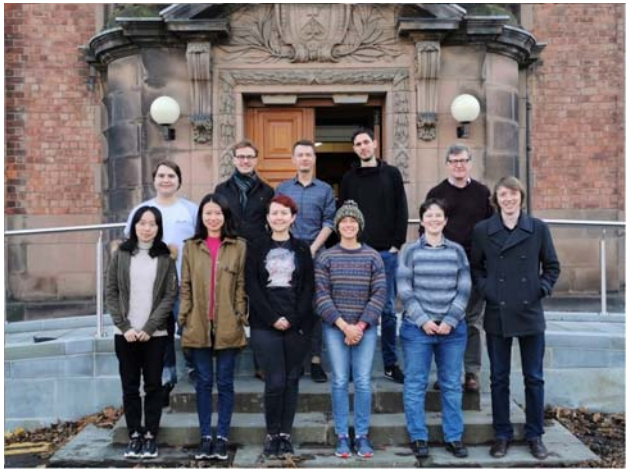
NMR and Kinetics

Yael Ben-Tal
SNUG Postgraduate NMR course
03 Dec 2019

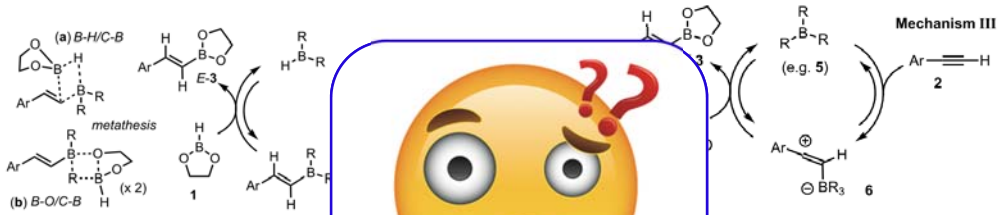
Introduction



Mechanistic studies!

Introduction

Case study: Alkyne Hydroboration

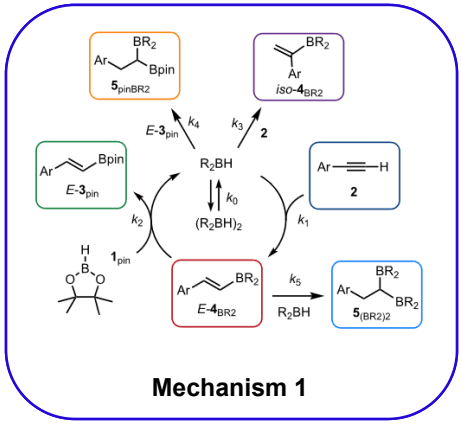


Which mechanism?

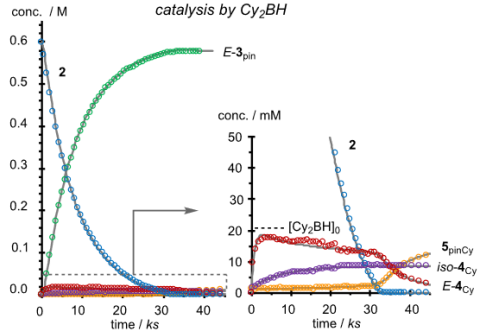
Lloyd-Jones, G.C. *J. Am. Chem. Soc.* **2019**, 141, 46, 18600-18611.

Introduction

Case study: Alkyne Hydroboration



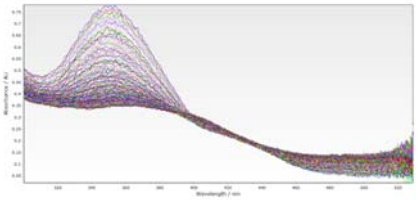
Mechanism 1



Many different kinetic experiments!

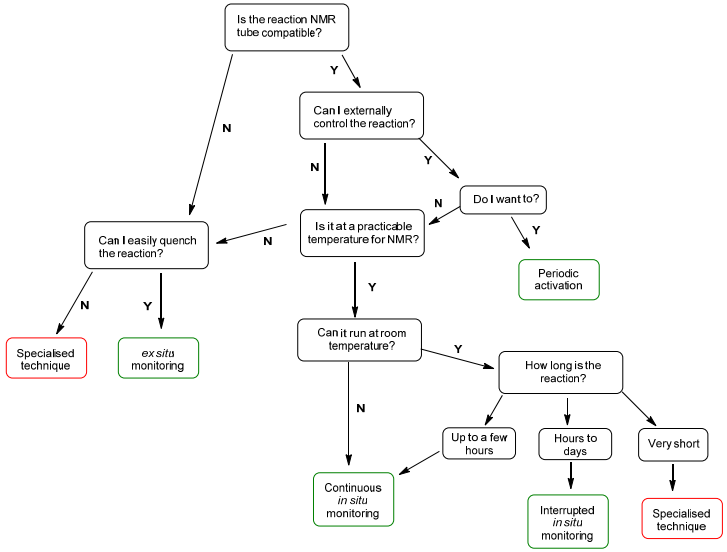
Lloyd-Jones, G.C. *J. Am. Chem. Soc.* **2019**, 141, 46, 18600-18611.

