# Biodegradable thiol-modified poly(vinyl alcohol) hydrogels

Yuri Svirkin, Adam Kozak, Gavin Braithwaite

MRS 2013

Cambridge Polymer Group,
56 Roland Street, Suite 310
Boston, MA 02129
www.campoly.com

Cambridge Polymer Group

# *Introduction*

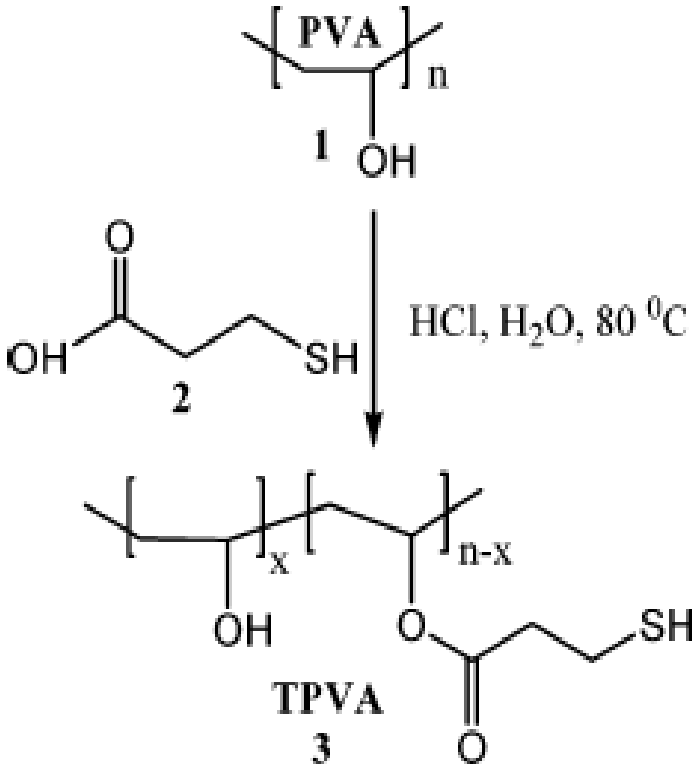
- PVA biocompatible
- Well respected biomaterial

- Not readily injectable and in situ crosslinkable
- Not intrinsically biodegradable
- Not sufficiently mucoadhesive

- This presentation will talk about
  - New method of making an injectable PVA hydrogel that is mucoadhesive and degradable

# *Synthesis of Thiolated Poly(vinyl alcohol)*

- Conversion of some OH groups to thiol groups adds thiol pendant groups directly to the PVA backbone



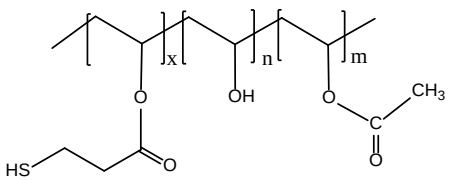



R.M. Dicharry, et al Biomacromolecules, Vol. 7, N 10, 2006

# *Synthesis of TPVA/PEGDA Hydrogels*

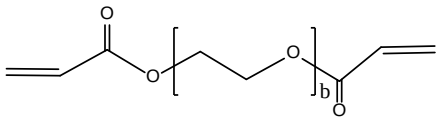
- TPVA crosslinking with difunctional poly (ethylene glycol) thiol-reactive molecules forms a hydrogel via Michael-Type addition reaction
  - Thiol groups control crosslink density
  - PEGDA chain length control molecular weight between crosslinks

