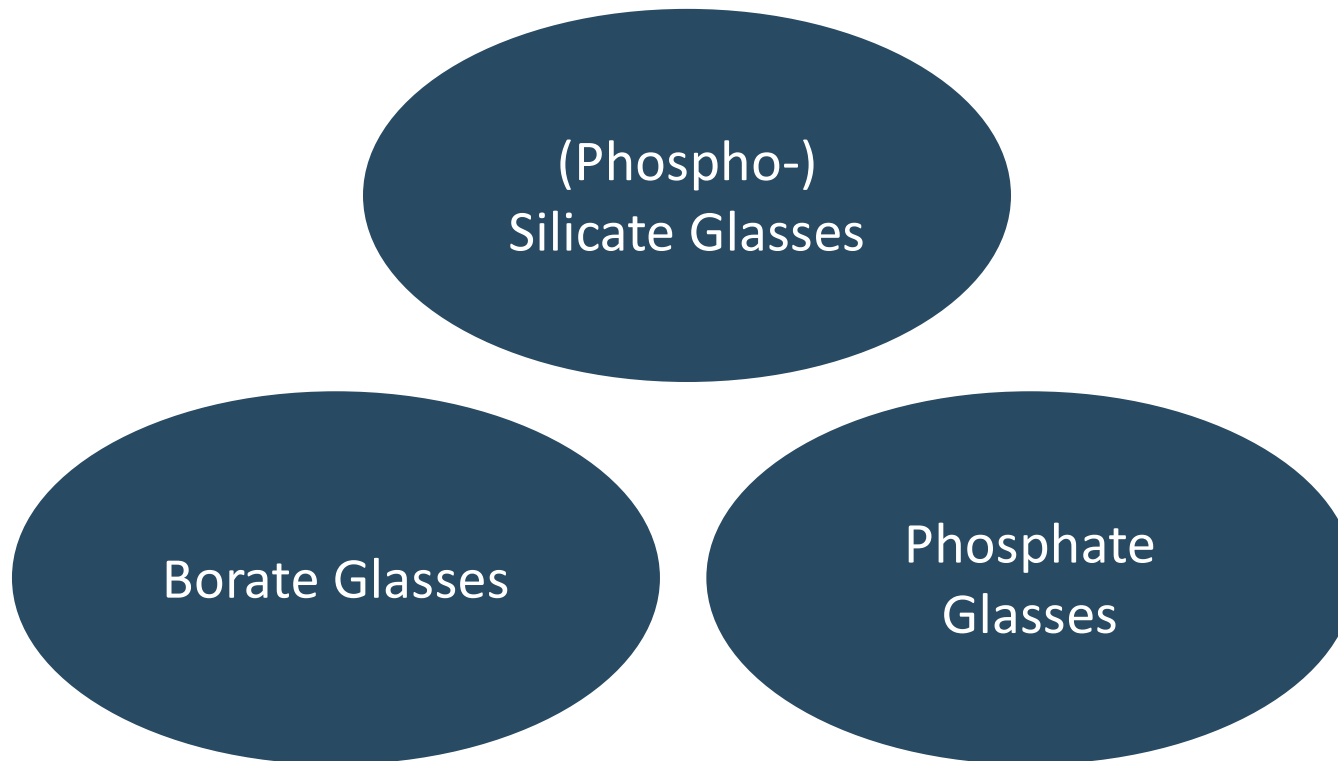
# Glass as a biomaterial

## Or why corrosion can be a good thing

**Delia S. Brauer**

Friedrich Schiller University

Otto Schott Institute of Materials Research



# "Bioactive glasses"

(Phospho-)  
Silicate Glasses

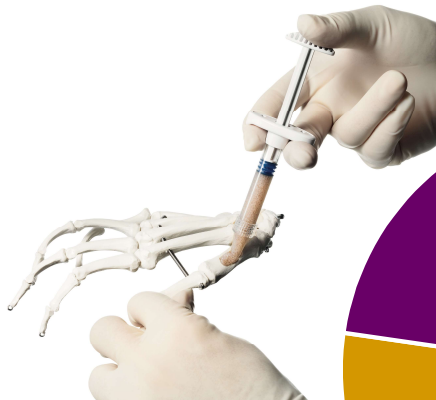
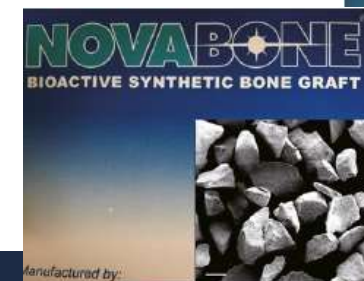
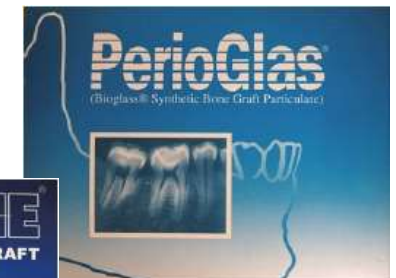
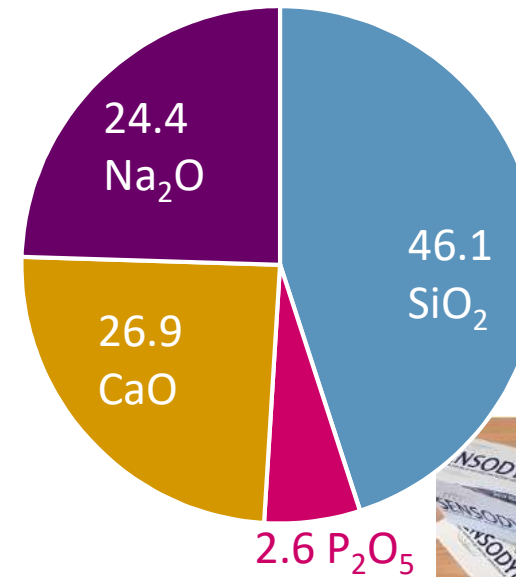
# "Bioactive glasses"



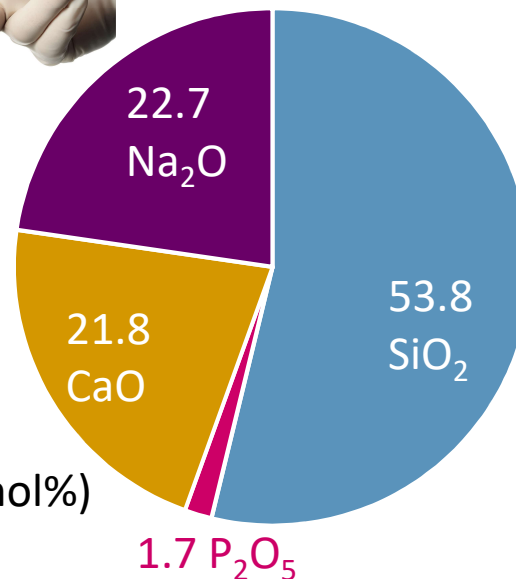
**Used Clinically for Bone Regeneration and Tooth Remineralisation**

# Commercial products

Composition of Bioglass 45S5 (mol%)



Composition of  
BonAlive® S53P4 (mol%)



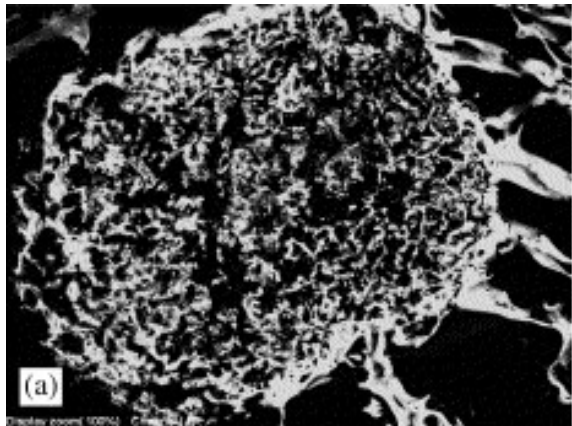
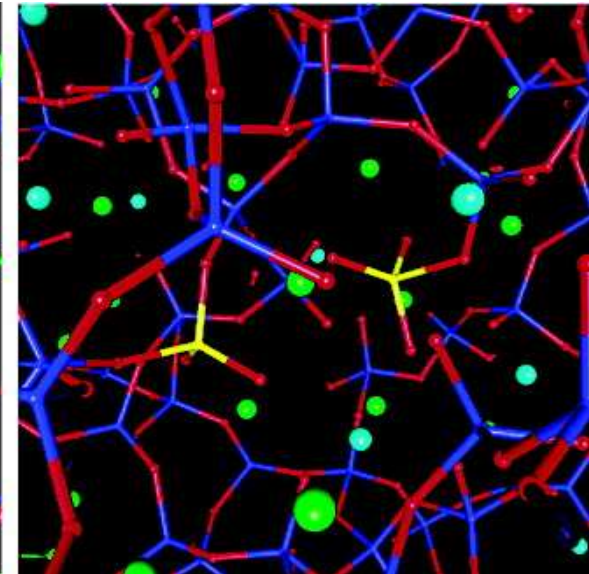
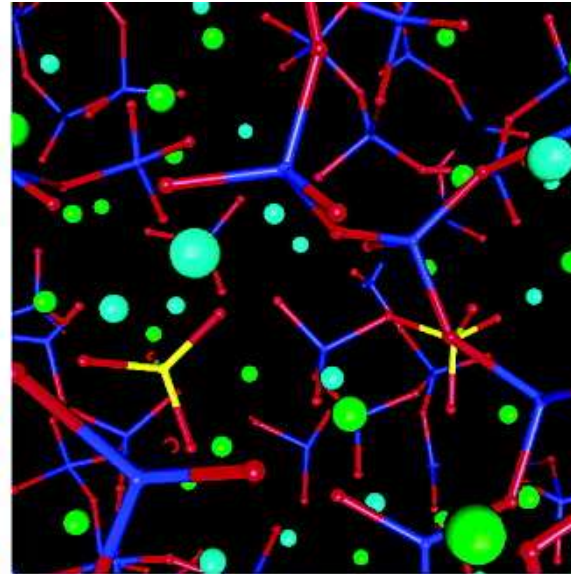
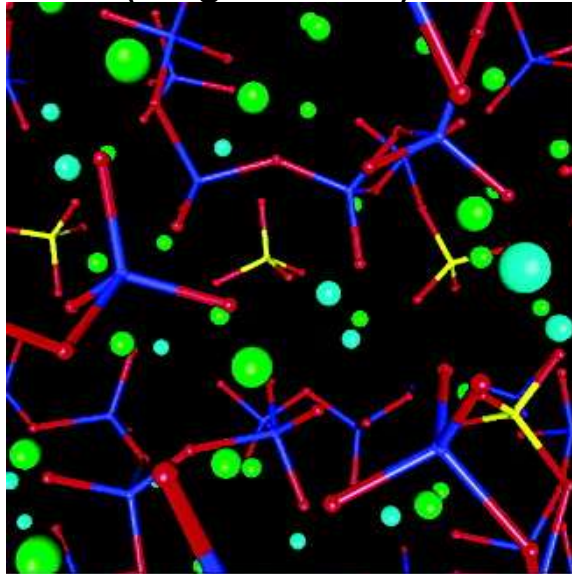
# Bone formation Na Ca silicate glass

46 mol% SiO<sub>2</sub>  
(Bioglass 45S5)