Introduction

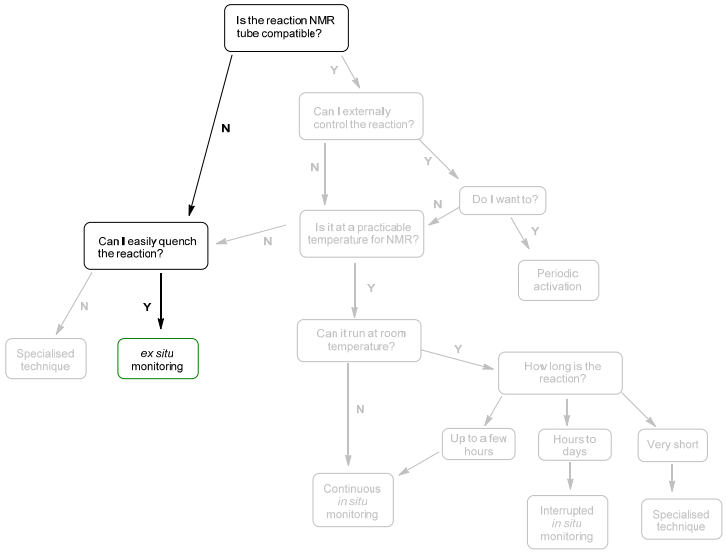


- High information density
- Non destructive

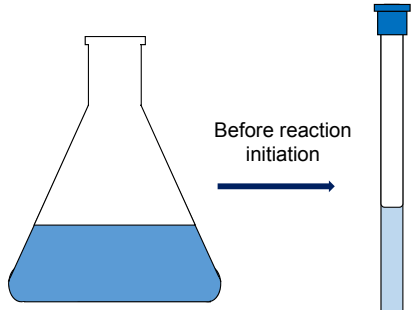
Sampling Methods



Sampling Methods



Sampling Methods – *ex situ* Monitoring

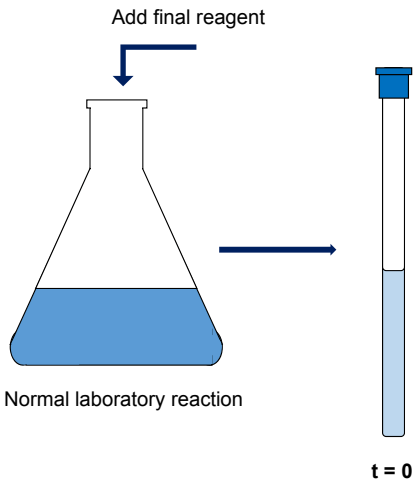


Before reaction initiation

Normal laboratory reaction

t = 0

Sampling Methods - *ex situ* Monitoring



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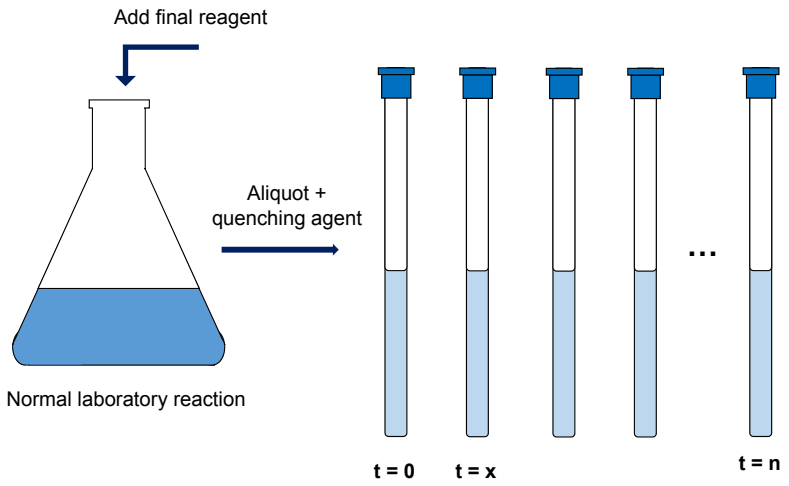
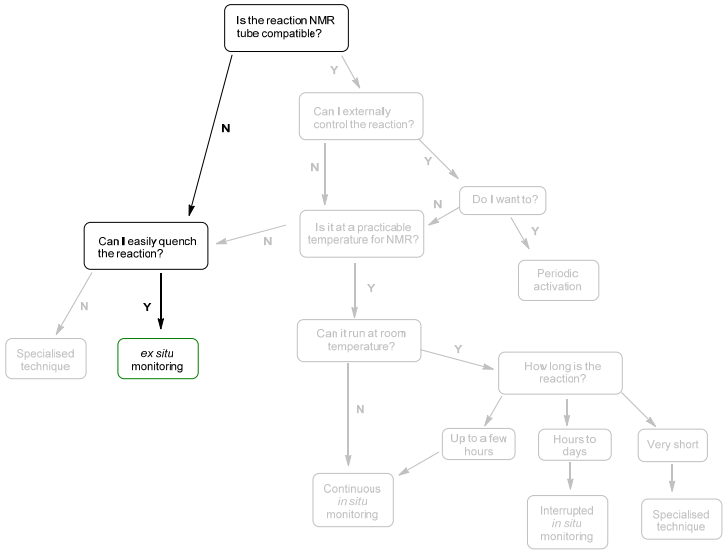