TPVA

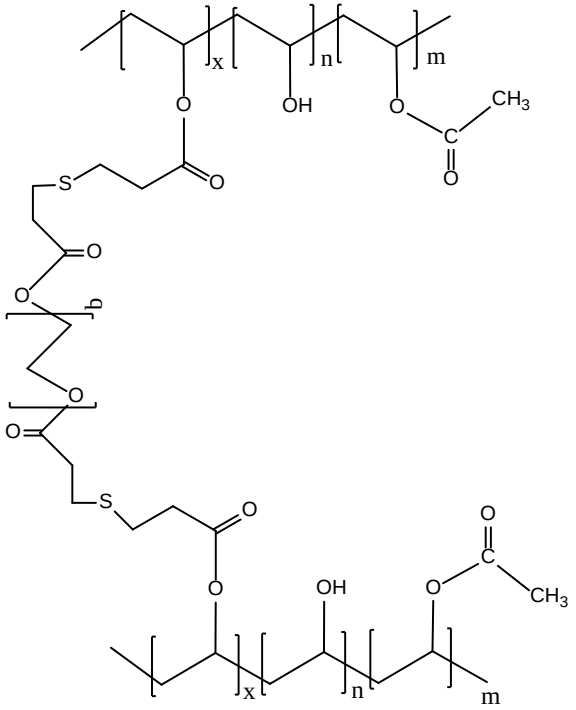


\+

PEGDA

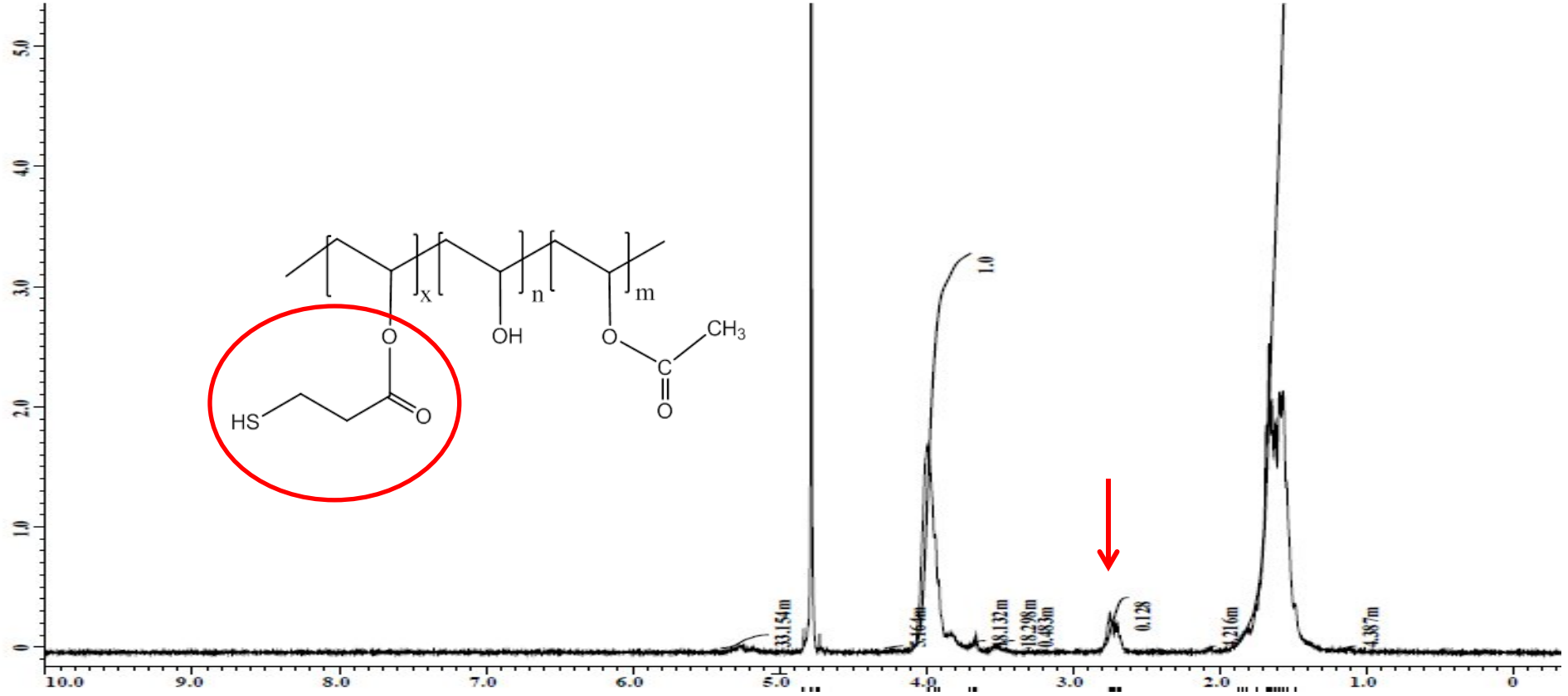


pH 7.4 1xPBS



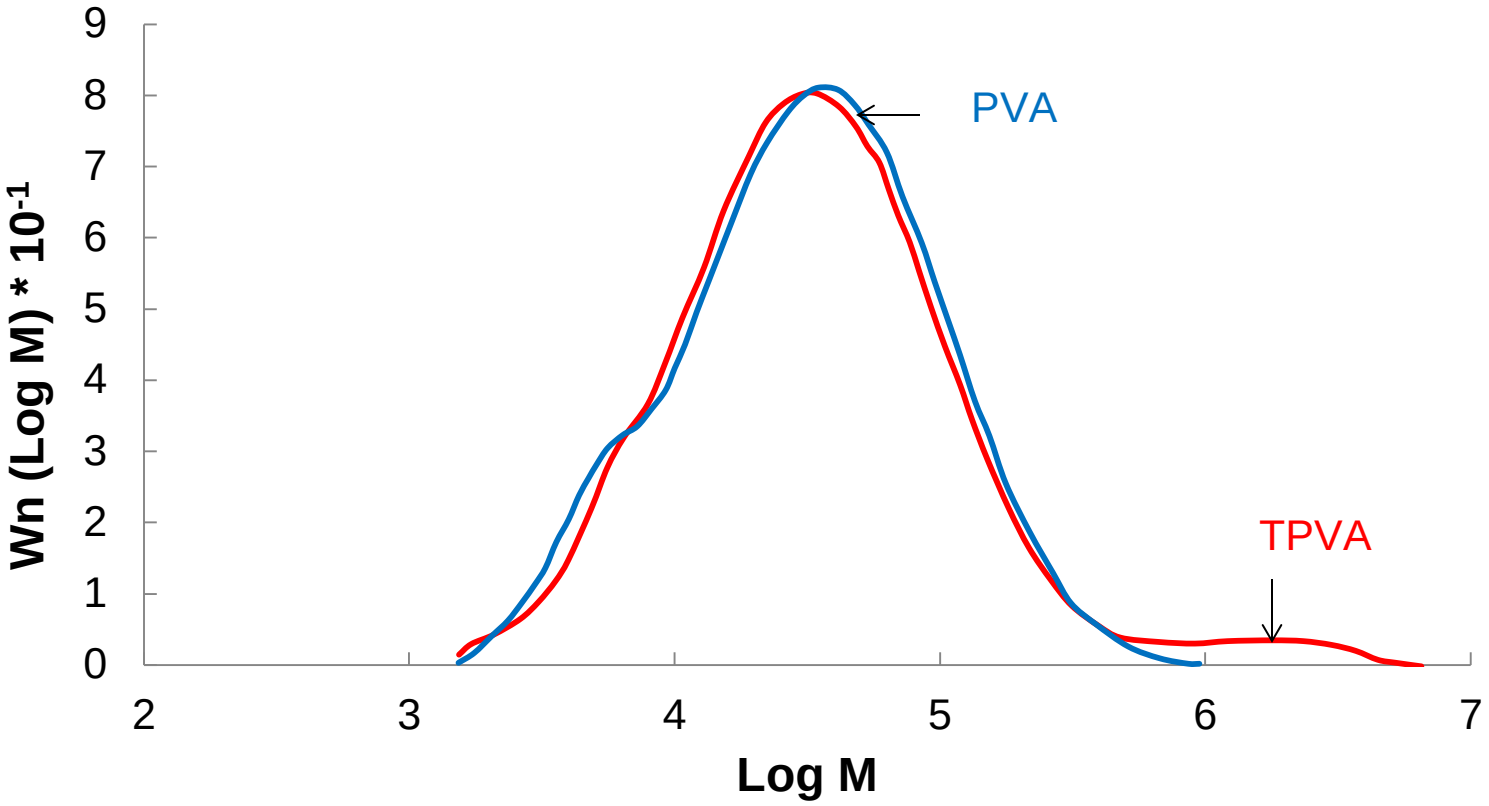
# *1H NMR of TPVA*

- 1H NMR of converted product indicate presence of mercaptopropionic ester fragment
  - Degree of modification ~3%