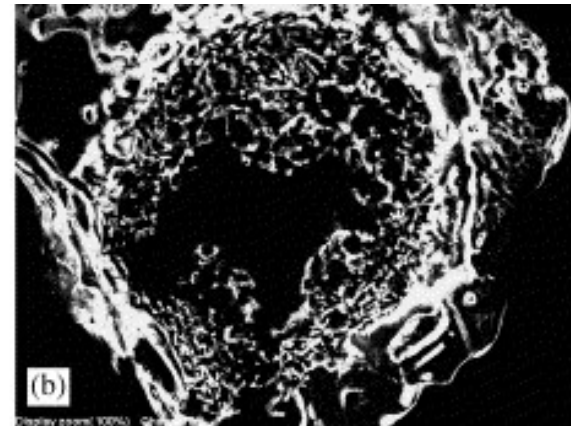
57 mol% SiO<sub>2</sub>

67 mol% SiO<sub>2</sub>

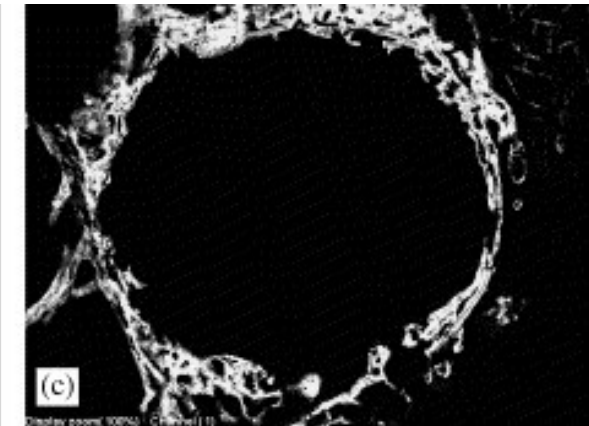
O  
Si  
P  
Ca  
Na



50mol% SiO<sub>2</sub>



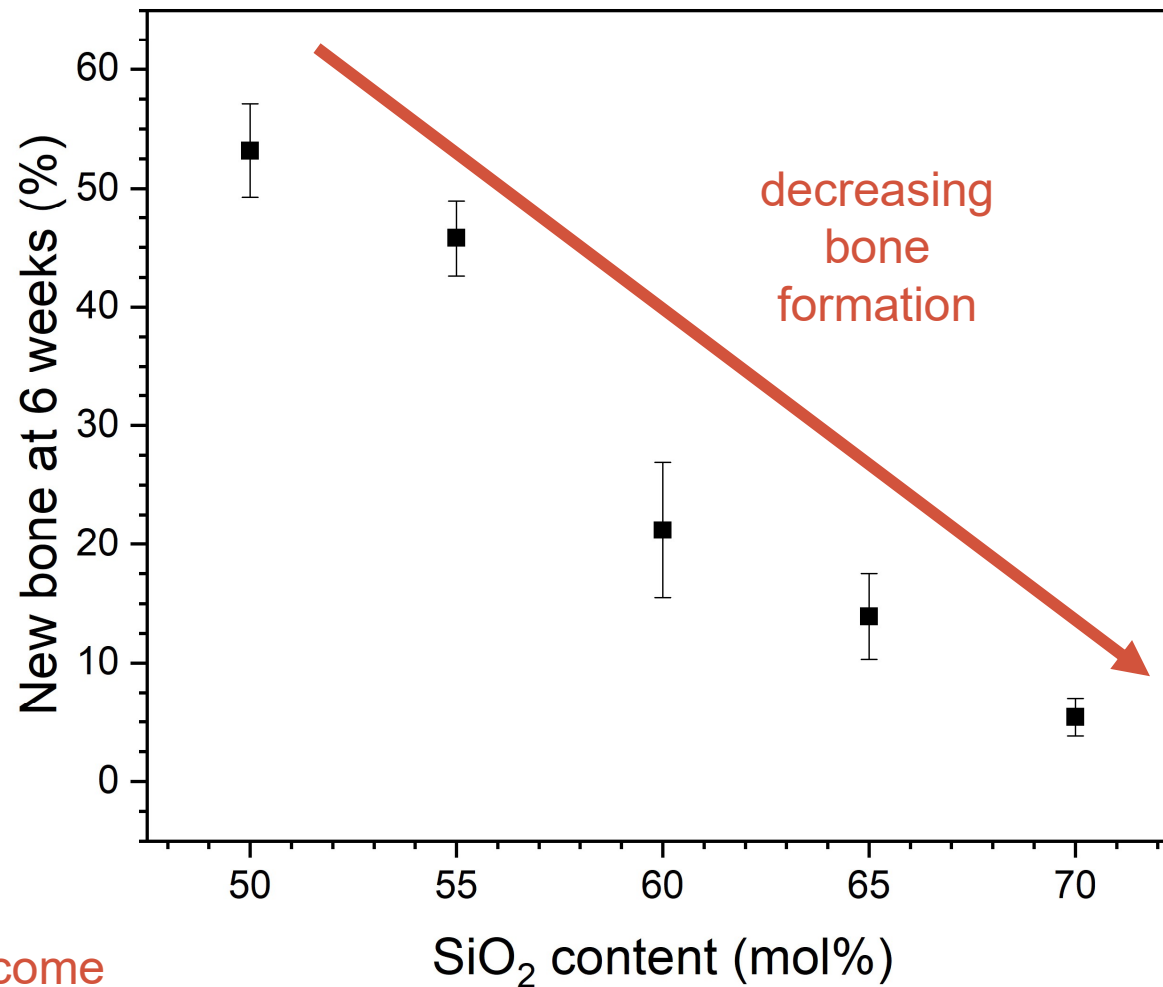
60mol% SiO<sub>2</sub>



70mol% SiO<sub>2</sub>

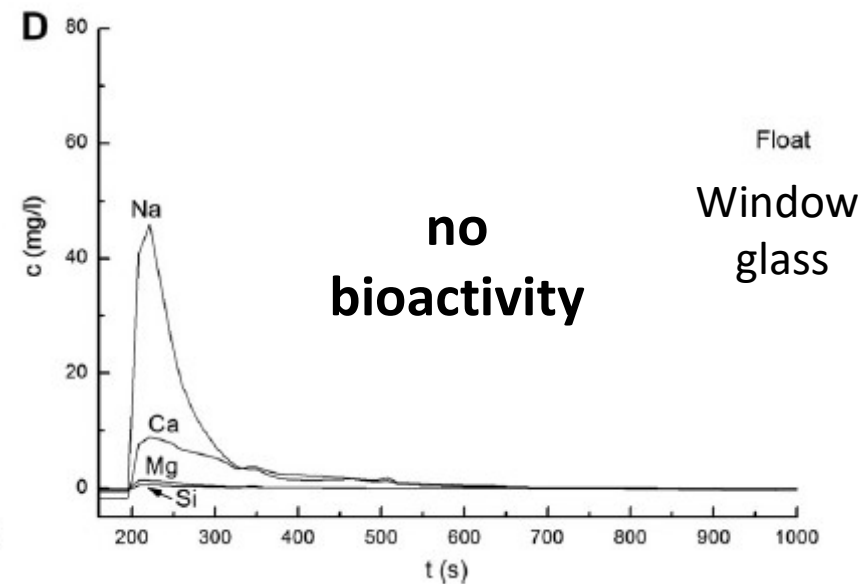
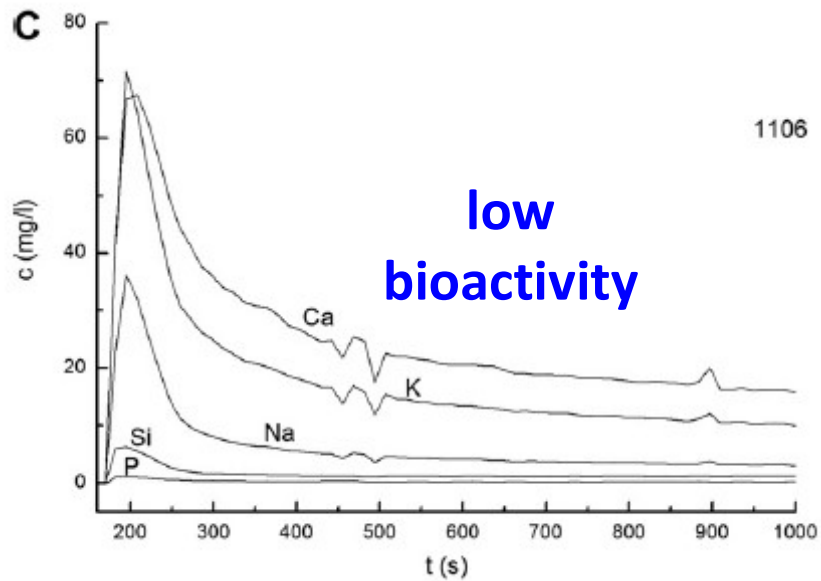
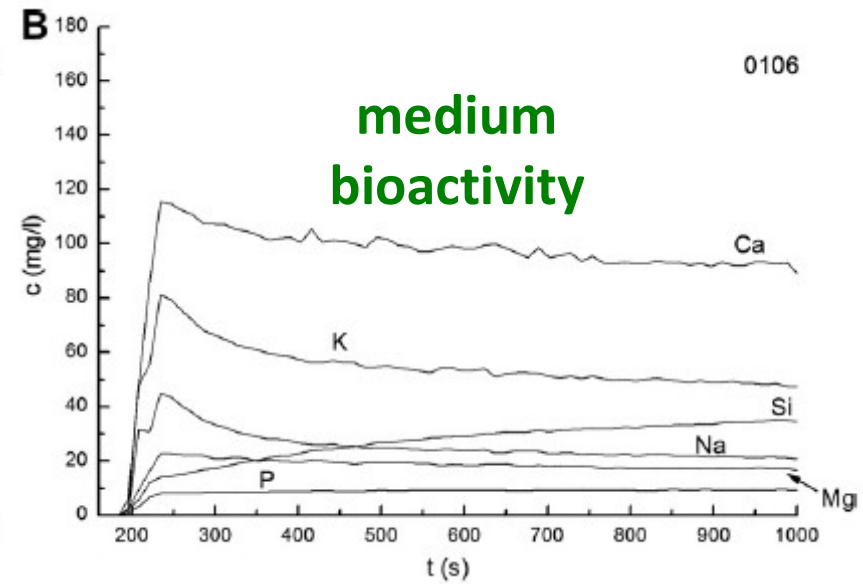
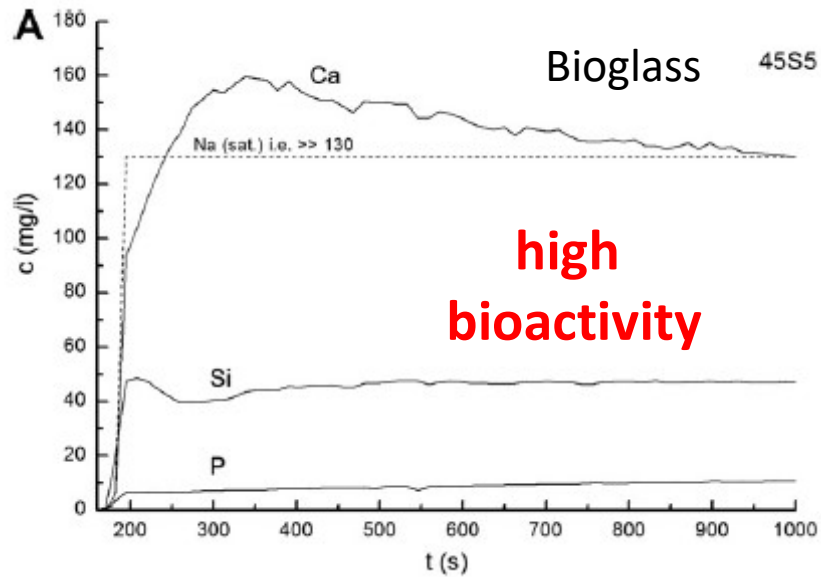
Tilocca et al., Chem. Mater. 19 (2007) 95-103  
Fujibayashi et al., Biomaterials 24 (2003) 1349-1356

# Bone formation Na Ca silicate glass



glasses become  
more cross-linked

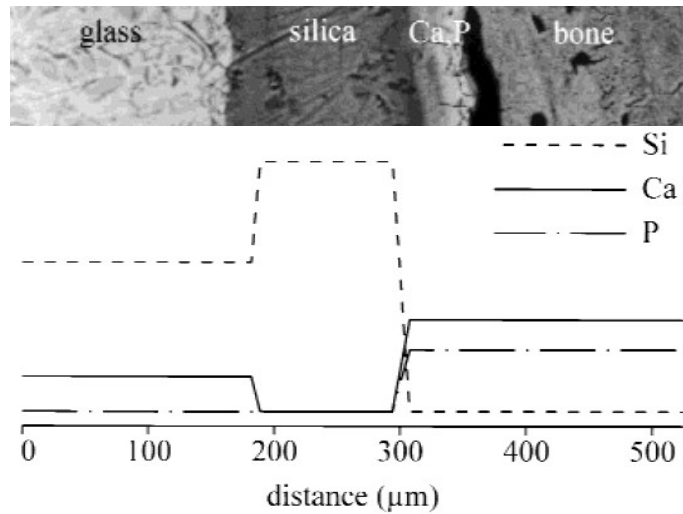
# Ion release



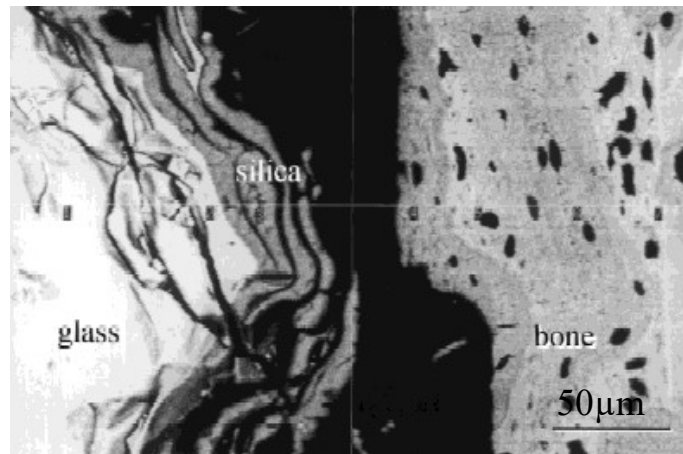


# Surface layer formation *in vivo*

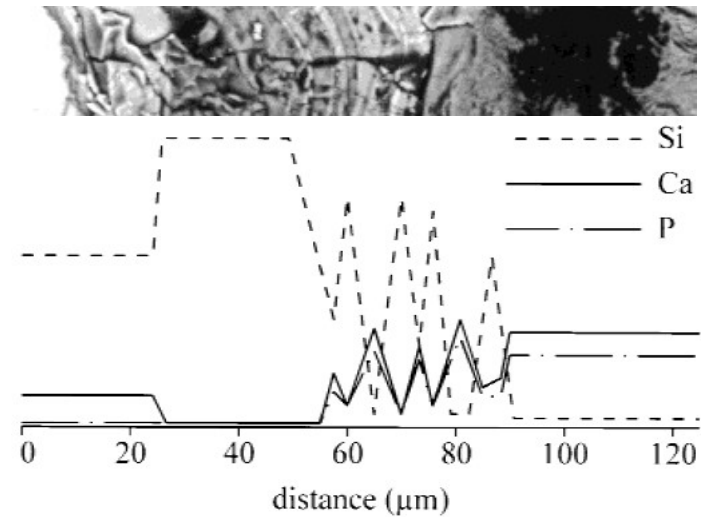
## high bioactivity:



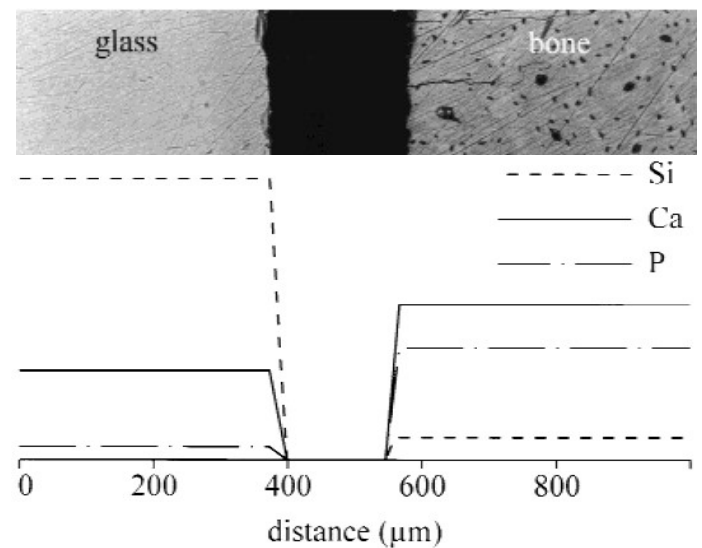
## low bioactivity:



## medium bioactivity:

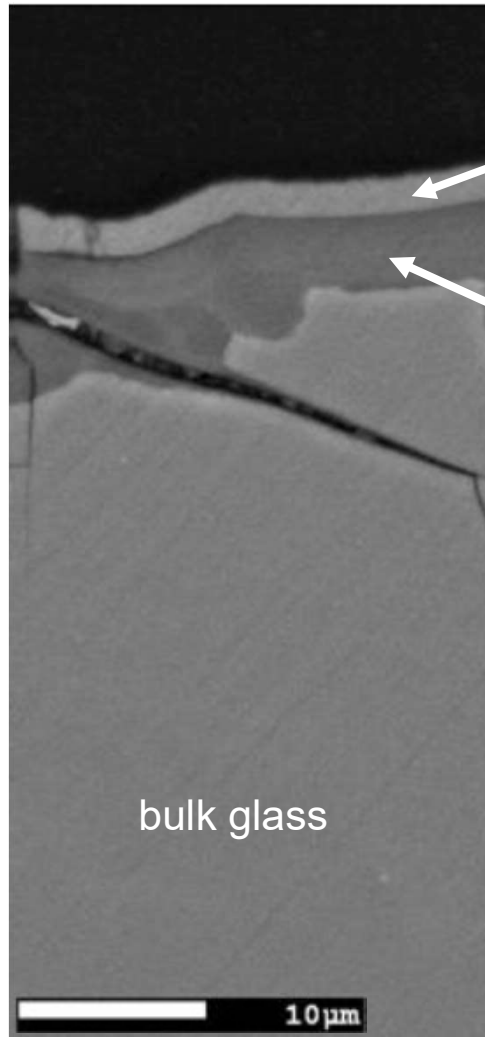


## no bioactivity:



# Surface layer formation *in vitro*

## Bioglass 45S5



surface layer:  
hydroxycarbonate  
apatite

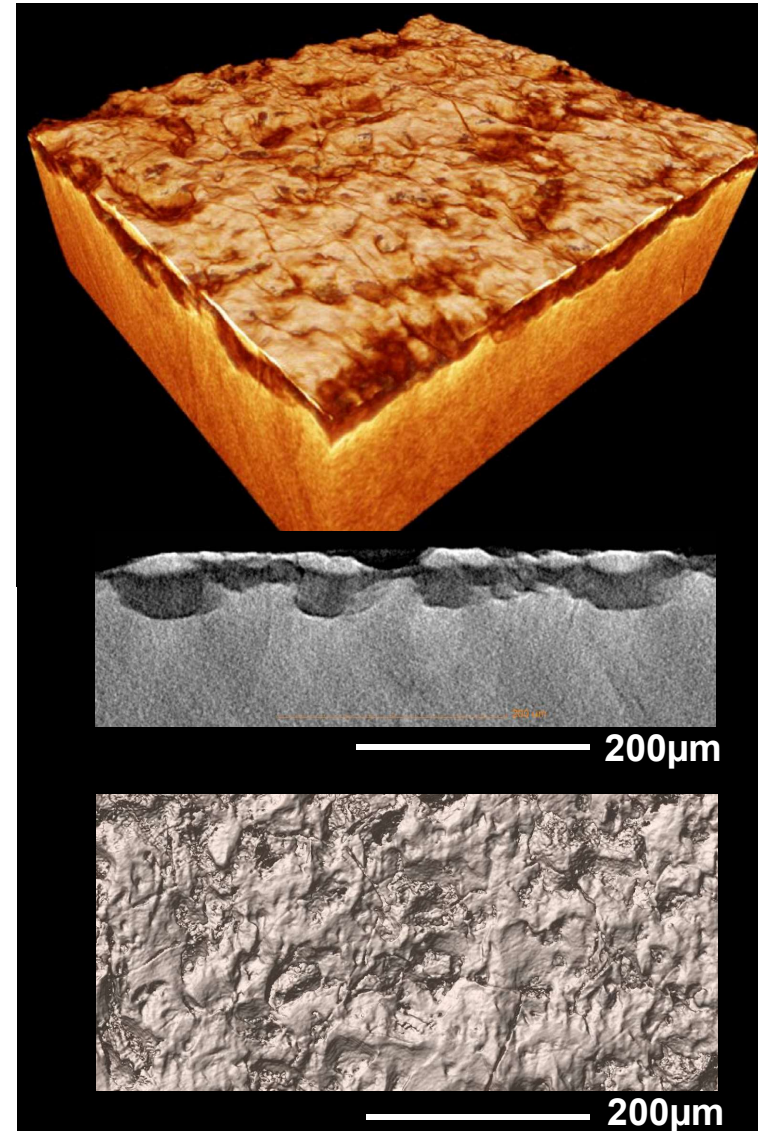
silica-rich layer:  
"silica gel"

Layer formation  
during immersion  
in simulated  
body fluid

bulk glass

10 μm

SEM



3D  
view

cross  
section

top  
view

200 μm

200 μm

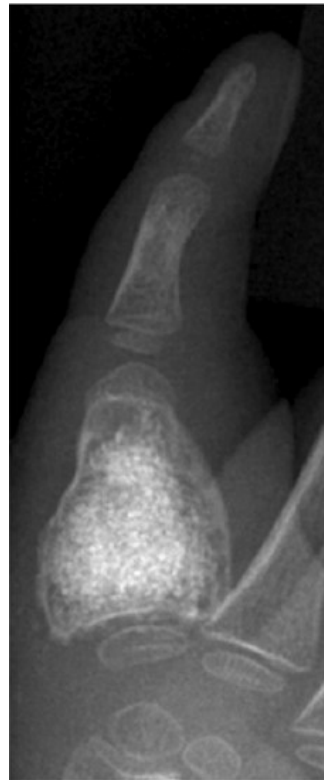
3D X-ray microscopy

## Treatment of a recurrent aneurysmal bone cyst in a 2 year old child

Bone cyst treated in the proximal phalanx of a finger:



Preoperative X-ray



at one month



at two years

Postoperative X-ray after treatment with BonAlive

Borate Glasses

# Borate glasses

images: ETS Wound Care



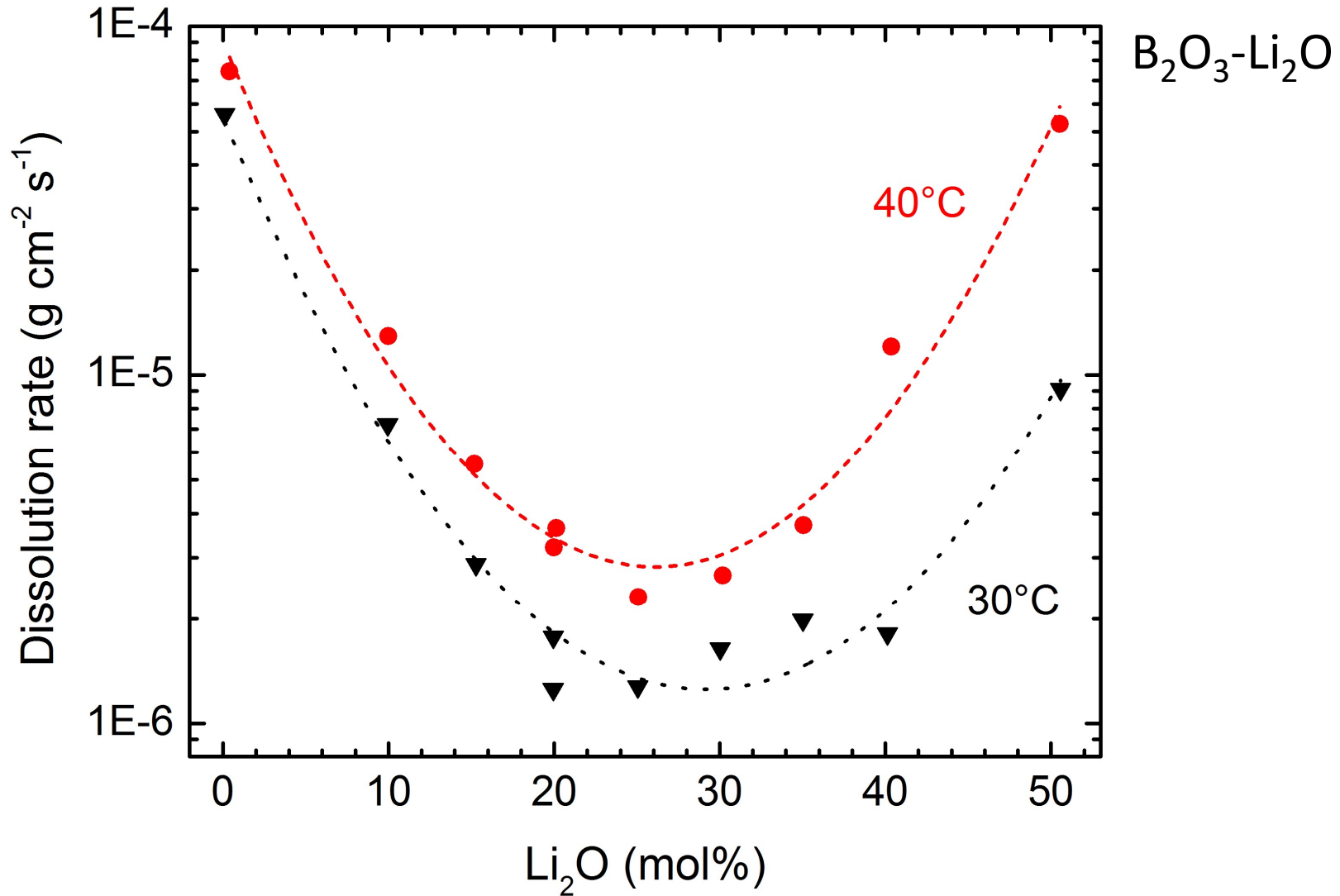
Borate Glasses



image: Avalon Medical

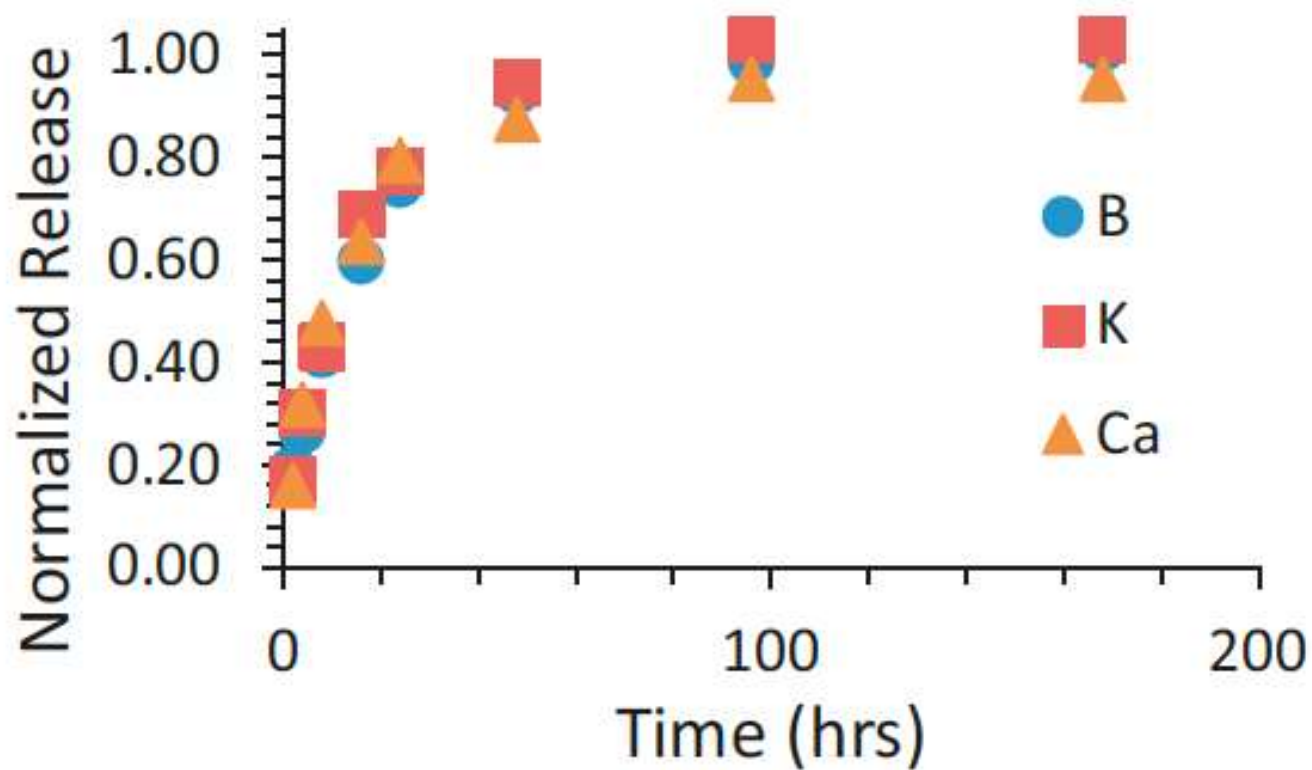
**Used Clinically for Wound Healing**  
(i.e. soft tissue application)

# Borate glass dissolution



# Borate glass dissolution

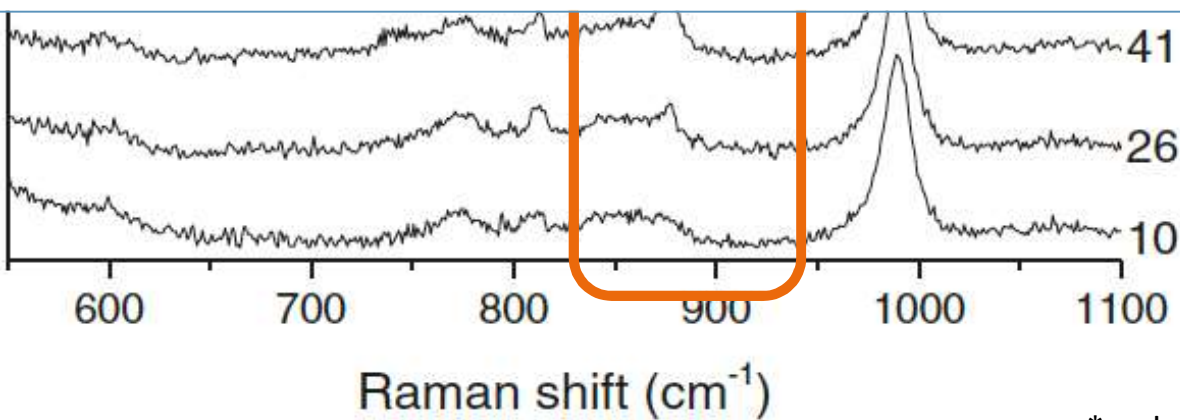
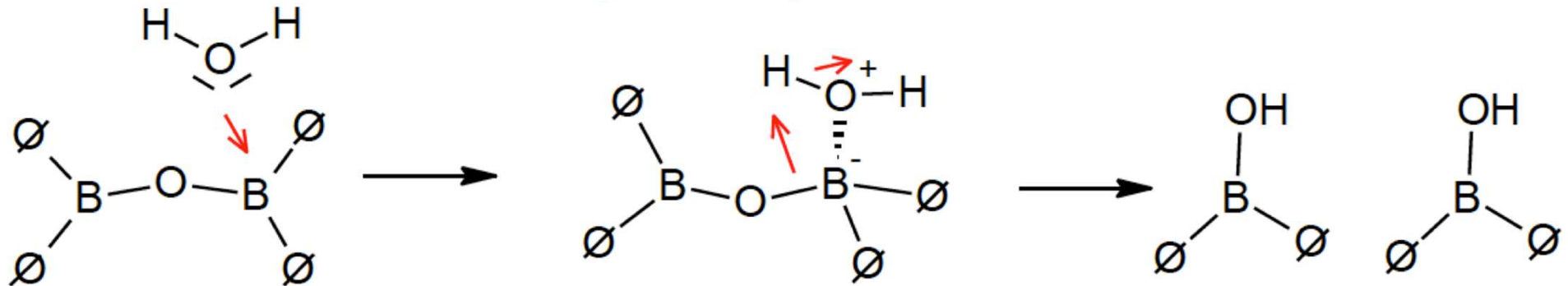
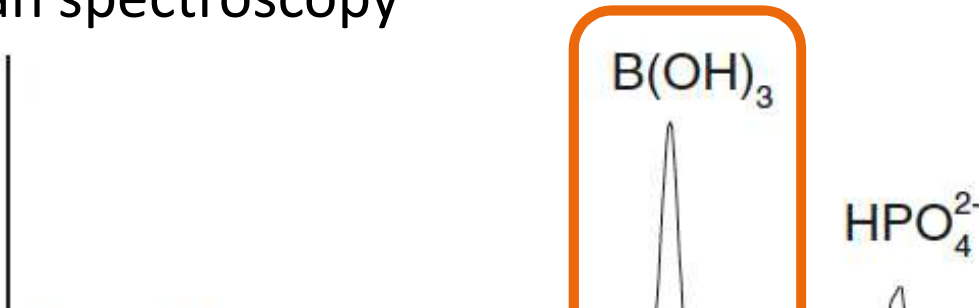
15 K<sub>2</sub>O-15 CaO-70 B<sub>2</sub>O<sub>3</sub>



# Borate glass dissolution

## Raman spectroscopy

80 B<sub>2</sub>O<sub>3</sub>-20 Na<sub>2</sub>O



\* polycarbonate sample holder



Phosphate  
Glasses

# Soluble phosphate glasses



**COSECURE™**

**rumen-available:** ✓ IONIC COBALT  
✓ SELENIUM  
✓ IONIC COPPER

available for cattle, sheep and lambs

[Read More](#)



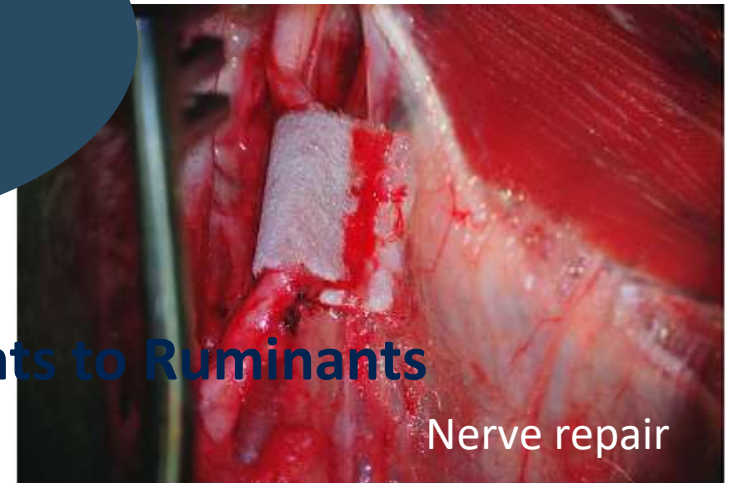
Specialised fertilisers

Therapeutic ion release

Fluoride release



Used to Deliver Trace Elements to Ruminants

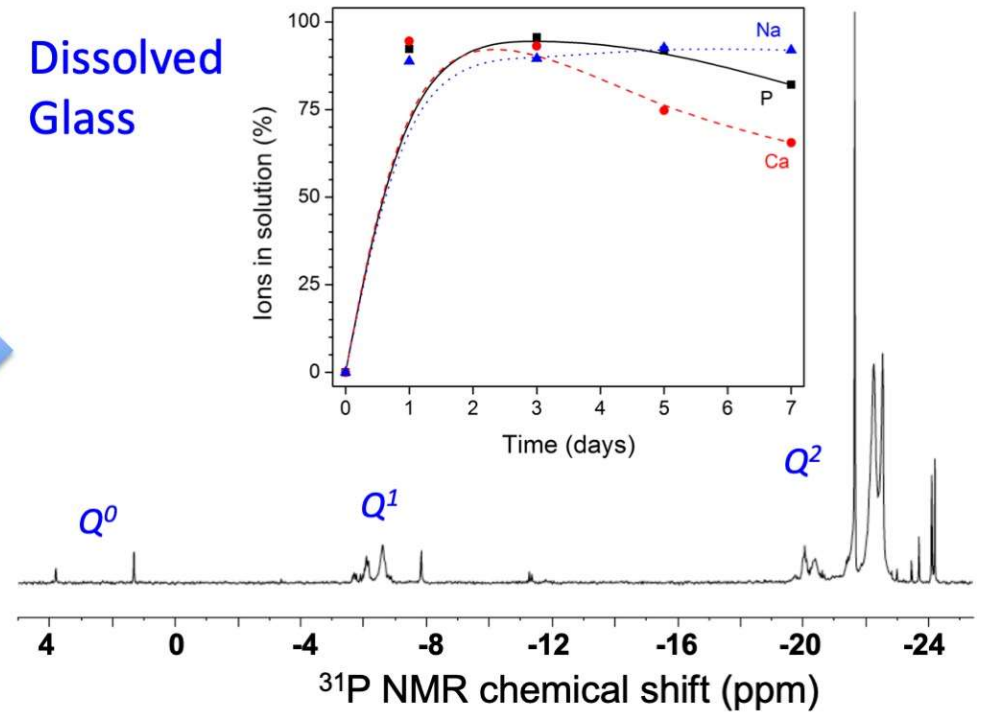
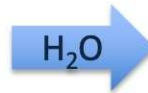
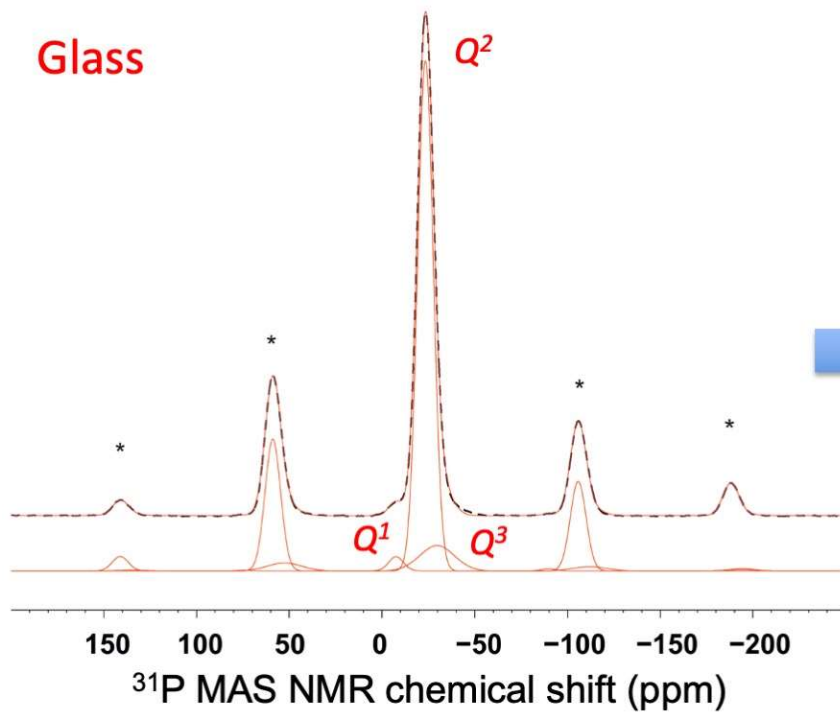


Nerve repair

Pessan et al., J Appl Oral Sci 16 (2008) 238-44  
Toumba & Curzon, Caries Res 39 (2005) 195-200

Lenihan et al., J Hand Surg 23B (1998) 588-593  
Jeans et al., J Plastic, Reconstr Aesth Surg 60 (2007) 1302-1308