- Same conditions as lab
- Parallel experiments
- Labour intensive
- Long NMR experiments possible
- Lose transient/unstable intermediates
- Incomplete quenching
- Large reaction volume

Sampling Methods



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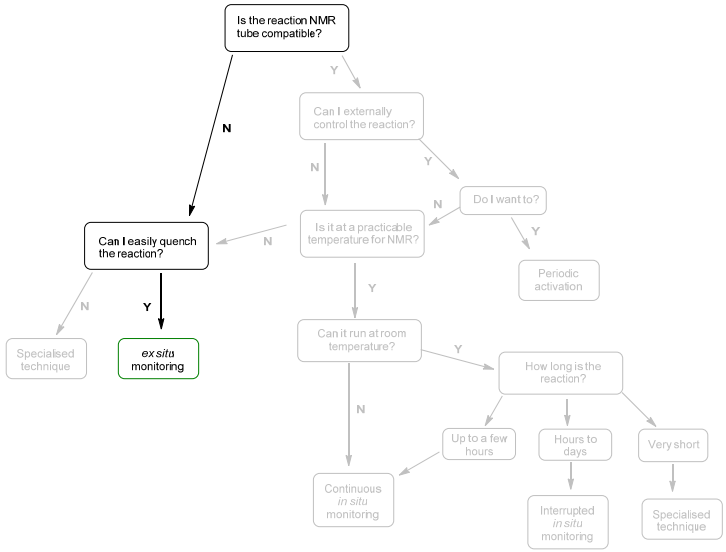
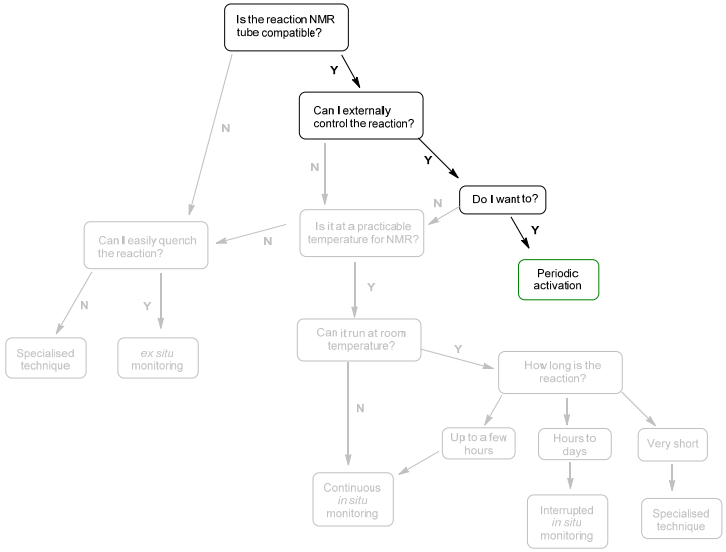
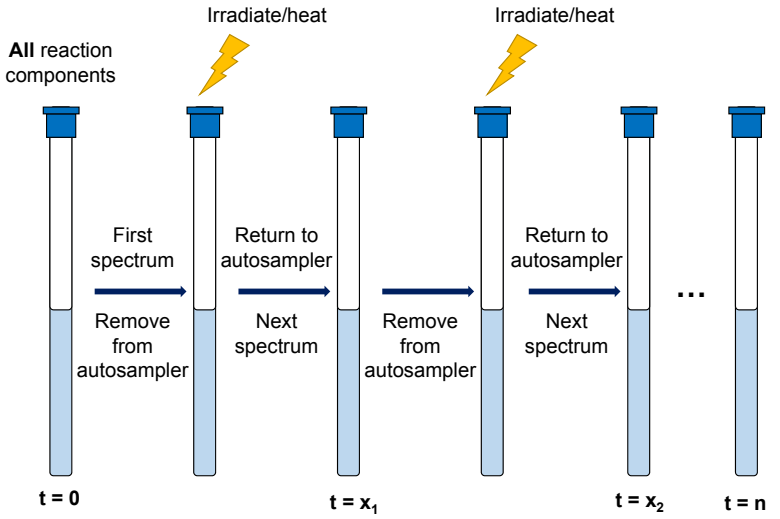


Sampling Methods



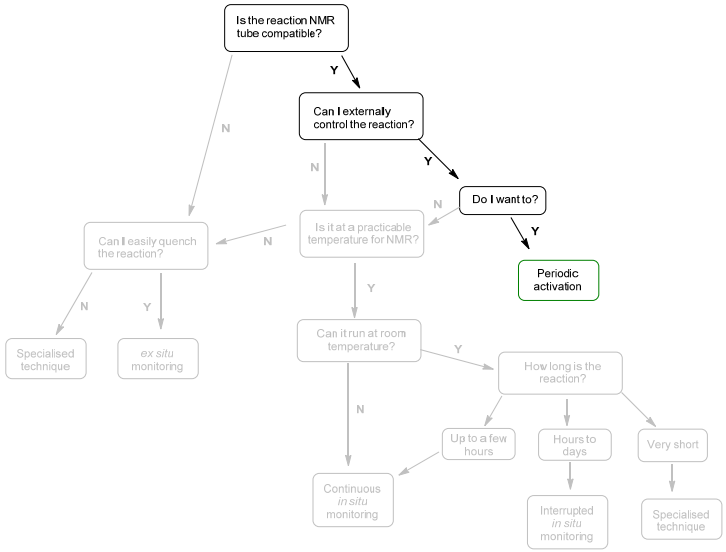
Sampling Methods – *in situ* Monitoring

Periodic Activation



- Long NMR experiments possible
- Parallel reactions possible
- Labour intensive
- Possibly lose transient species
- Limited reaction compatibility