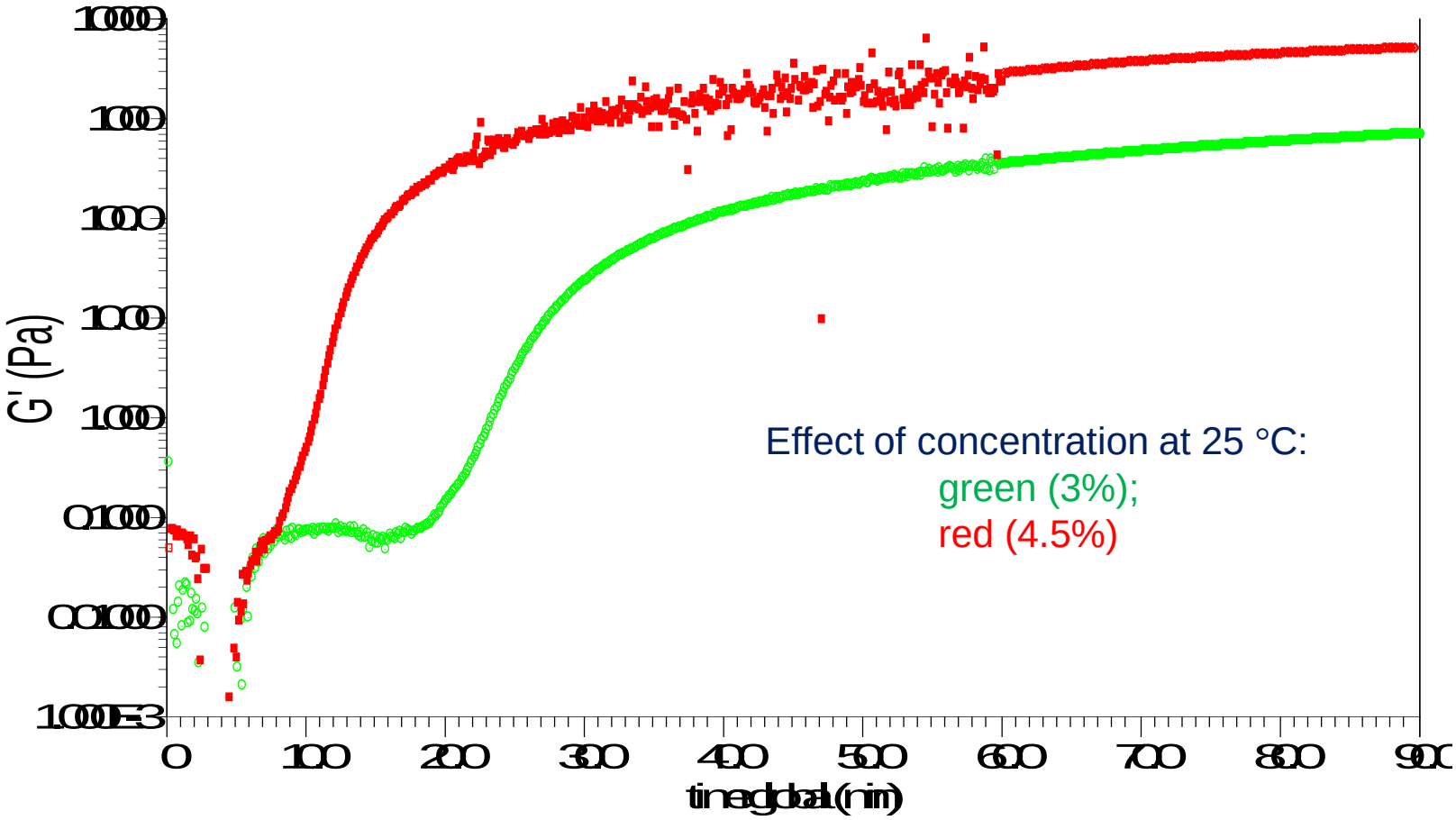
# *Molecular Weight Distribution of PVA and TPVA*