# Dissolution studies



2-amino-2-hydroxymethyl-propane-1,3-diol + HCl  
(Tris-HCl) buffer

# Dissolution experiments

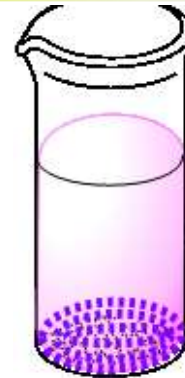
## 2. Glass immersion

- 125-315  $\mu\text{m}$
- $\text{H}_2\text{O}$ , Tris, EDTA



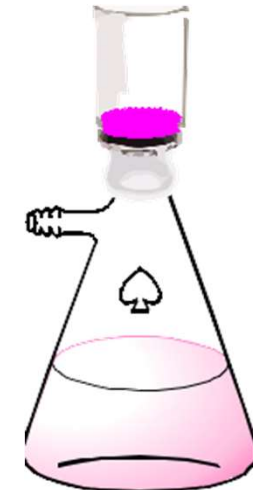
## 3. Dissolution

- 37  $^{\circ}\text{C}$   
1,3,...,7 days



- pH at 37  $^{\circ}\text{C}$

## 4. Filtration

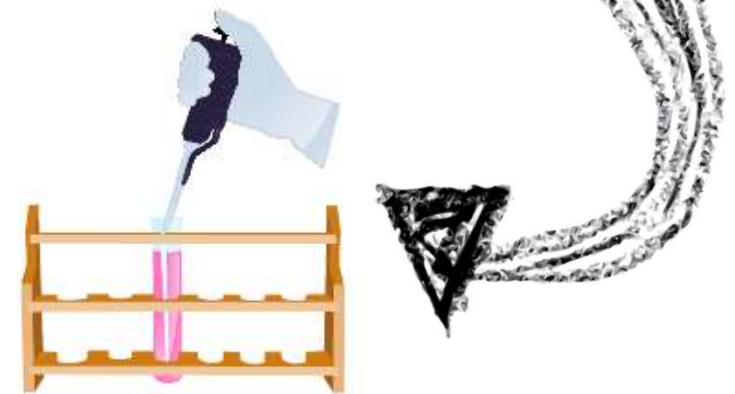


## 1. Glass analysis

- ICP-OES
- $^{31}\text{P}$  MAS-NMR

- ICP-OES
- $^{31}\text{P}$  NMR

## 5. Solution analysis



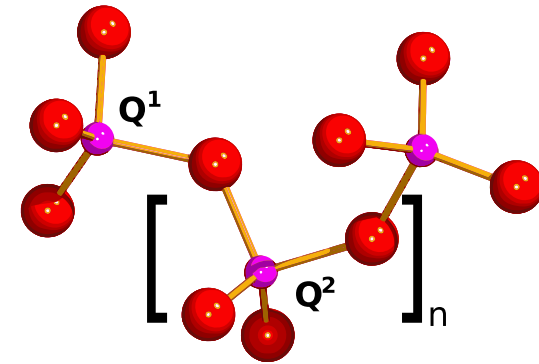
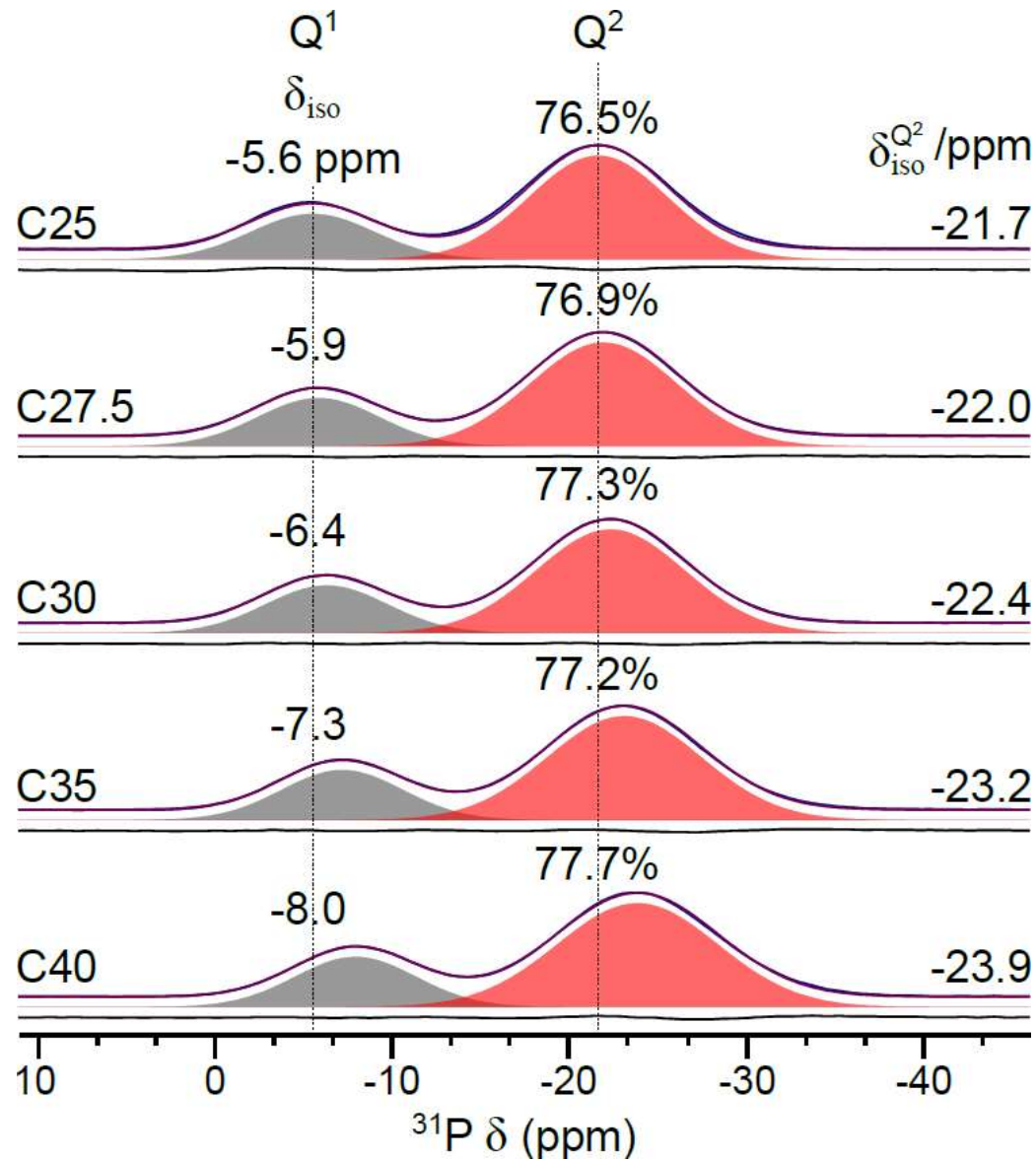
# Glass composition

Polyphosphate glasses of varying Na<sub>2</sub>O/CaO ratio

Glass	P <sub>2</sub> O <sub>5</sub>	Na <sub>2</sub> O	CaO
C25	45	30	25
C27.5	45	27.5	27.5
C30	45	25	30
C35	45	20	35
C40	45	15	40

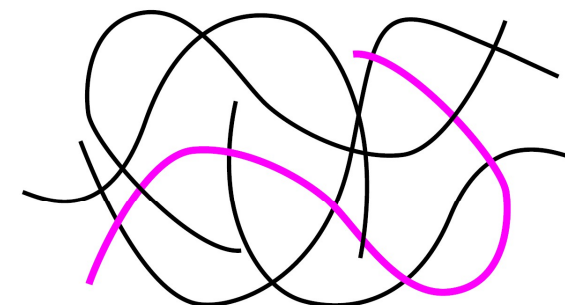
(mol%)

# $^{31}\text{P}$ MAS NMR



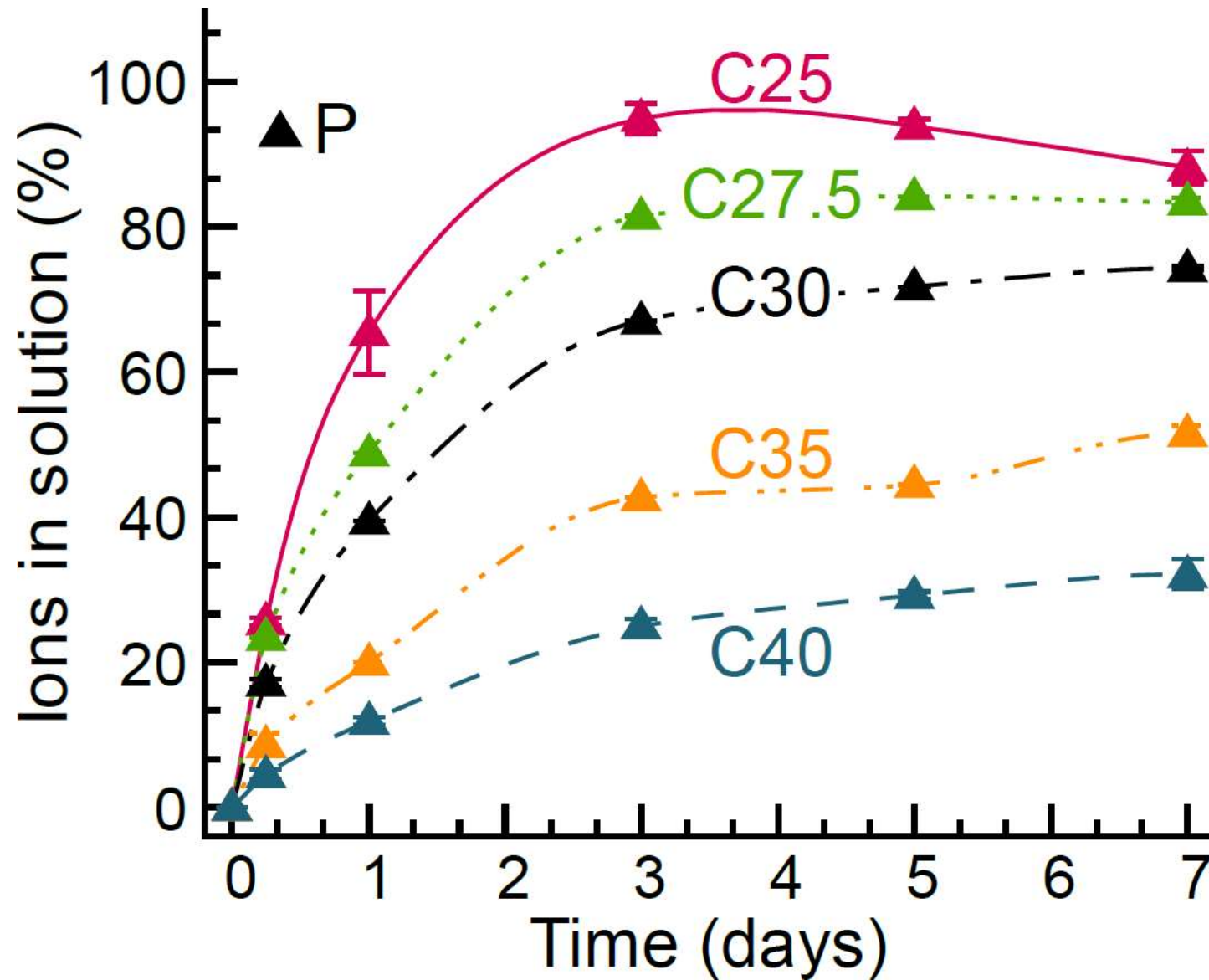
$$2\text{Q}^1 + n\text{Q}^2$$

$$\approx 8 - 9$$



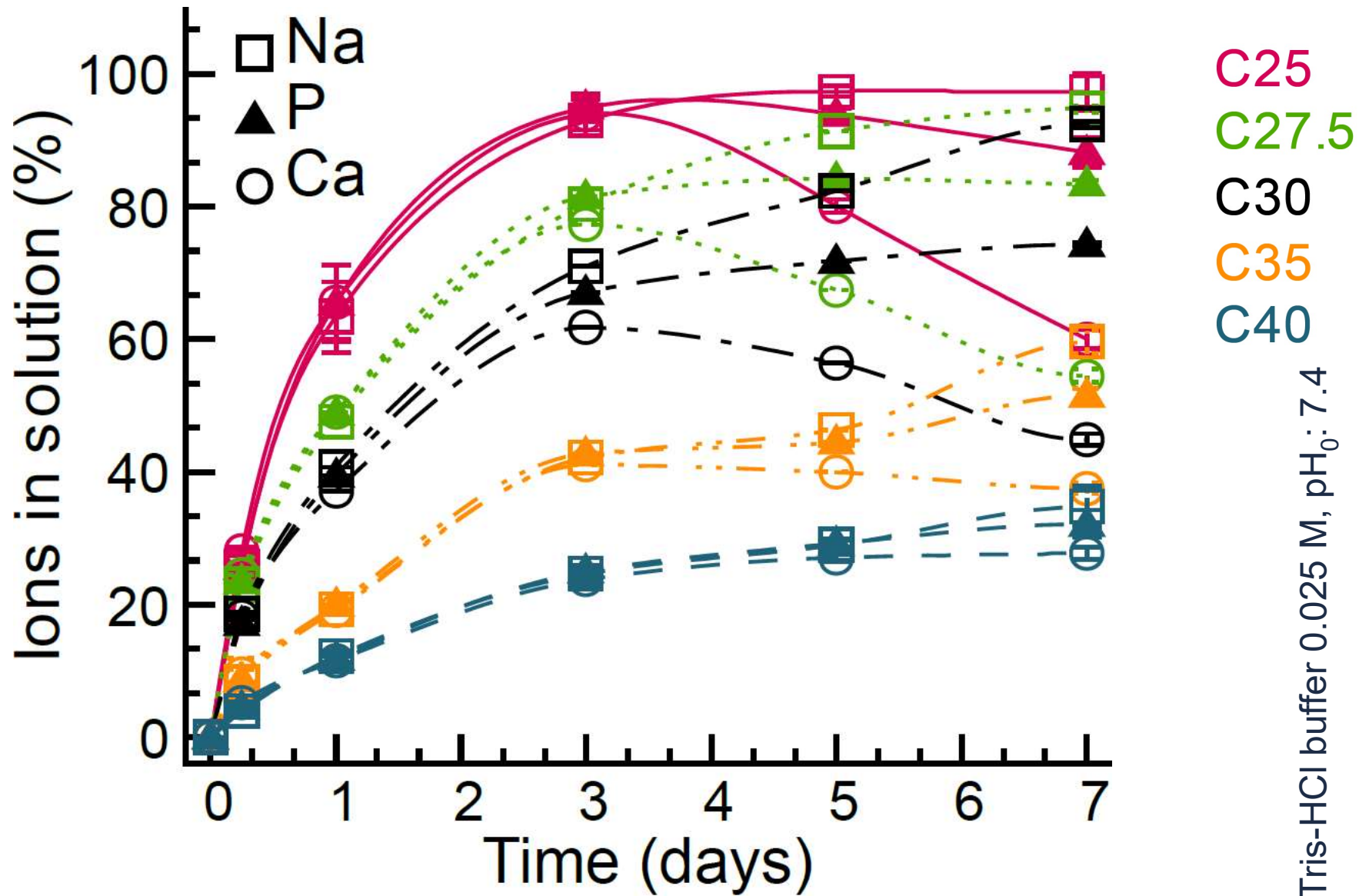
**Glass**

# Glass dissolution



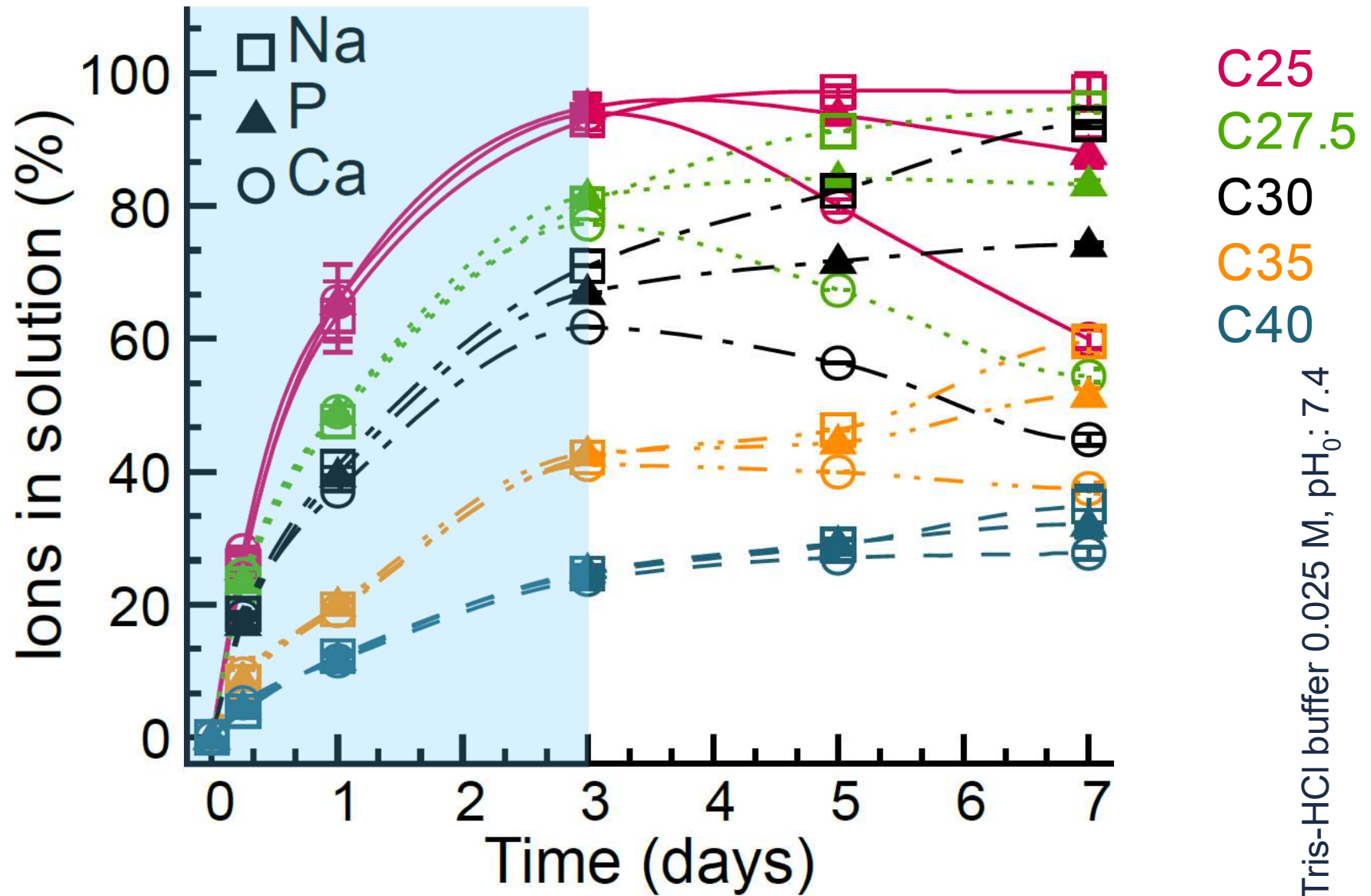
Tris-HCl buffer 0.025 M, pH<sub>0</sub>: 7.4