Sampling Methods



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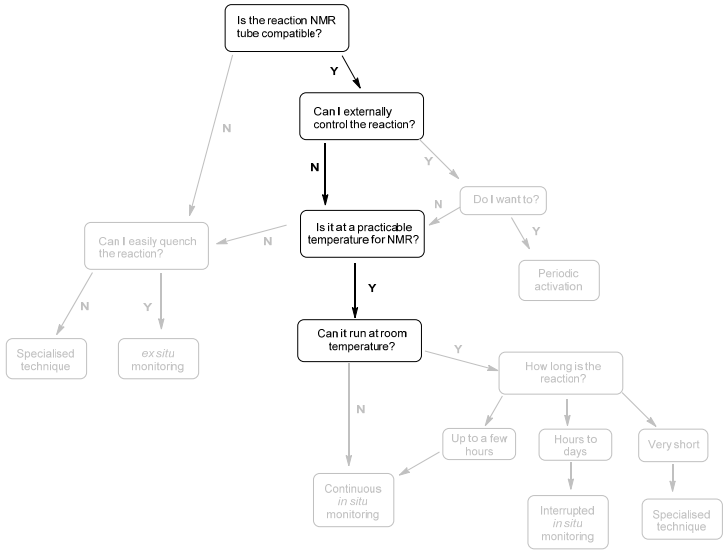

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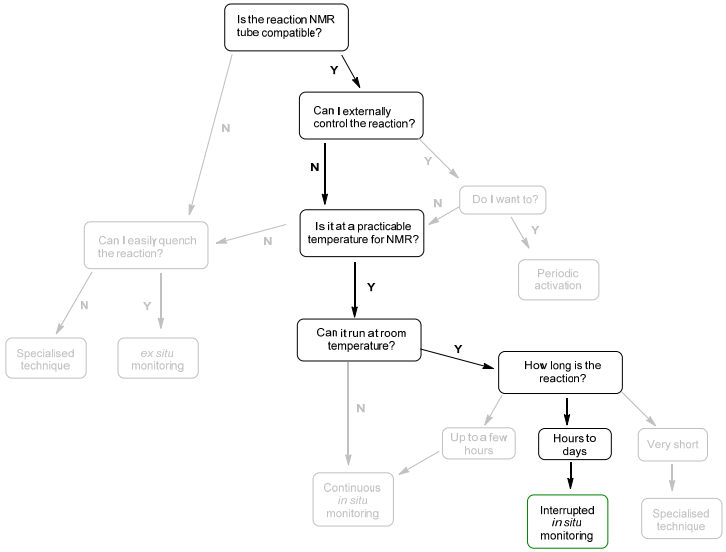
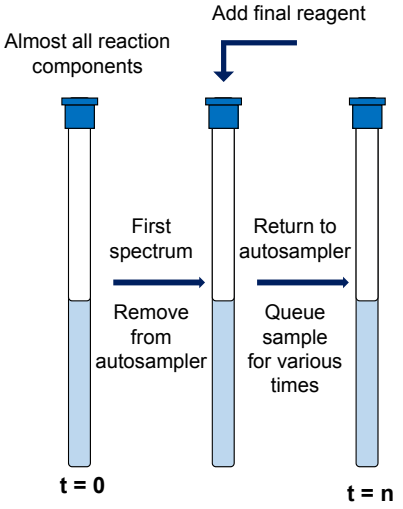
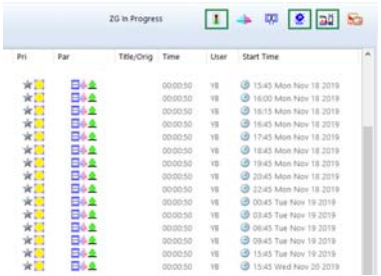