- Gel Permeation Chromatography indicates a small fraction of higher molecular weight species



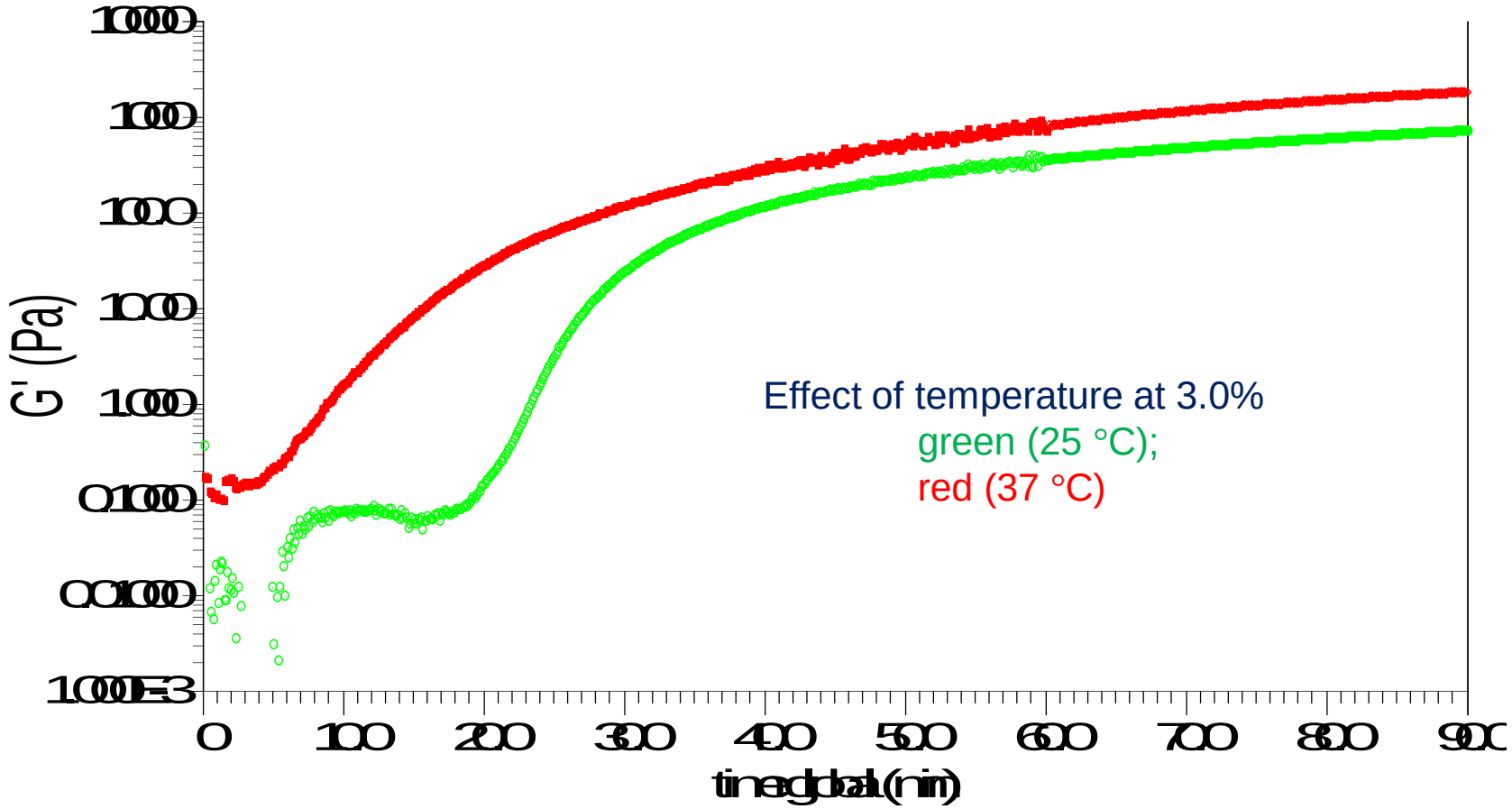
# *Gelation kinetics of TPVA/PEGDA (concentration)*