# Glass dissolution

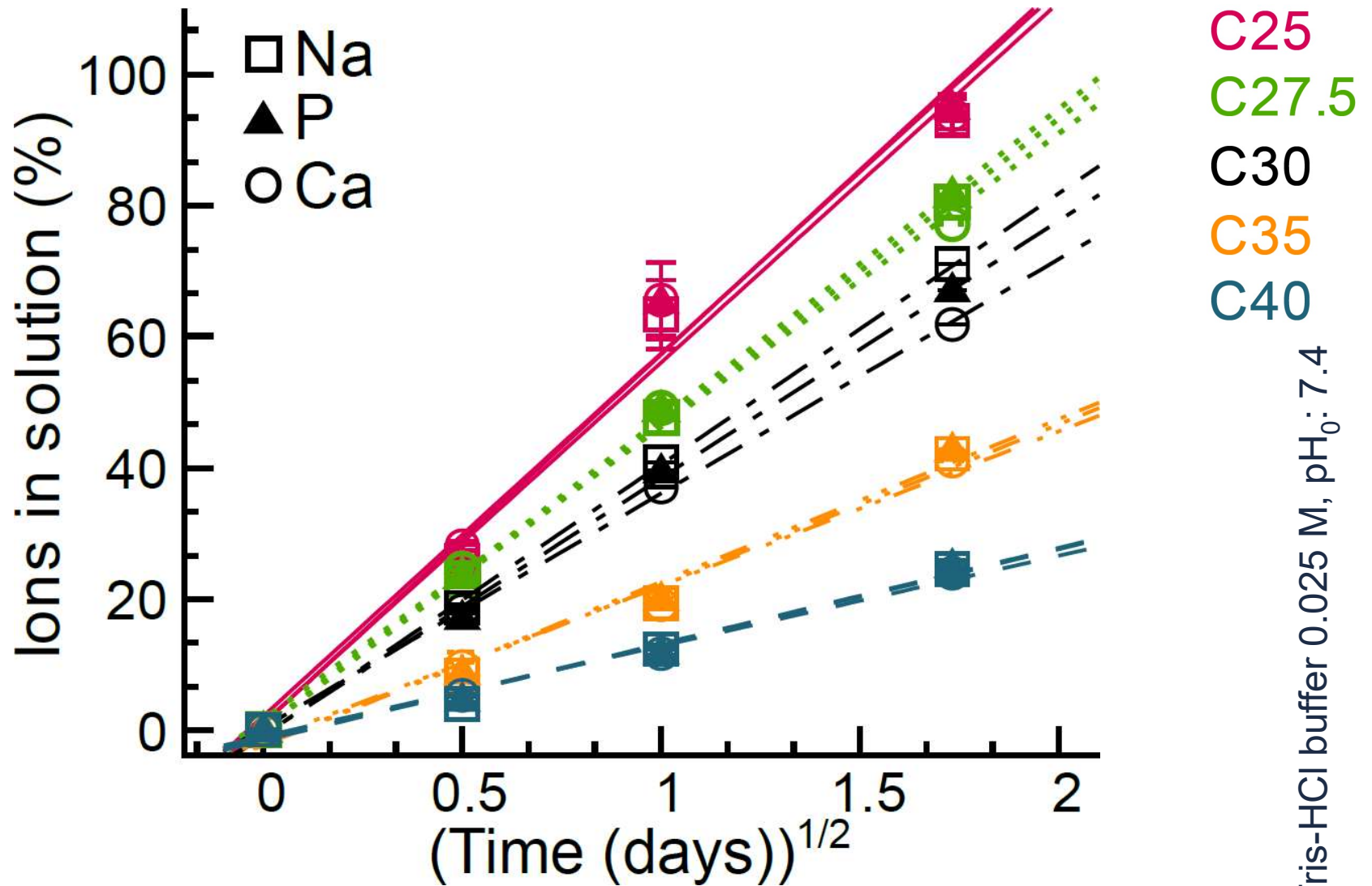




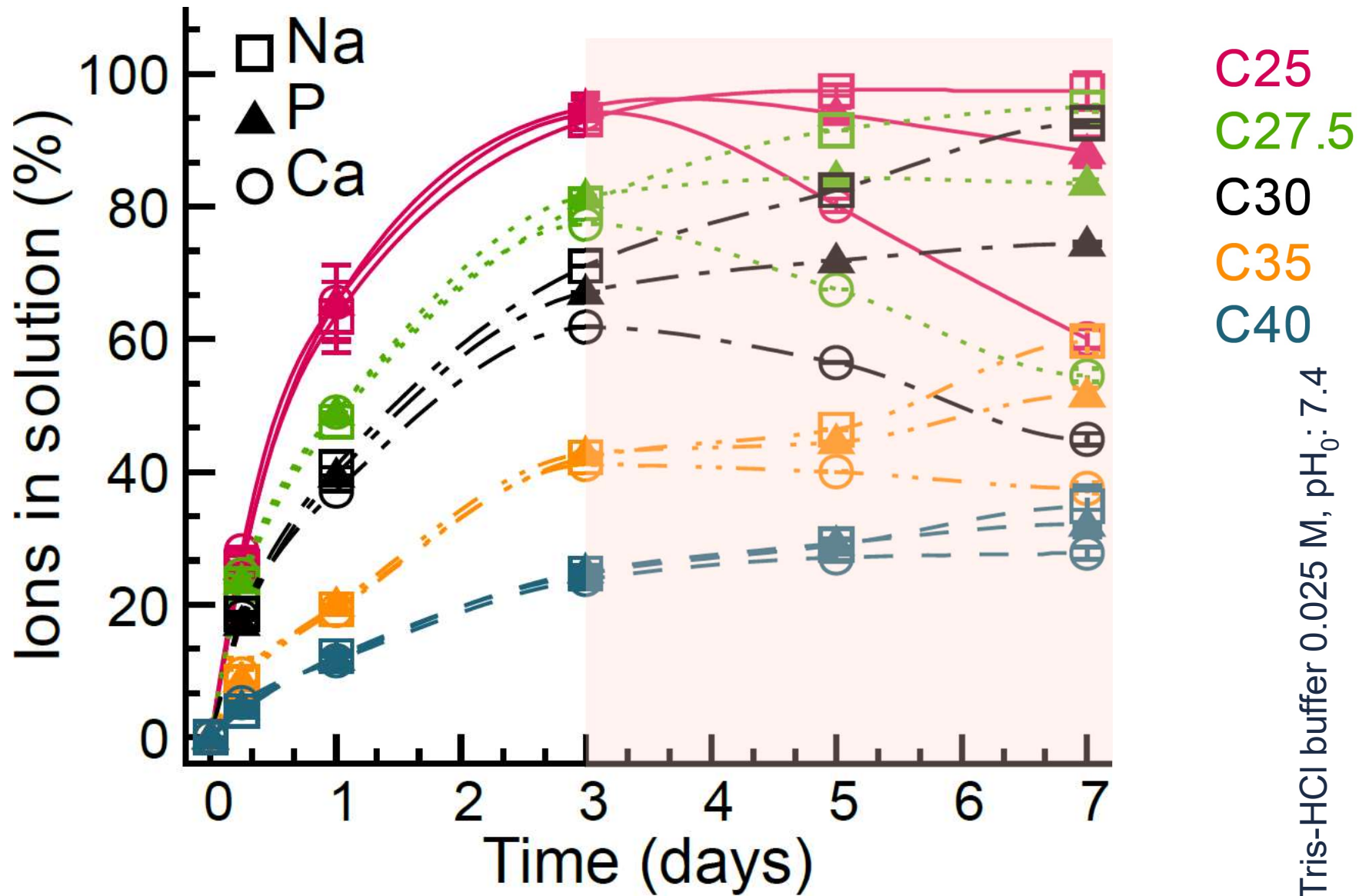
# Glass dissolution



# Glass dissolution

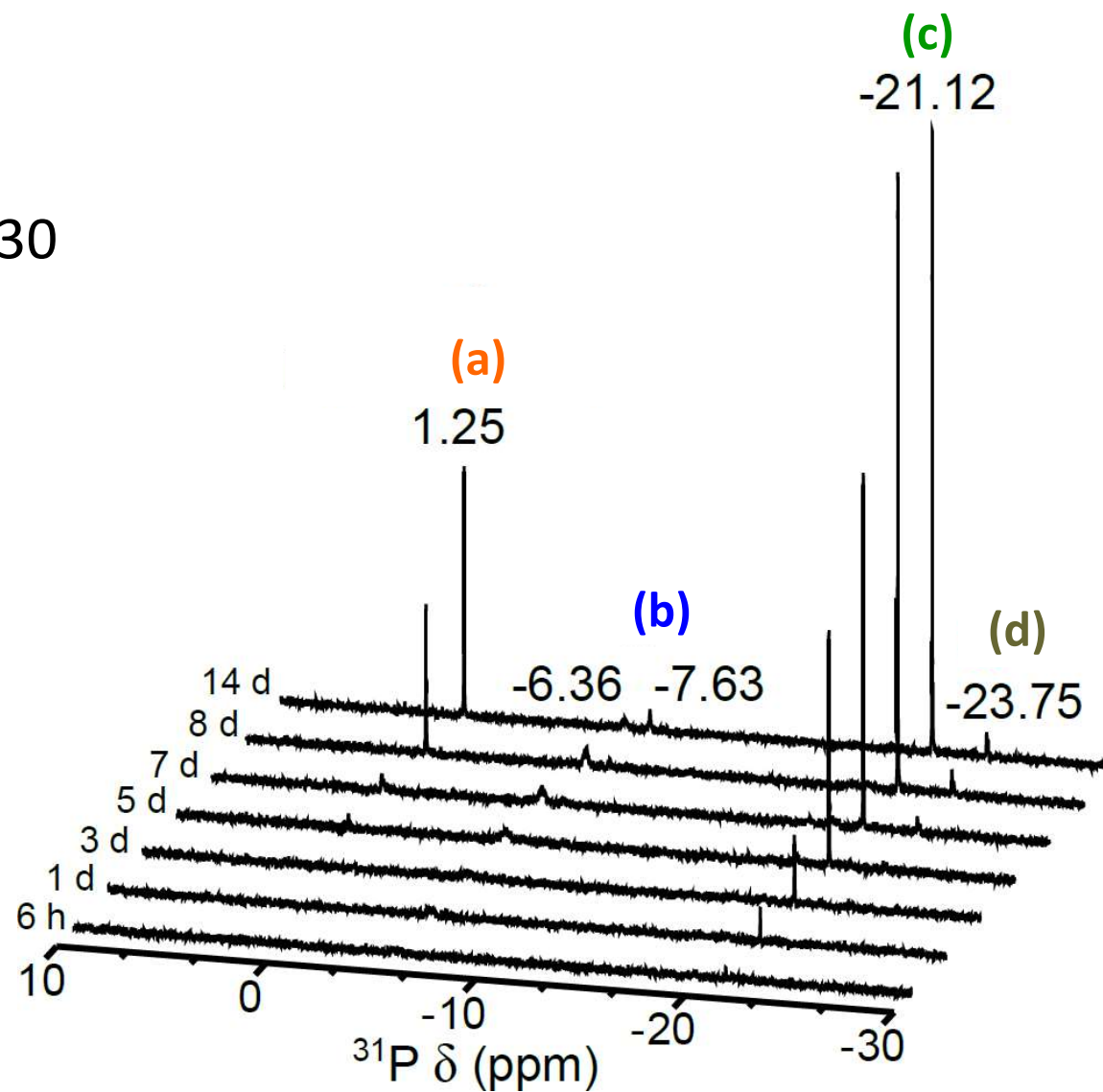


# Glass dissolution



# $^{31}\text{P}$ liquid NMR

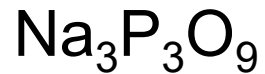
Glass C30



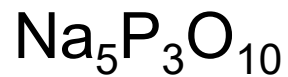
Tris-HCl buffer 0.025 M,  $\text{pH}_0$ : 7.4

# Peak assignment in $^{31}\text{P}$ NMR

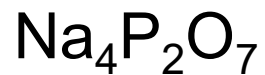
## Standards:



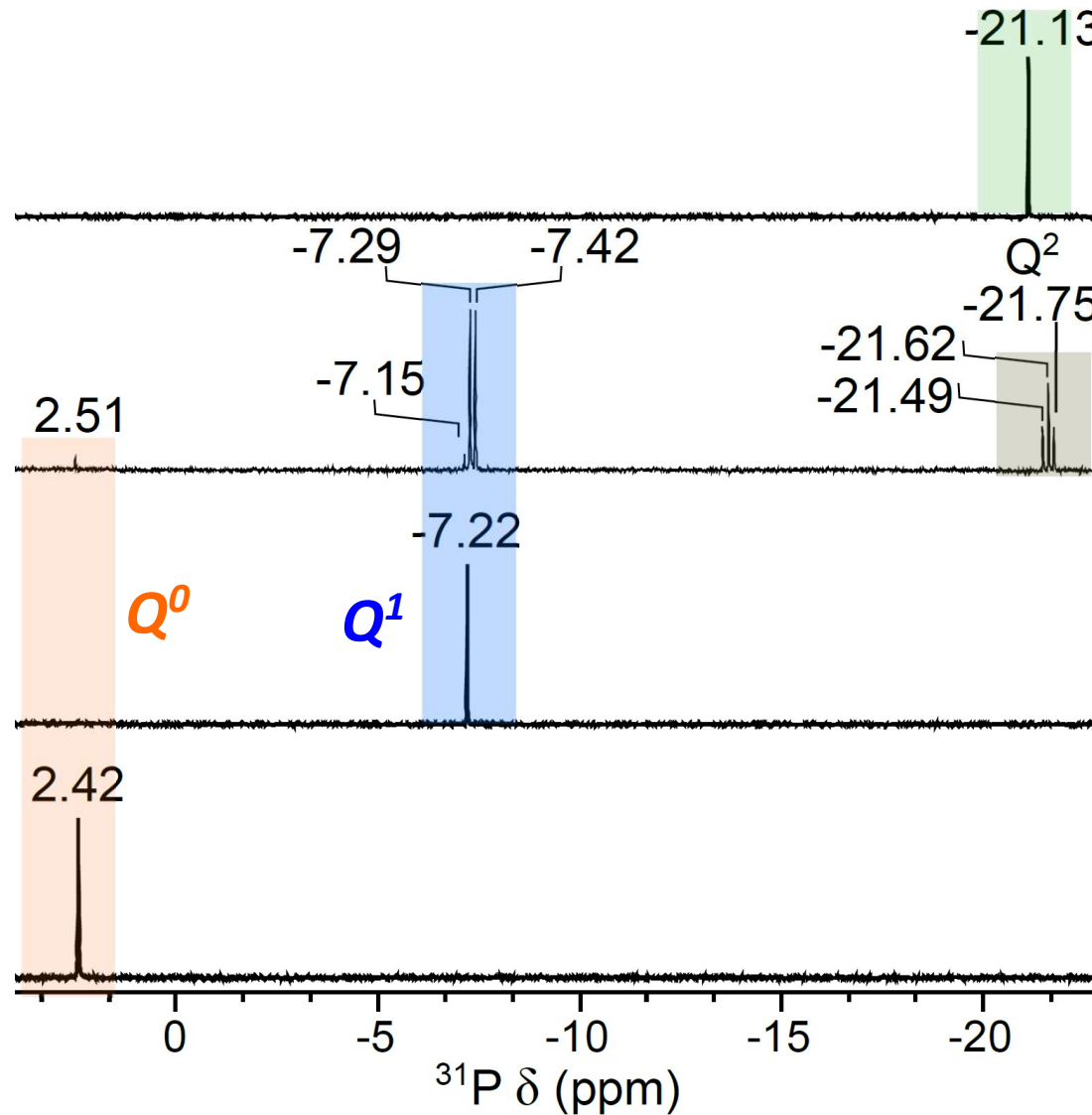
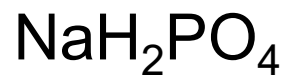
-21.13  $Q^2$   
ring