Sampling Methods – *in situ* Monitoring

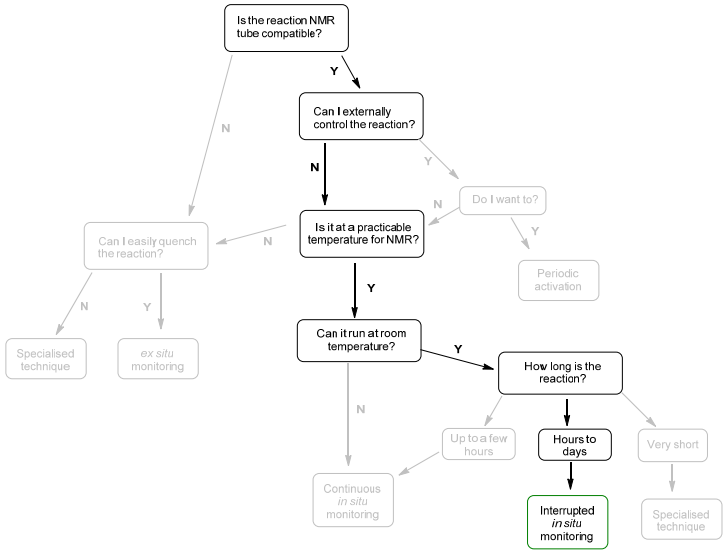
'Interrupted' Monitoring





- Easy
- Parallel experiments
- Relatively slow reactions

Sampling Methods



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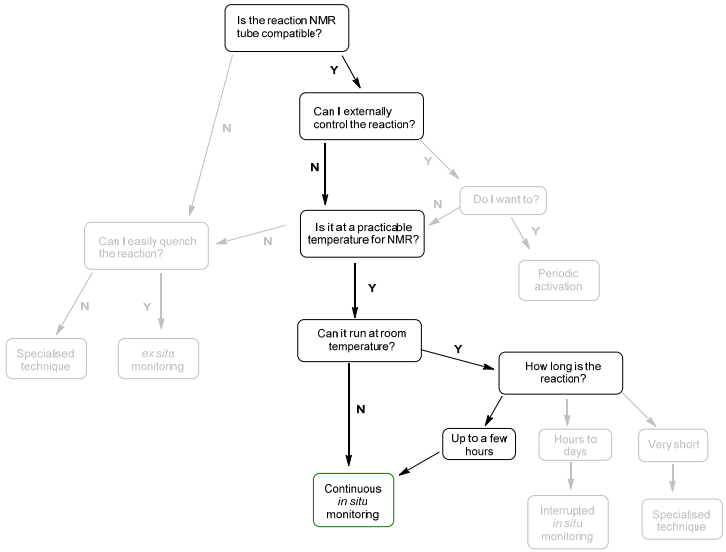
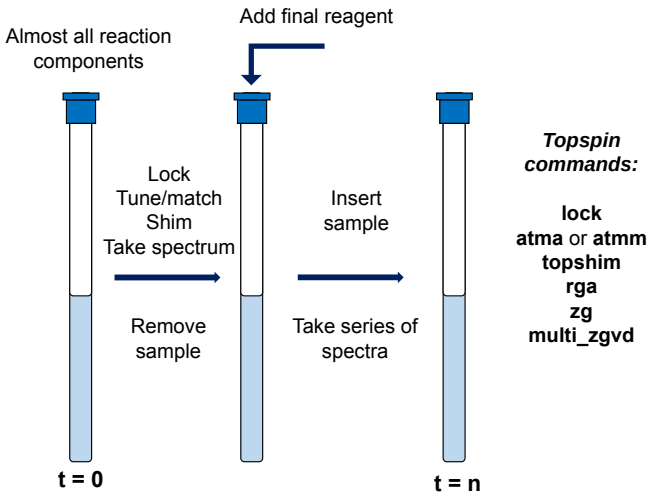


Sampling Methods – *in situ* Monitoring

Continuous Monitoring

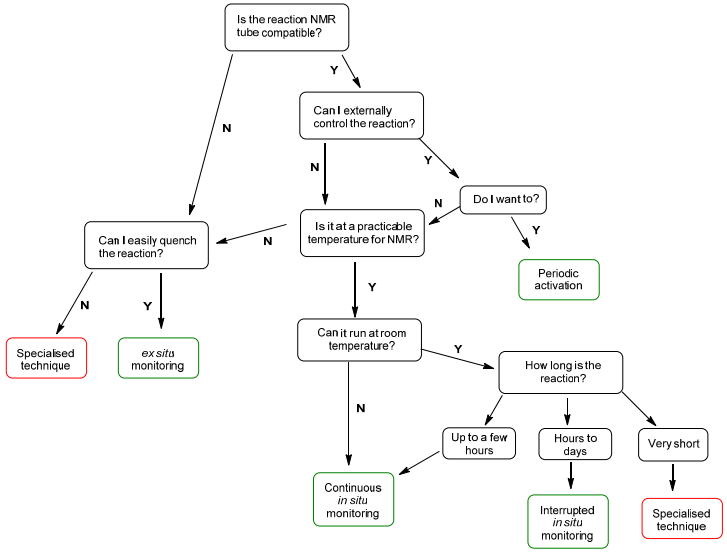


Topspin commands:

lock
atma or **atmm**
topshim
rga
zg
multi_zgvd

- Not labour intensive
- Uses entire instrument time
- Much faster reactions

Sampling Methods



Considerations – Nucleus

Nucleus	Abundance (%)/ Sensitivity (% ^{1}H)	NMR experiment time	Level of structural information	Likelihood of presence in target system	Solvent
^{1}H	99.99 / 100	Fast	High	High	Deuterated
^{19}F	100 / 83	Fast	Medium	Medium	Non-deuterated
^{31}P	100 / 7	Slow	Medium	Medium	Non-deuterated
^{29}Si	4.68 / 0.03	Slow	Medium	Medium	Non-deuterated
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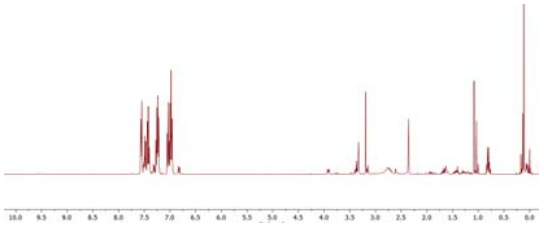