- Rheology provides a sensitive tool for tracking gelation kinetics as a function of concentration

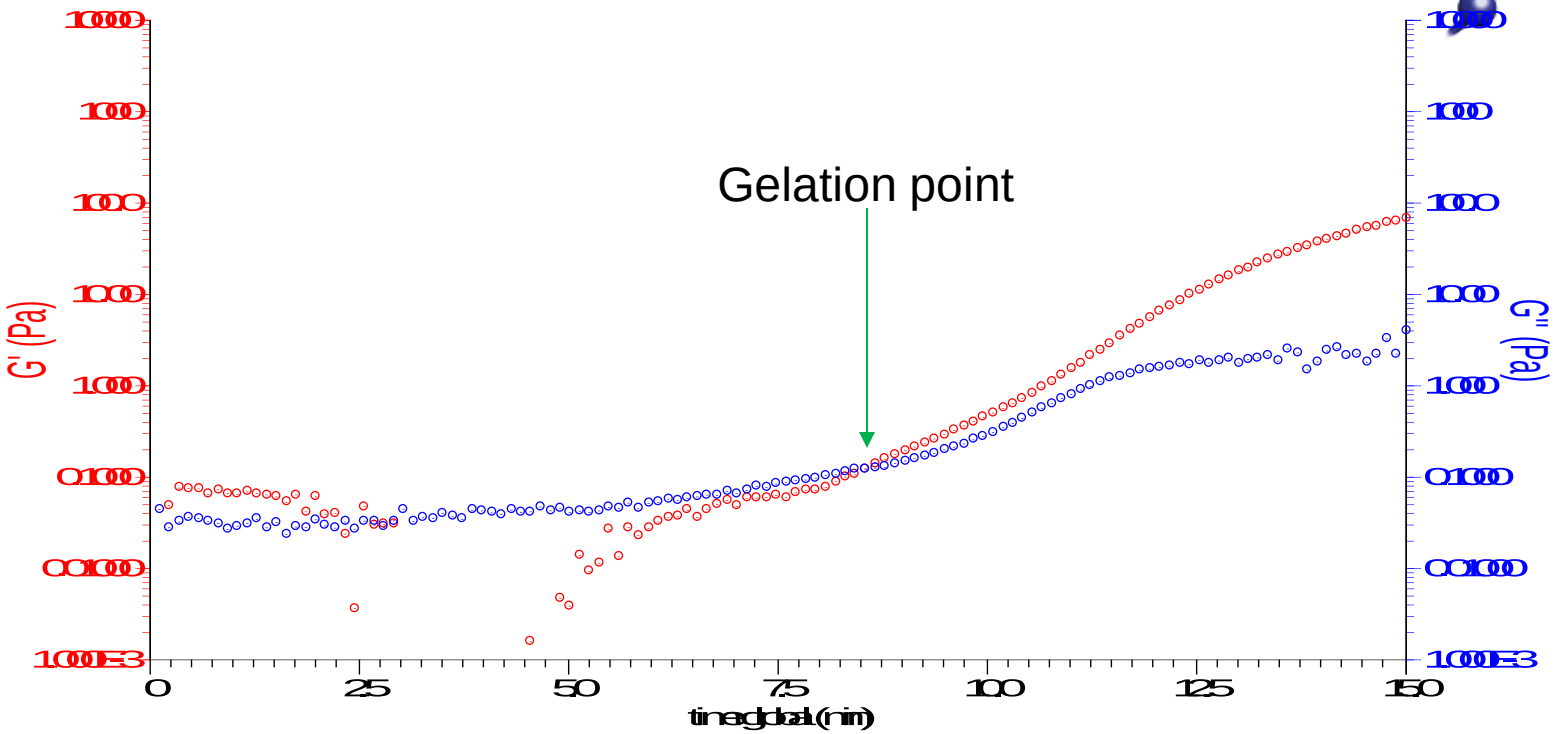


# *Gelation kinetics of