-21.62  $Q^2$   
-21.49 chains

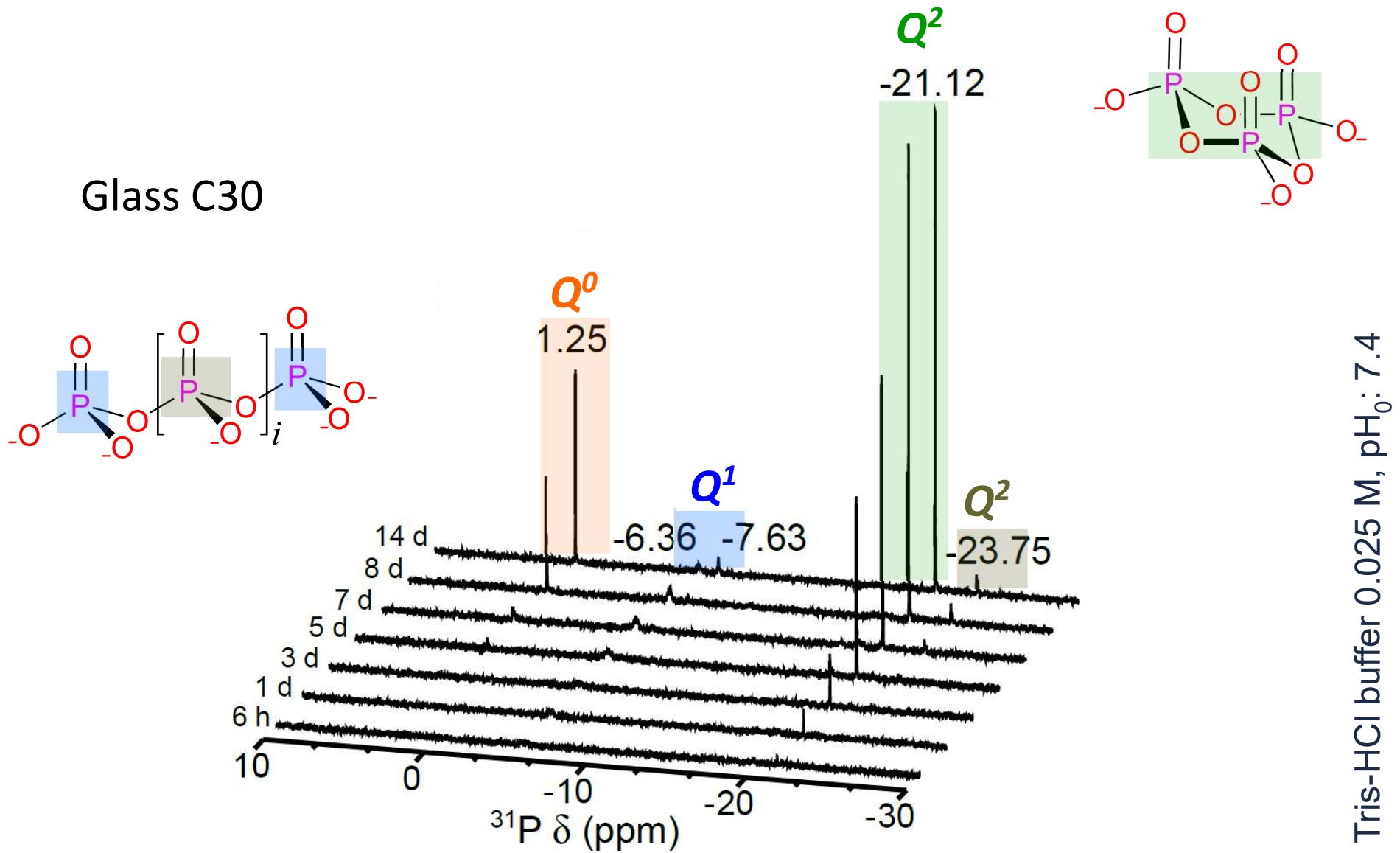


$Q^0$   $Q^1$



Tris-HCl buffer 0.025 M,  $\text{pH}_0$ : 7.4

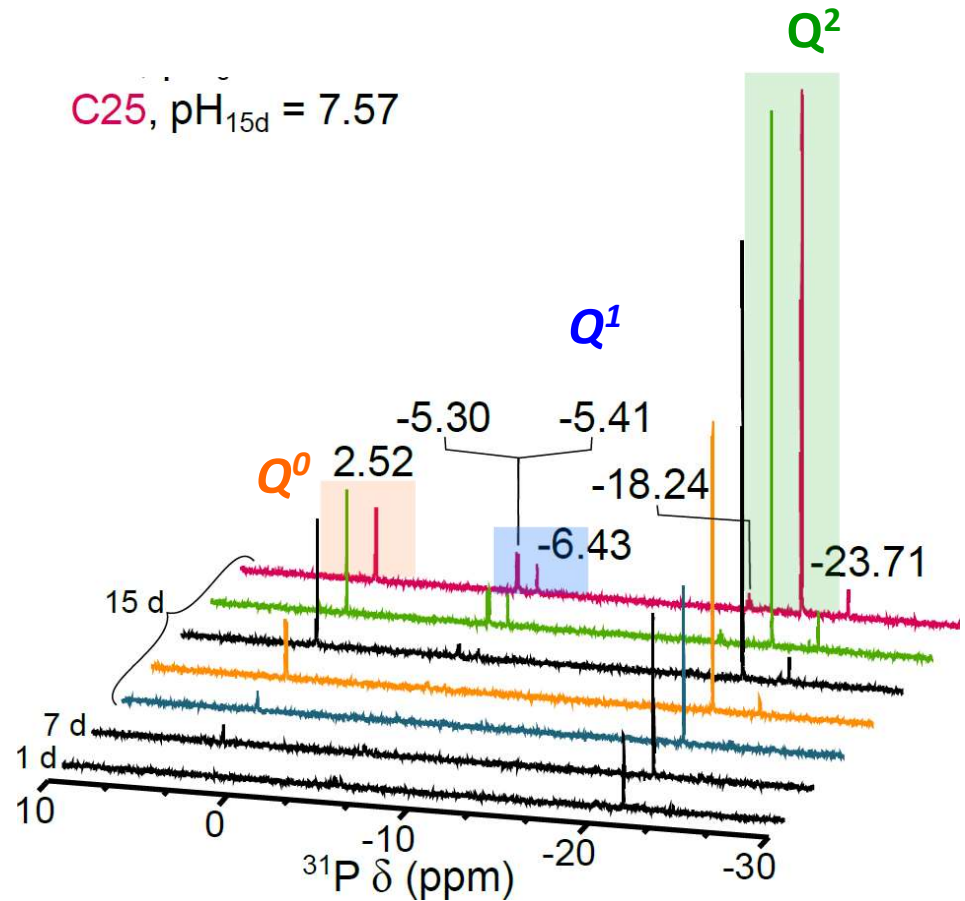
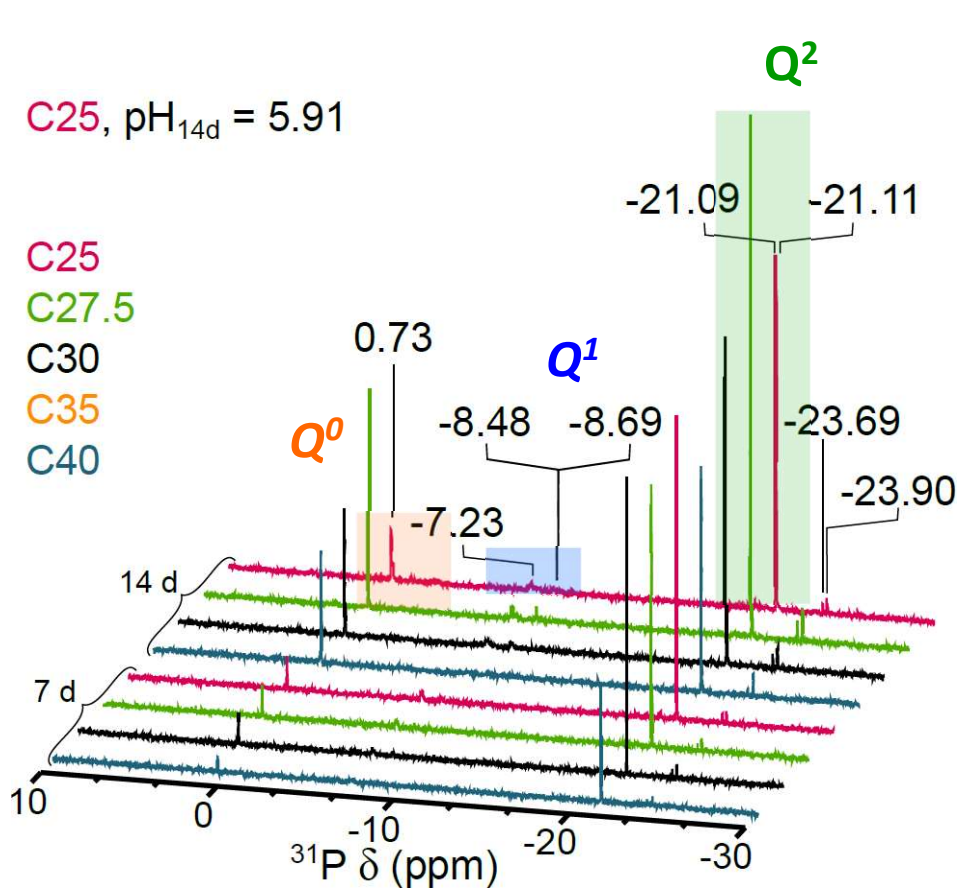
# $^{31}\text{P}$ liquid NMR



# DI H<sub>2</sub>O vs. Tris

Deionised water, pH<sub>0</sub>: ≈5.5

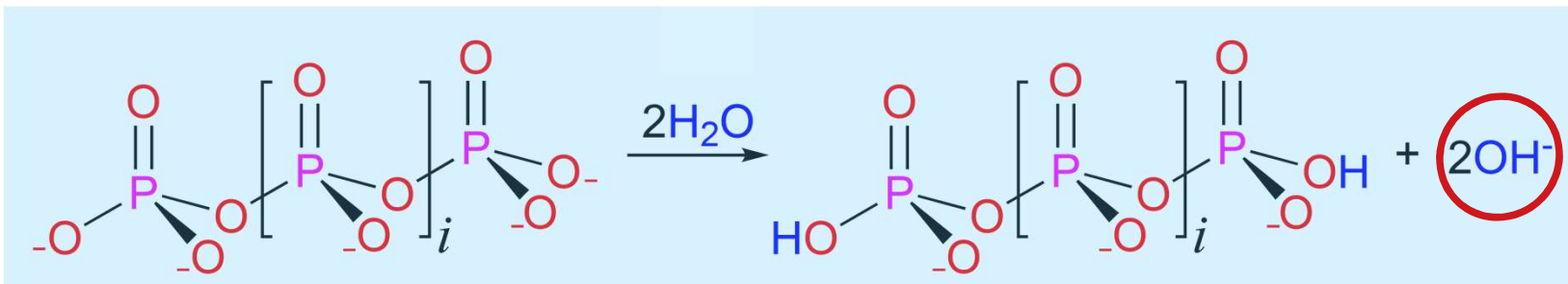
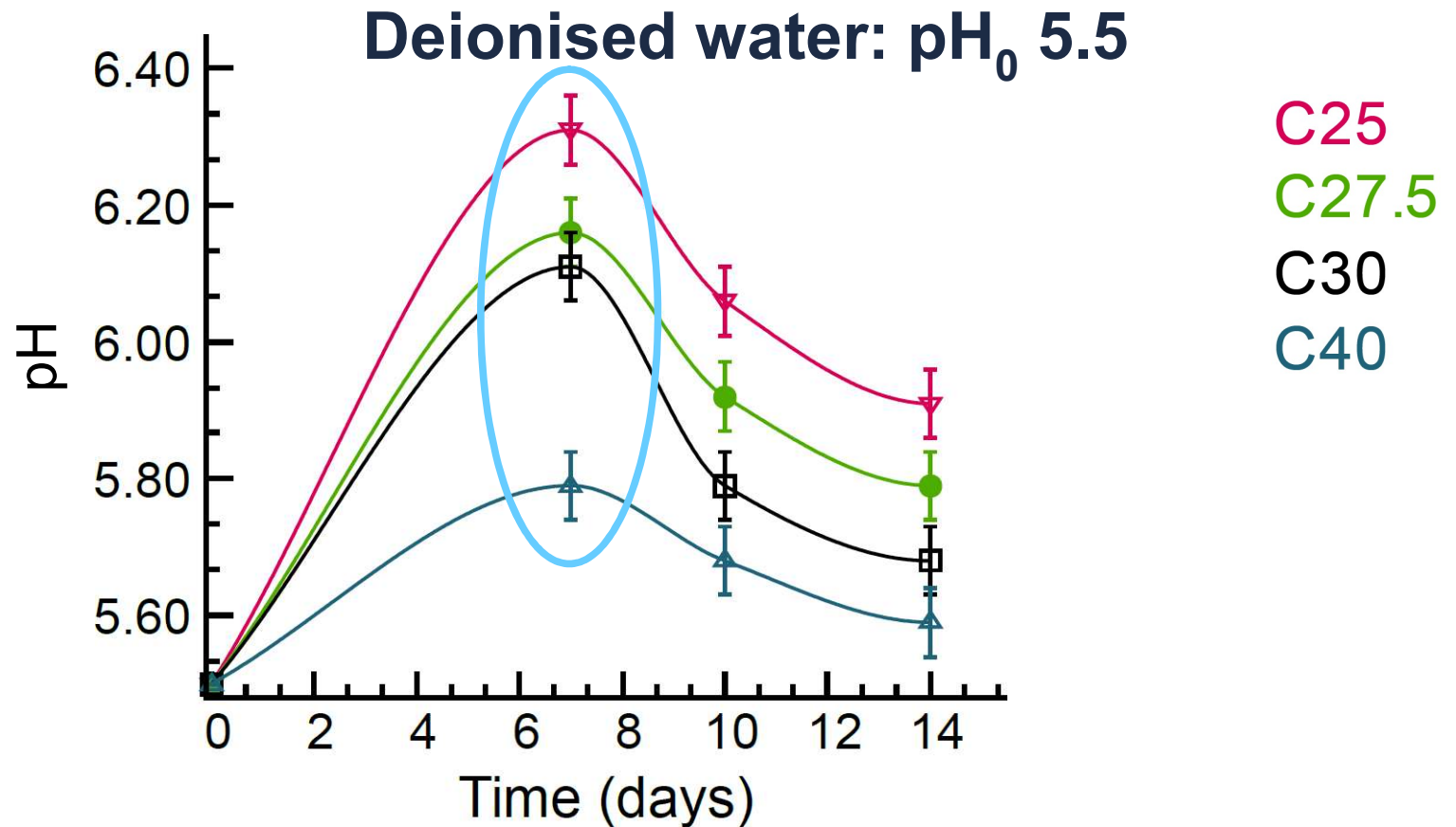
Tris pH<sub>0</sub>: 7.9



H<sub>2</sub>O: hydrolysis **faster**

Tris (pH<sub>0</sub>: 7.9): hydrolysis **slower**

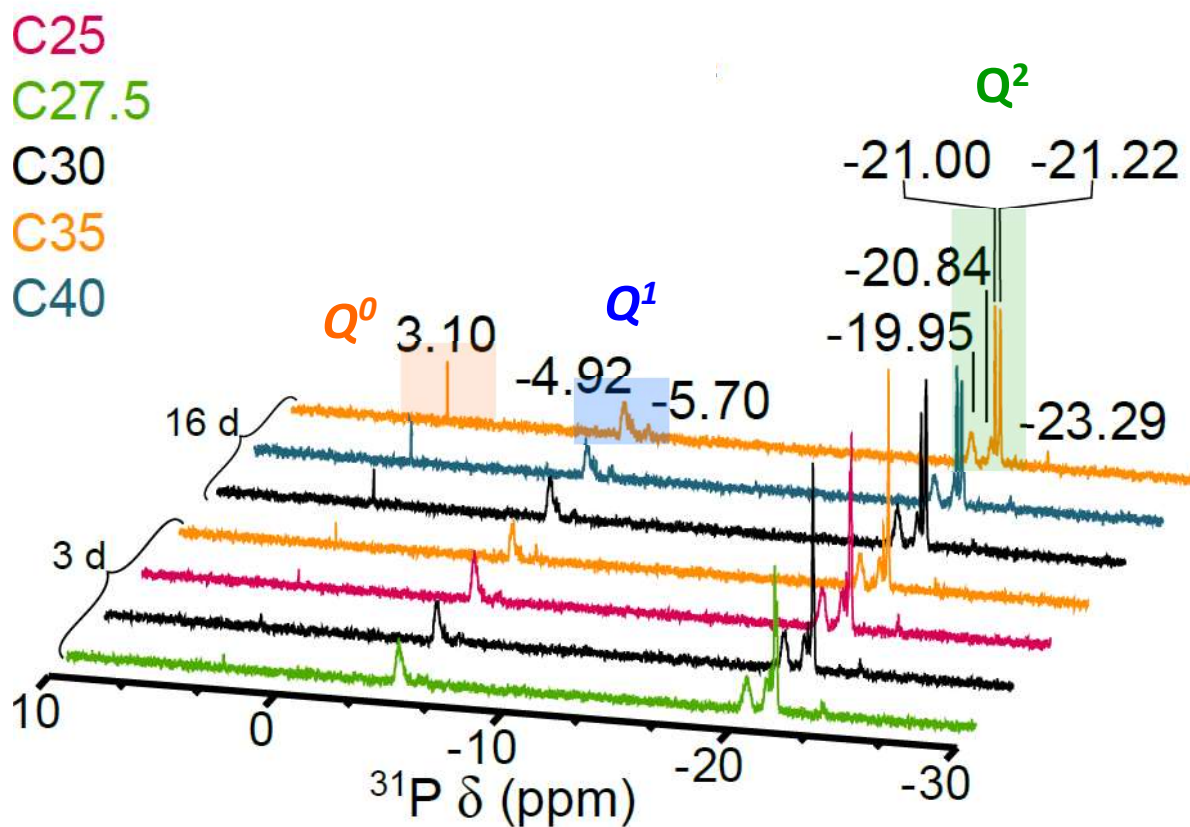
# pH effects





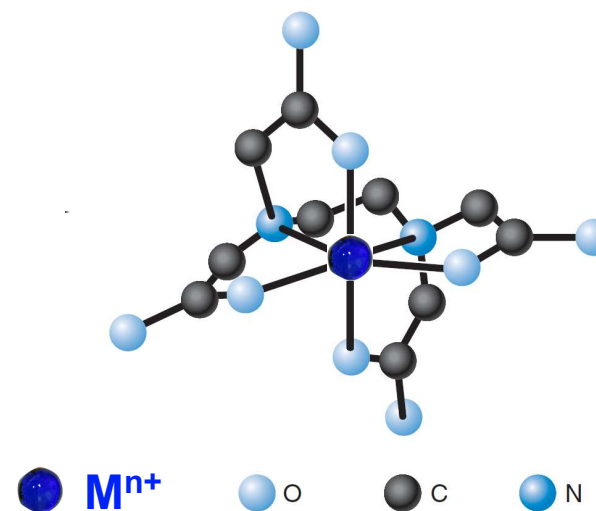
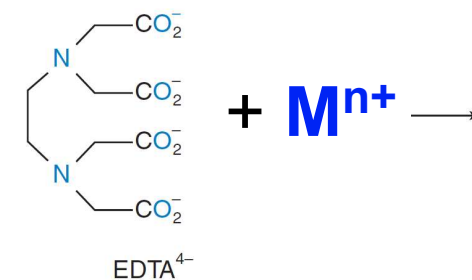
# $^{31}\text{P}$ NMR in EDTA

EDTA,  $\text{pH}_0$ : 10.0

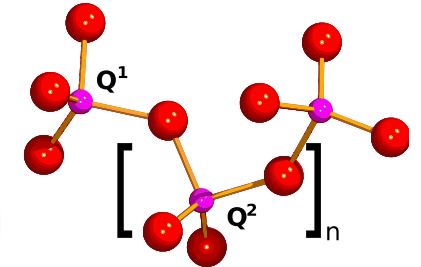
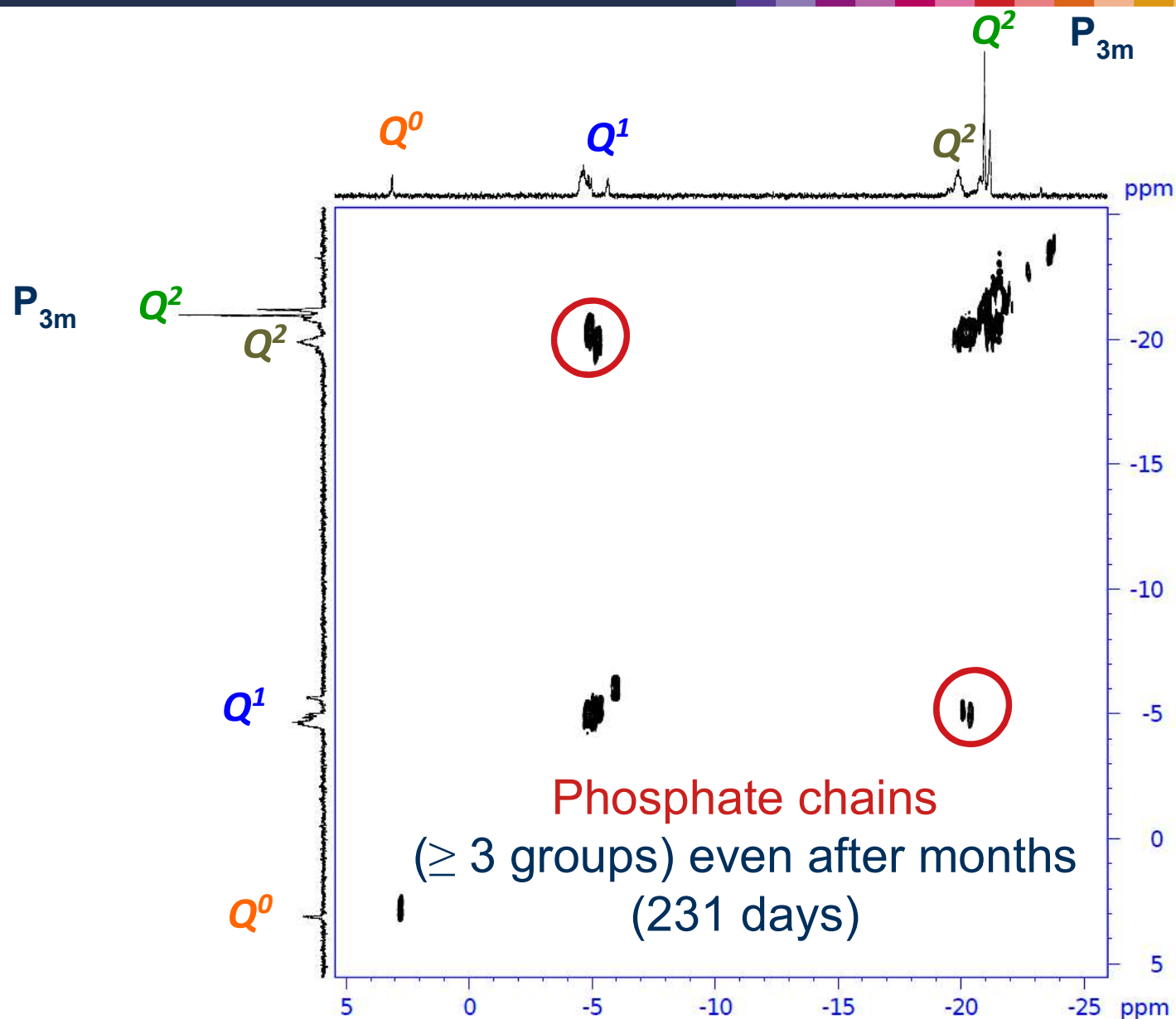