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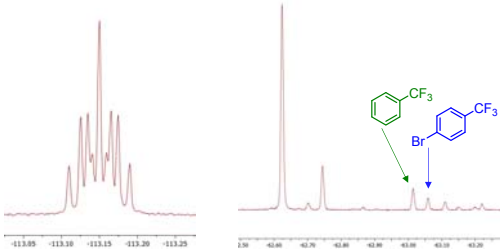
- Coupling
- Highly sensitive to chemical environment
- Assignment by independent isolation



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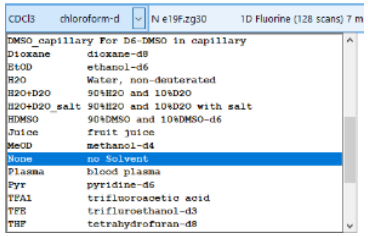
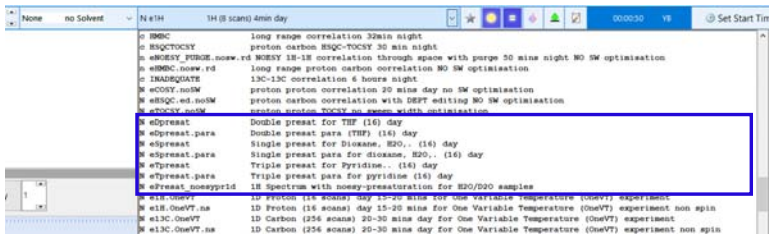
Sometimes very useful!
- Quenched reactions
- Slow reactions
- Equilibria

Considerations – Solvent

Deuterated solvent
- ^{1}H
- Expensive!

Non-deuterated solvent
- Much cheaper!
- Non ^{1}H nuclei
- 1H with solvent suppression
  - longer pulse sequence takes time

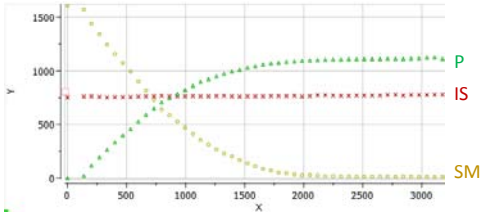




Considerations - Internal Standards

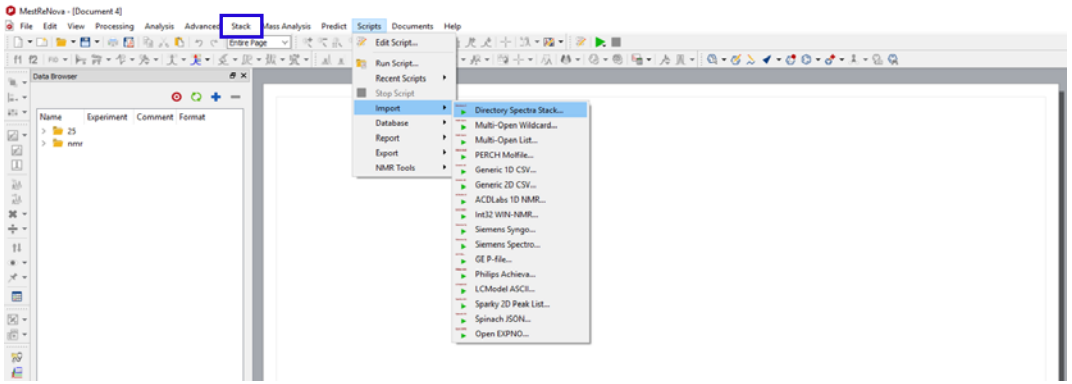
Why?
- Reference chemical shift
- Integral normalisation

Good internal standard
- Concentration stays fixed over reaction
  - (relatively) nonvolatile
  - innocent
- No signal overlap
- Similar T_1 to reagents



$$[\mathrm{A}] = \frac{s(A)}{s(IS)} \times \frac{n(IS)}{n(A)} \times [IS]$$

Data Processing - Mestrenova



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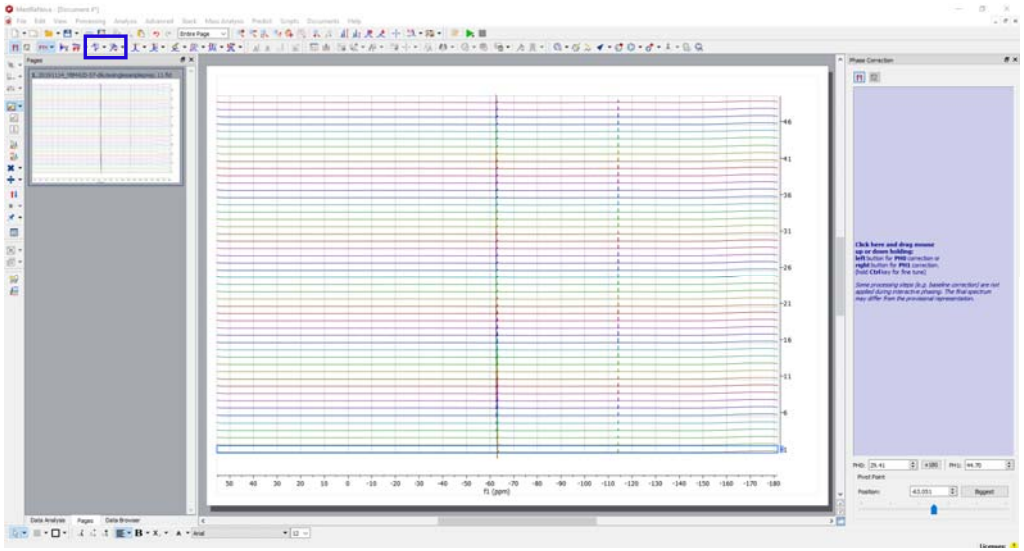