TPVA/PEGDA (temperature)*

- Temperature also controls gelation kinetics



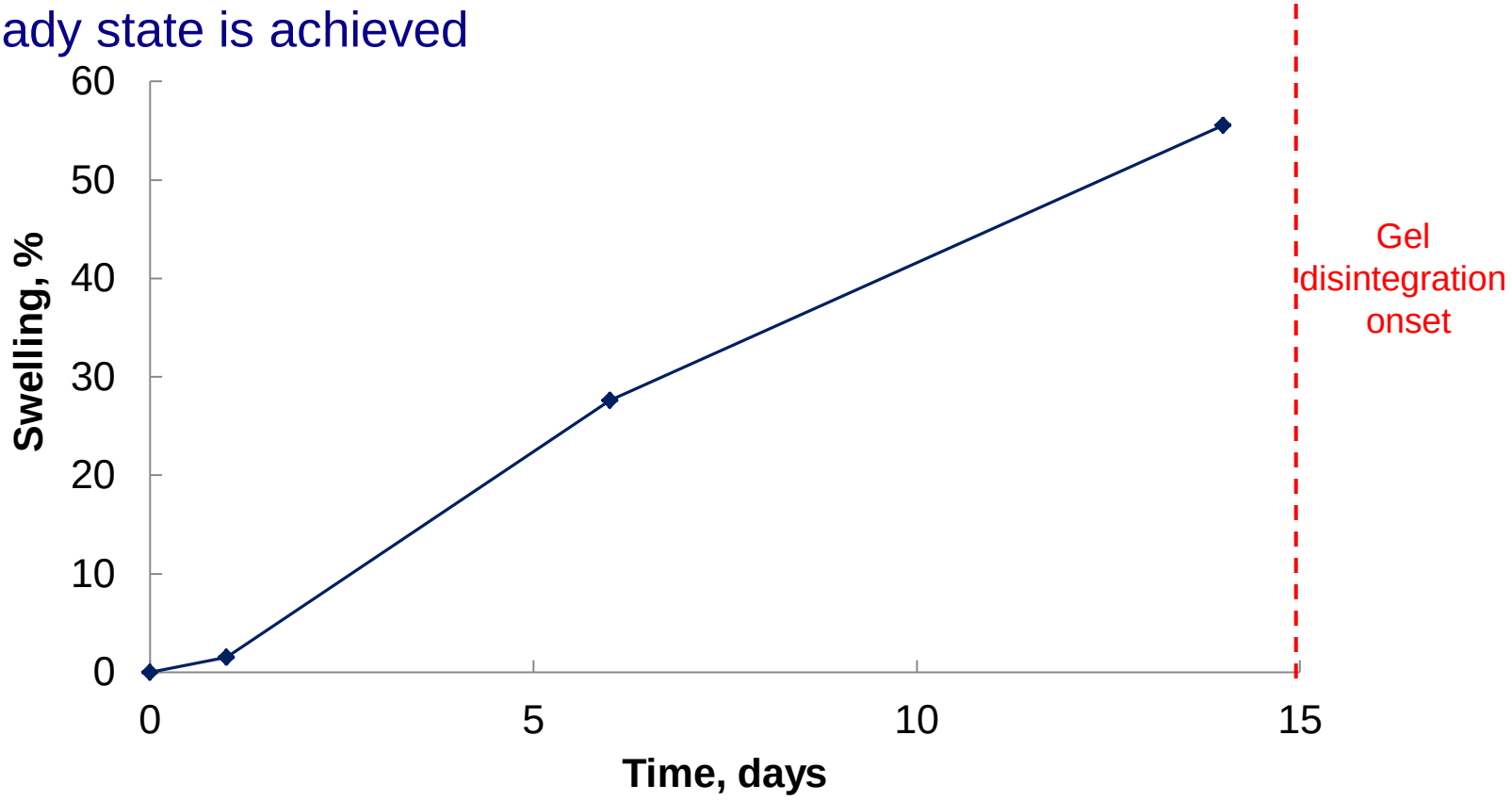
# *Kinetics and Properties of TPVA/PEGDA Hydrogels*