EDTA: Hydrolysis **very slow**

**EDTA complex**  
(ethylenediaminetetra acetate)



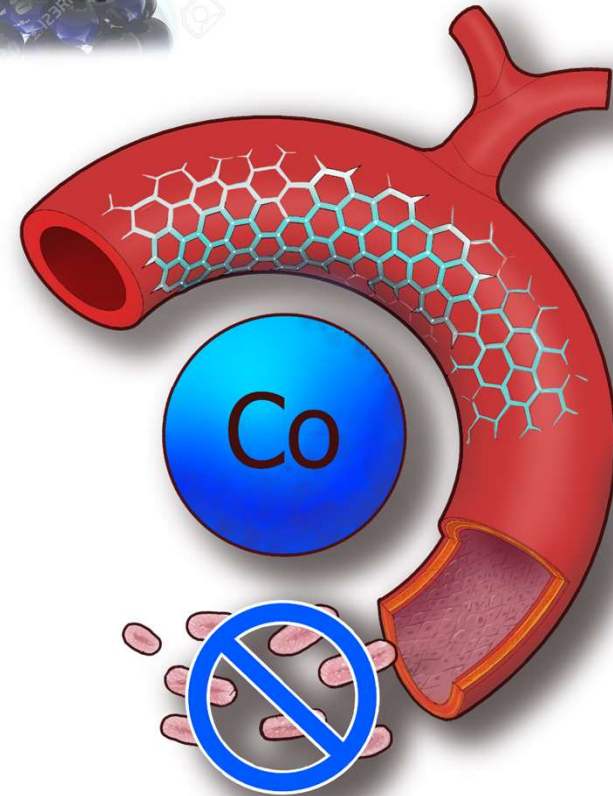
# 2D $^{31}\text{P}$ NMR (COSY) in EDTA



# Cobalt phosphate glasses as biomaterials

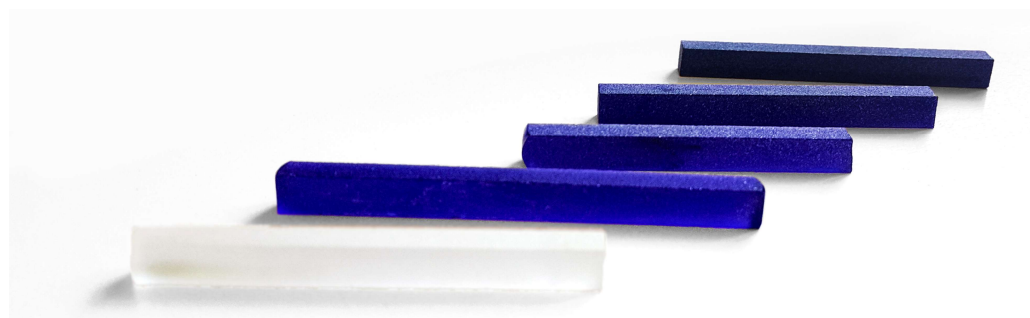


Drug delivery



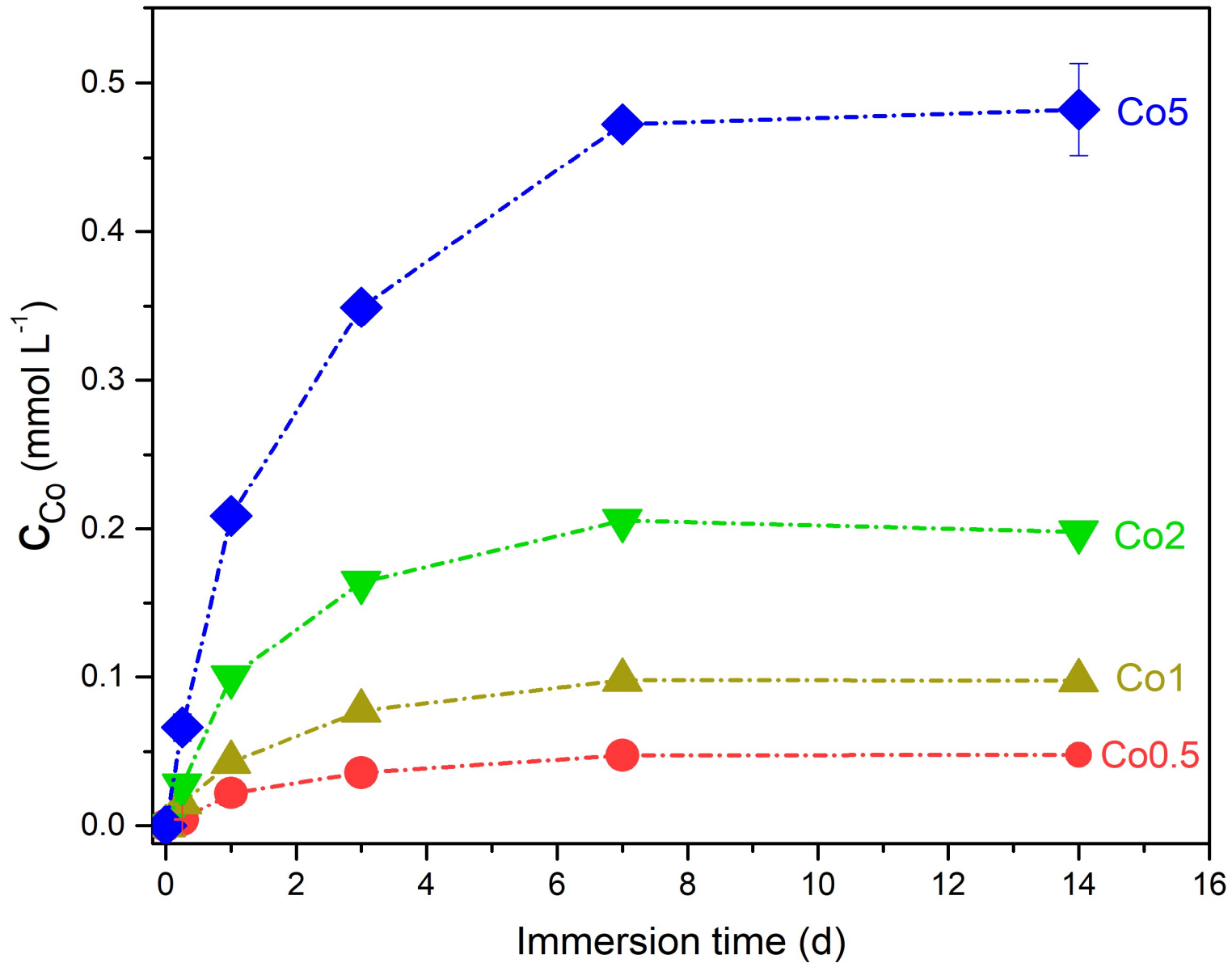
## Polyphosphate glasses with cobalt for calcium substitution

Glass	P <sub>2</sub> O <sub>5</sub>	Na <sub>2</sub> O	CaO	CoO
Co0	45	30	25	-
Co0.5	45	30	24.5	0.5
Co1	45	30	24	1
Co2	45	30	23	2
Co5	45	30	20	5



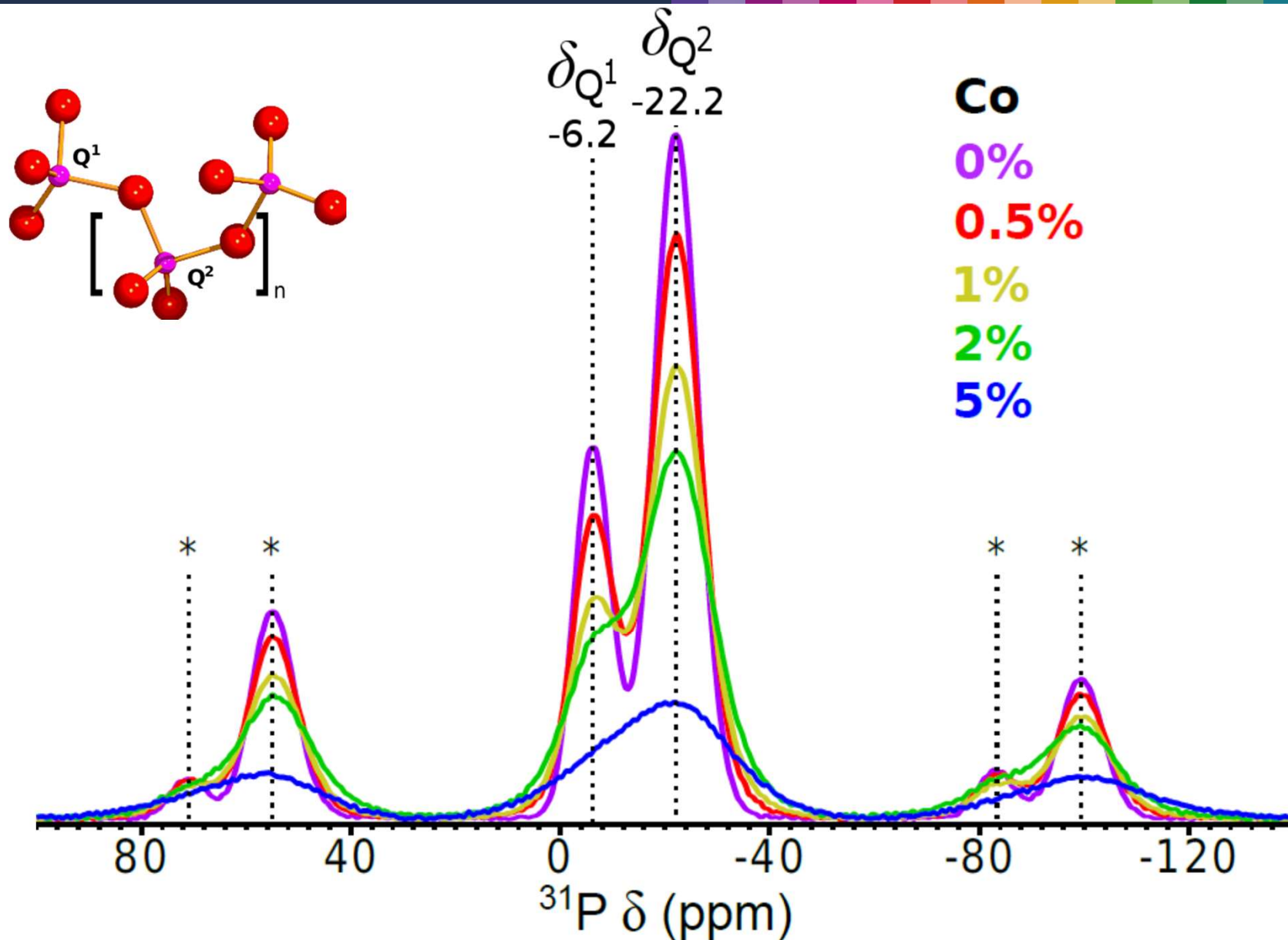
(mol%)