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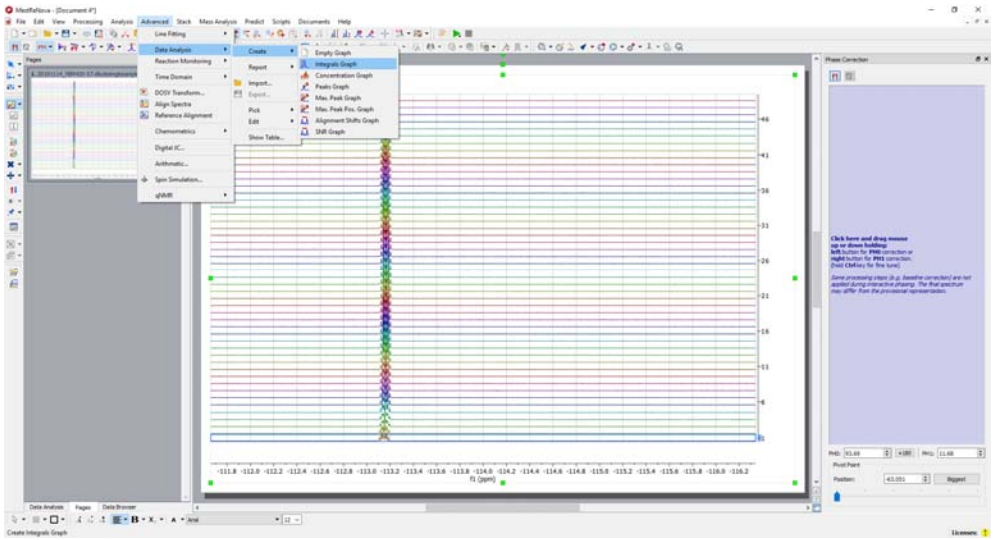

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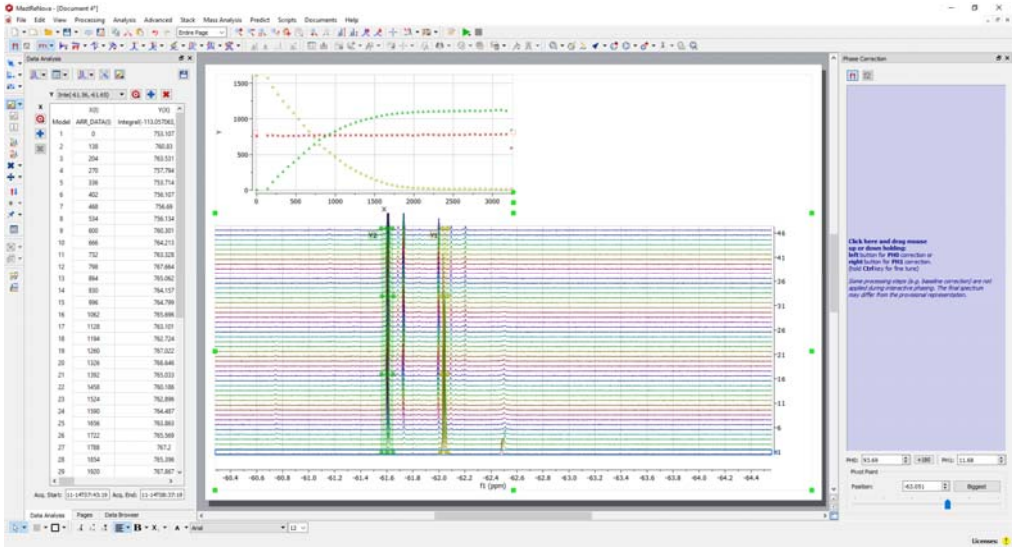
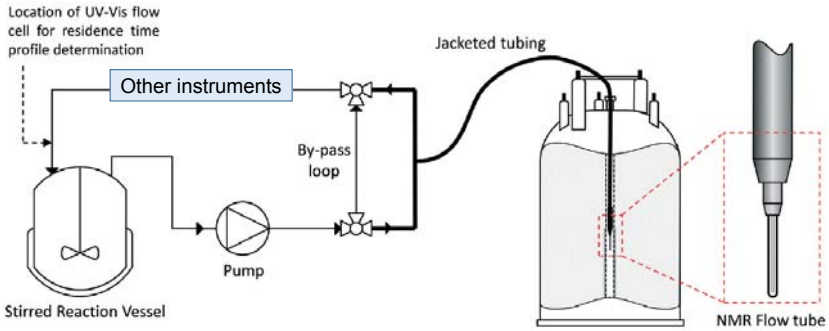


Specialised Techniques – Flow NMR

On-line monitoring

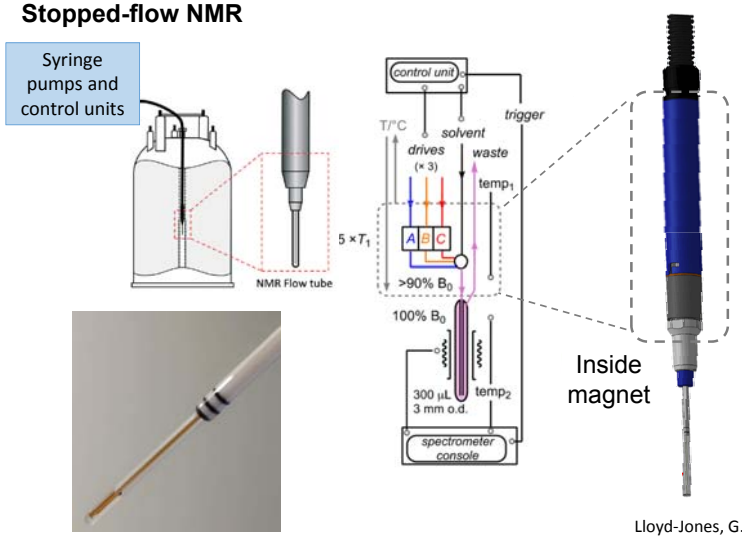


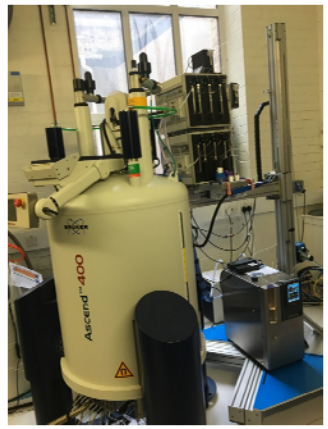
Hintermair, U. *Catal. Sci. Technol*. **2016**, 6, 8406-8417.

Specialised Techniques – Stopped-Flow NMR

Stopped-flow NMR

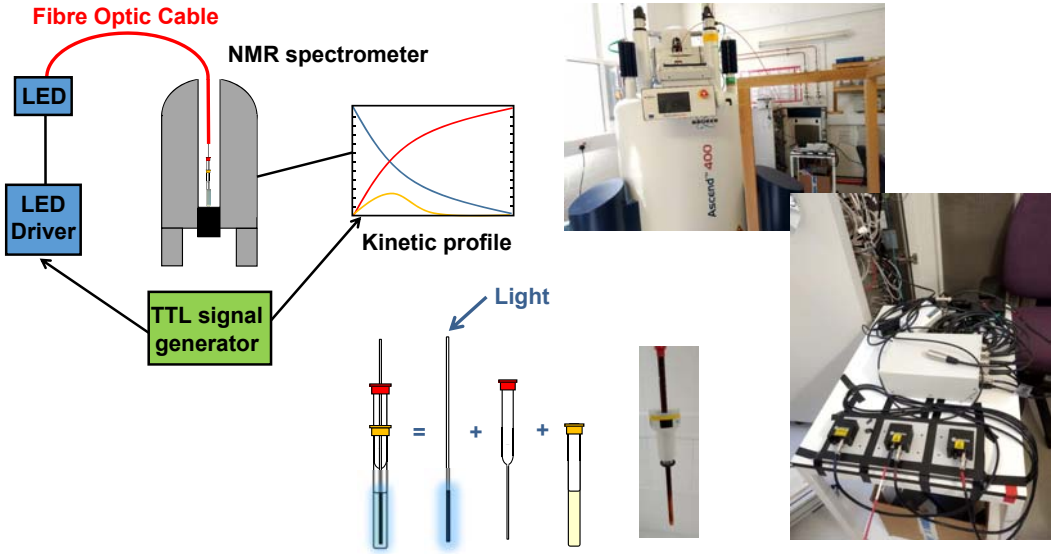
Syringe pumps and control units





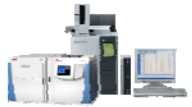
Lloyd-Jones, G.G. *J. Am. Chem. Soc.* **2018**, 140, 11112-11124.

Specialist Techniques – *in situ* Illumination



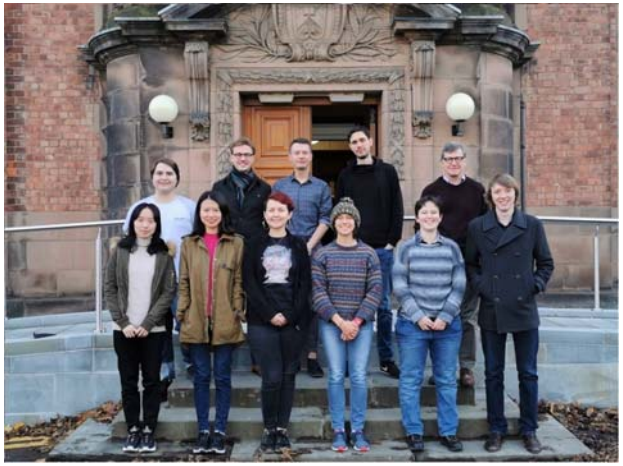
Key Messages

- **Lots of different ways to monitor kinetics by NMR**
  - **Sampling methods**
  - **Signal to monitor**
- **Lots of different factors to consider**
- **Often don't need specialised equipment**



- **… remember that other techniques exist too**

Acknowledgements



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