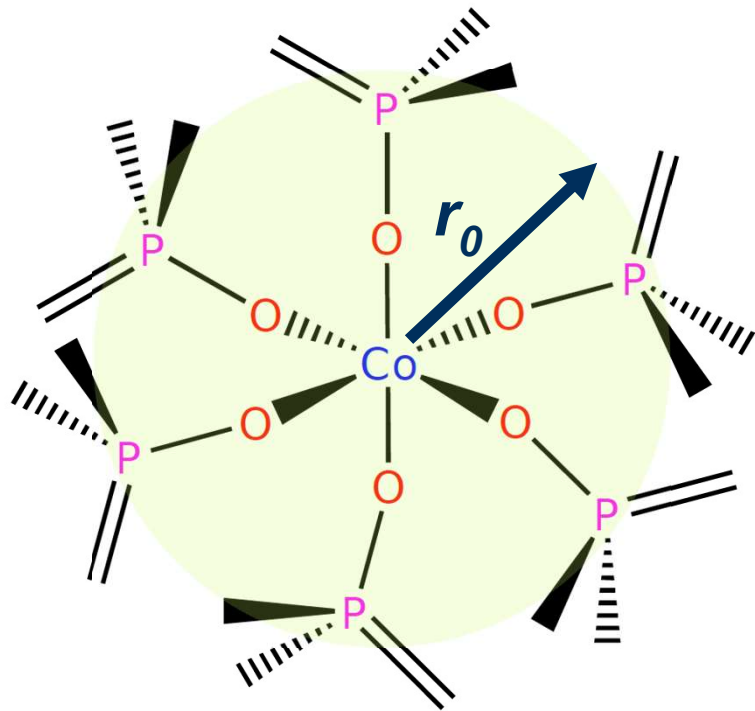
# Ion release



Tris-HCl buffer 0.025 M, pH<sub>0</sub>: 7.4

# $^{31}\text{P}$ MAS NMR: the glass



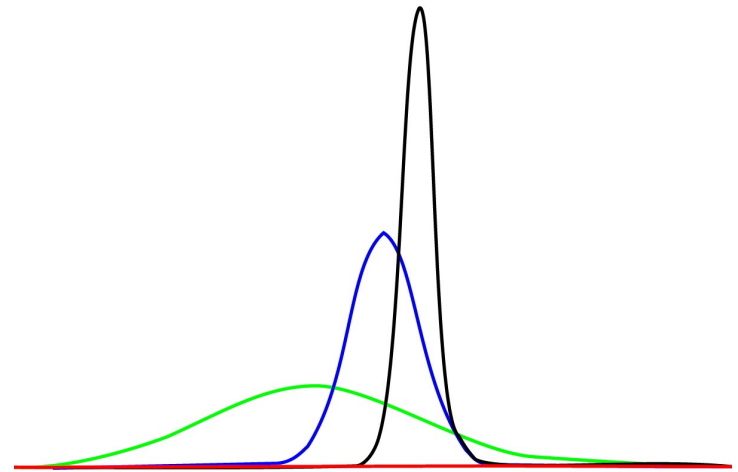


**Co<sup>2+</sup>**: paramagnetic centre

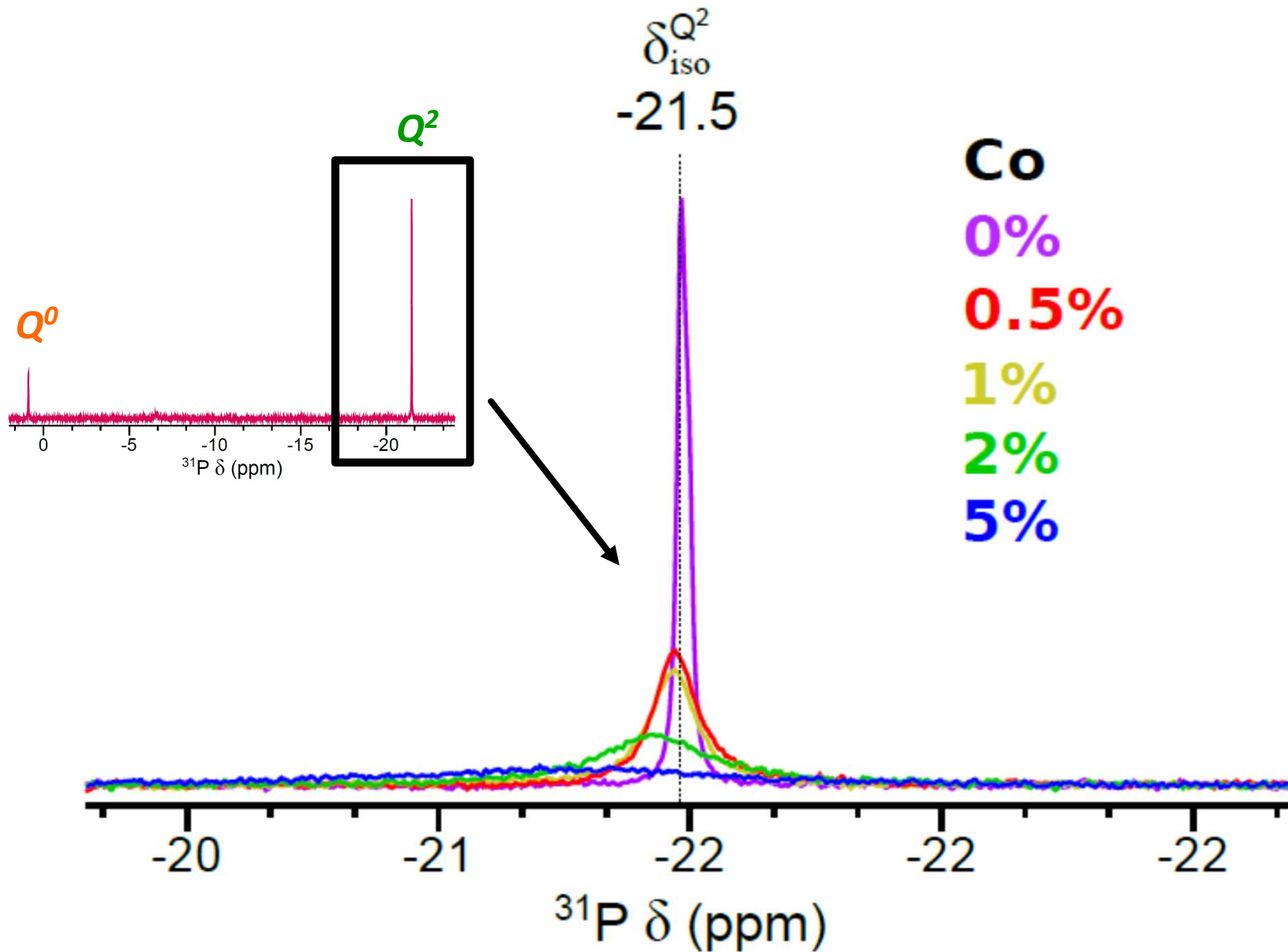
**$r_0$** : wipe out radius

## Paramagnetic effects

- shifts
- line broadening
- shorter  $T_1$  and  $T_2$



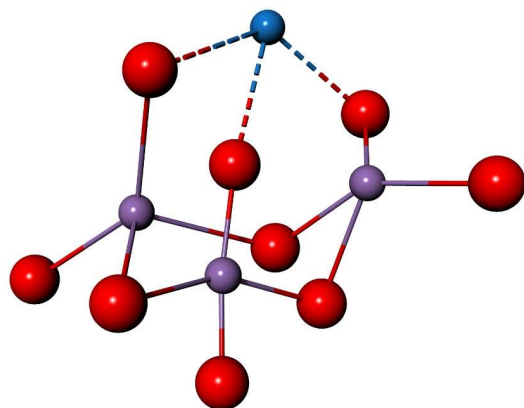
# $^{31}\text{P}$ NMR: in solution



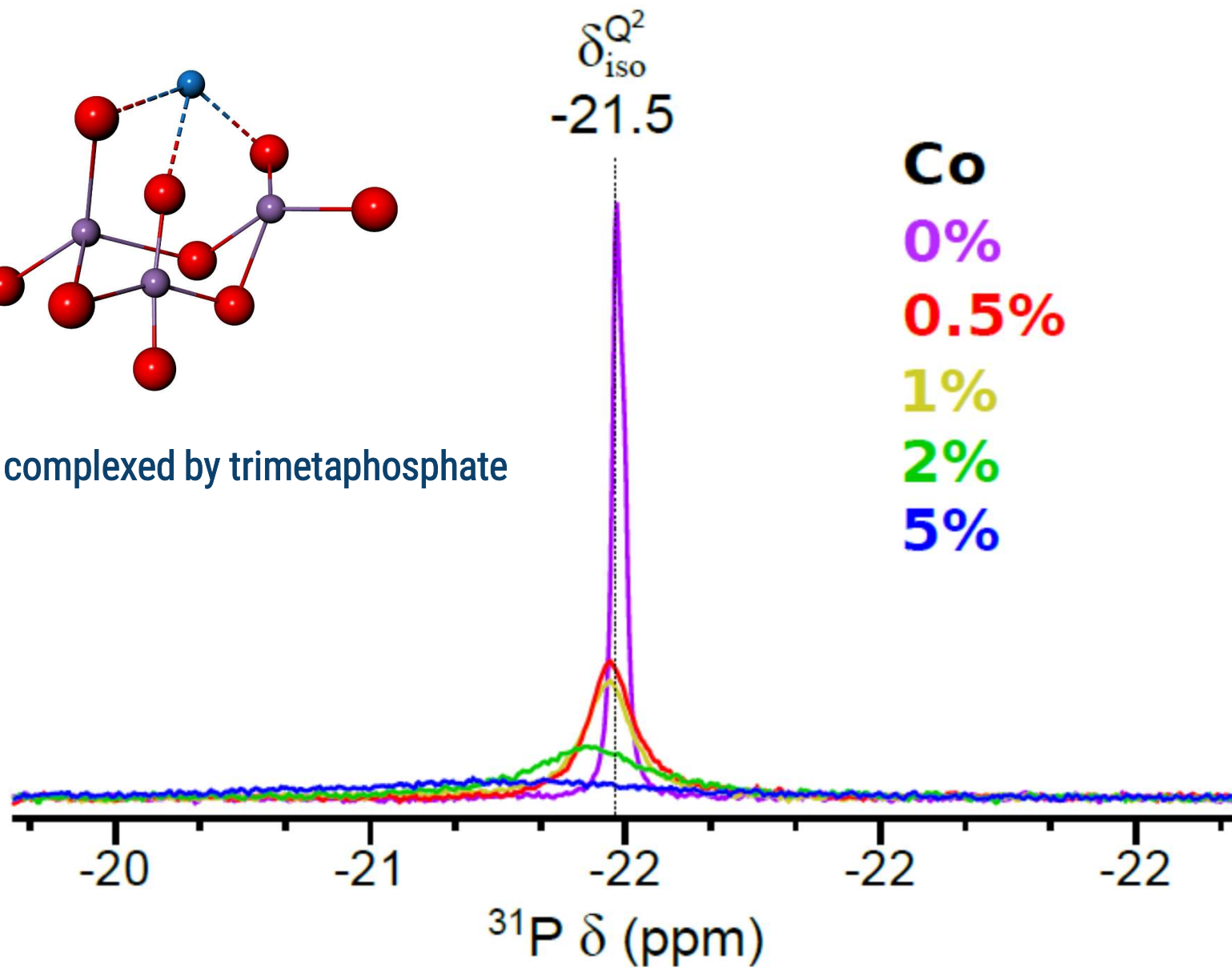
Tris-HCl buffer 0.025 M,  $\text{pH}_0$ : 7.4



# $^{31}\text{P}$ liquid NMR



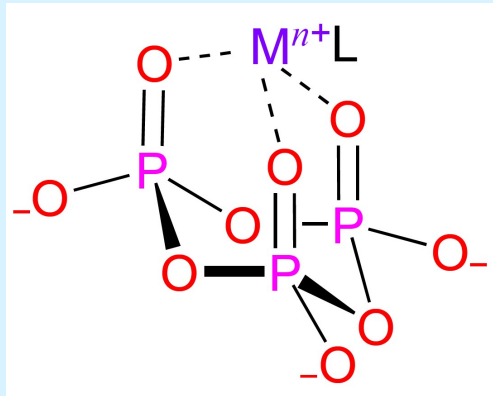
$\text{Co}^{2+}$  complexed by trimetaphosphate



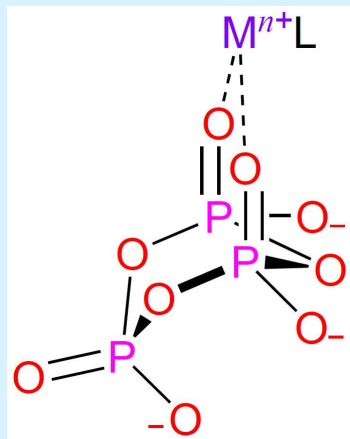
Tris-HCl buffer 0.025 M,  $\text{pH}_0$ : 7.4

# Ligands & complexing

## Rings



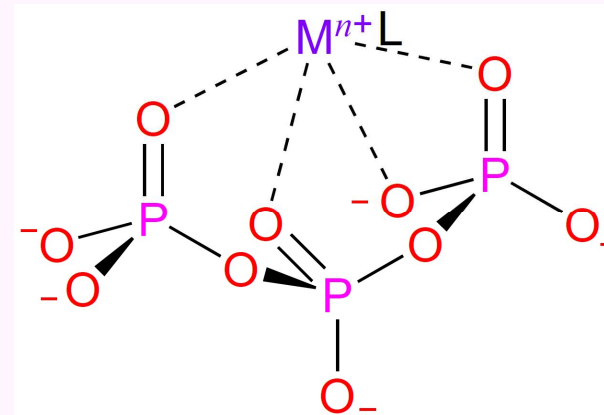
tridentate



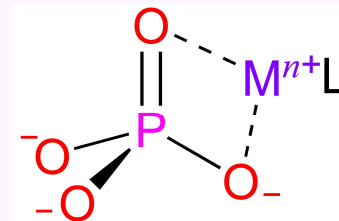
bidentate

**rigid, restricted denticity**

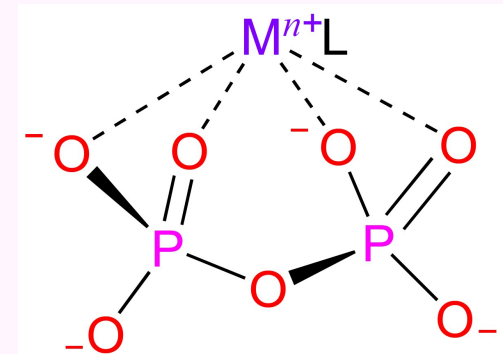
## Chains



tetradentate



bidentate

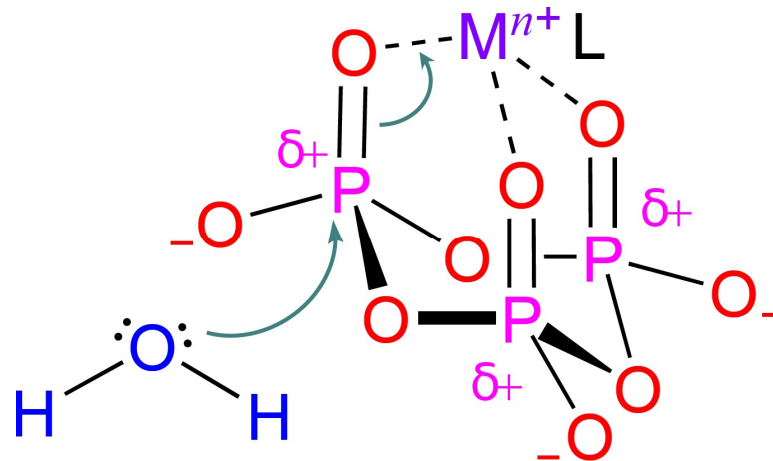


tridentate

**flexible, high denticity possible**

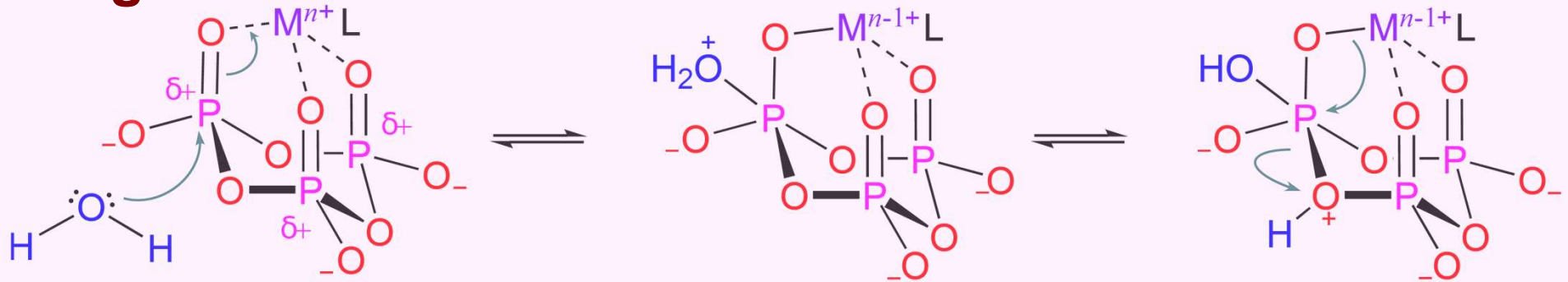
**Cations**, e. g.  $\text{Co}^{2+}$ , play a **catalytic** role in hydrolysis:

They make the phosphorus atom **electrophilic**, facilitating attack by  $\text{H}_2\text{O}$

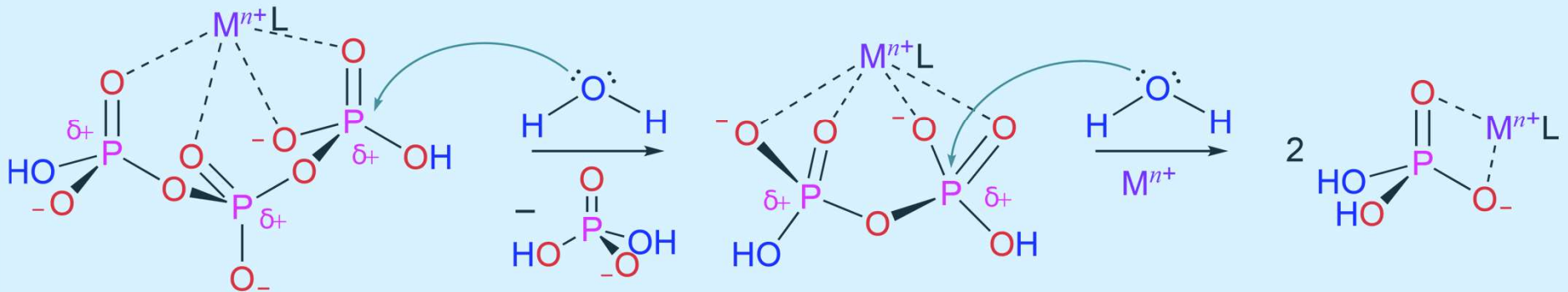


# Mechanism of hydrolysis

## Rings: slow



## Chains: fast



# Summary of phosphate dissolution

Na Ca polyphosphate glasses; **chains of 8-9** phosphate groups:

**Dissolution:**

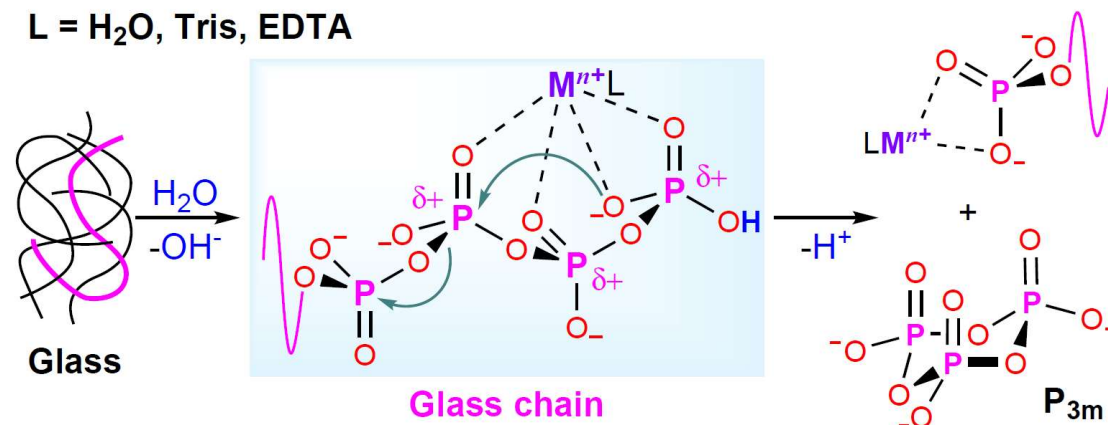
Glasses dissolve **congruently**

**Complexing:**

Competition of **ligands** for cations:  
EDTA >> **phosphate species** > Tris (pH 7.9) > Tris (pH:7.4) > H<sub>2</sub>O

**Mechanism of dissolution:**

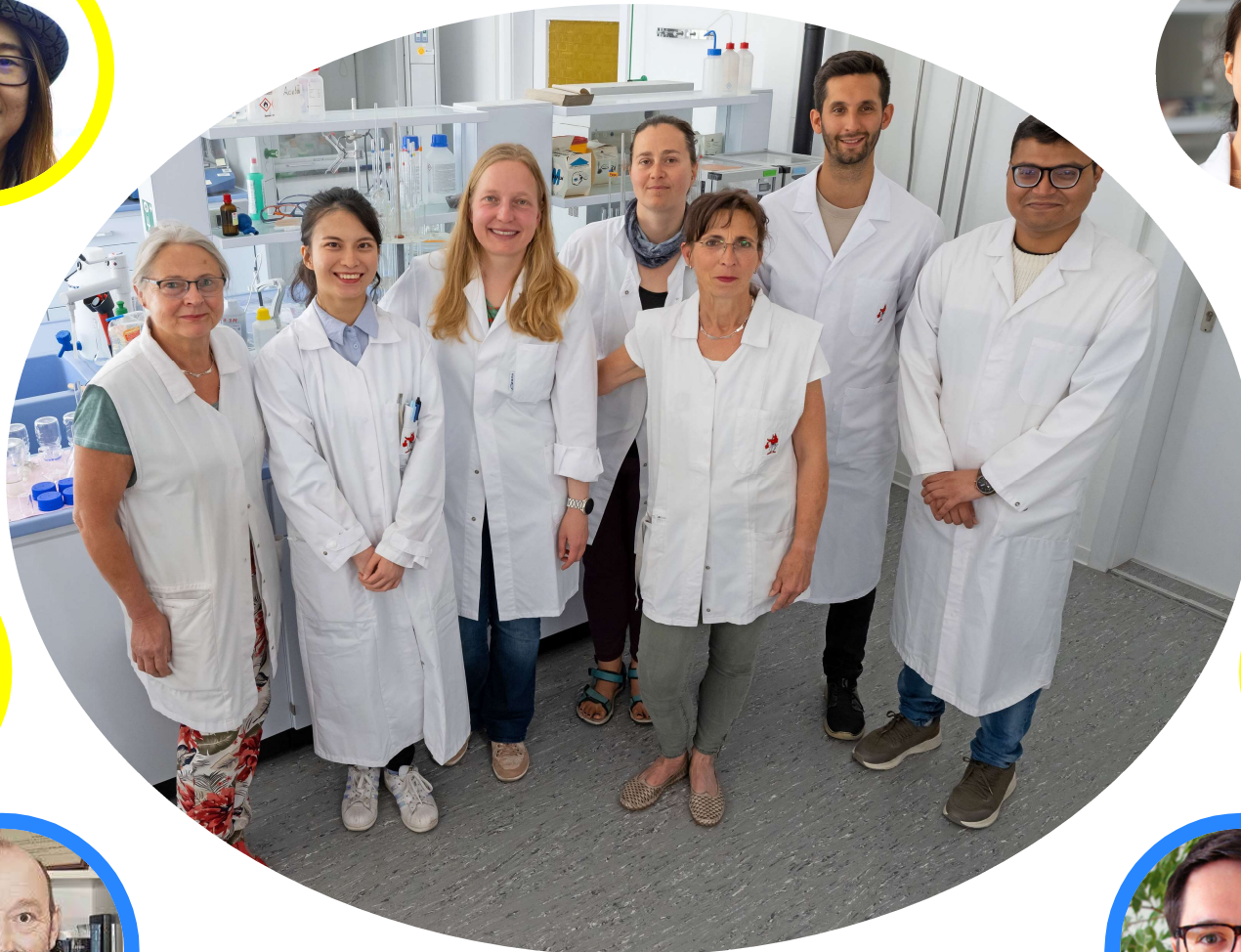
**Cations** activate the **P atom** as a suitable **electrophile** for H<sub>2</sub>O attack



# Conclusions

- Inorganic glasses used as biomaterials
- Borate glasses and (phospho-) silicate glasses have successfully made it to the clinic
- Phosphate glasses, so far, have not
- Most promising is use as delivery vehicles for e.g. inorganic therapeutic ions

# Acknowledgements



# Acknowledgements

Thank you for your attention

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# Glass as a biomaterial

## Or why corrosion can be a good thing

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