| Polymer concentration, % [w/v] | Temperature, °C | | | | | |
|---|---|---|---|---|---|---|
| | 25 °C | | | 37 °C | | |
| | Gelation time, [min] | G' [Pa] | G" [Pa] | Gelation time, [min] | G' [Pa] | G" [Pa] |
| 3.0 | 23.3 | 803 | 5 | 4.2 | 3607 | 480 |
| 4.5 | 9.2 | 6440 | 133 | 3.0 | 9860 | 280 |

# *Swelling kinetics of TPVA hydrogels*

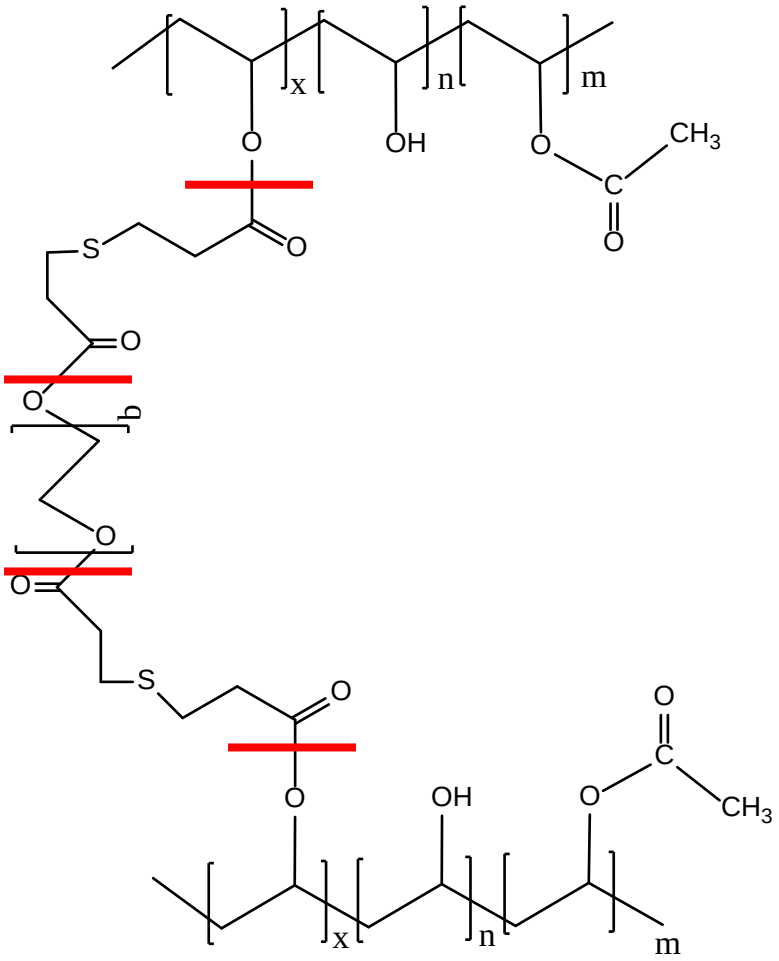
- Tracking unconfined swelling of the hydrogels in 1xPBS suggests no steady state is achieved




Swelling of 4.5 % w/v TPVA/PEGDA hydrogel in 1xPBS as a function of degradation time. Swelling percent=(W-Wo)/Wo;

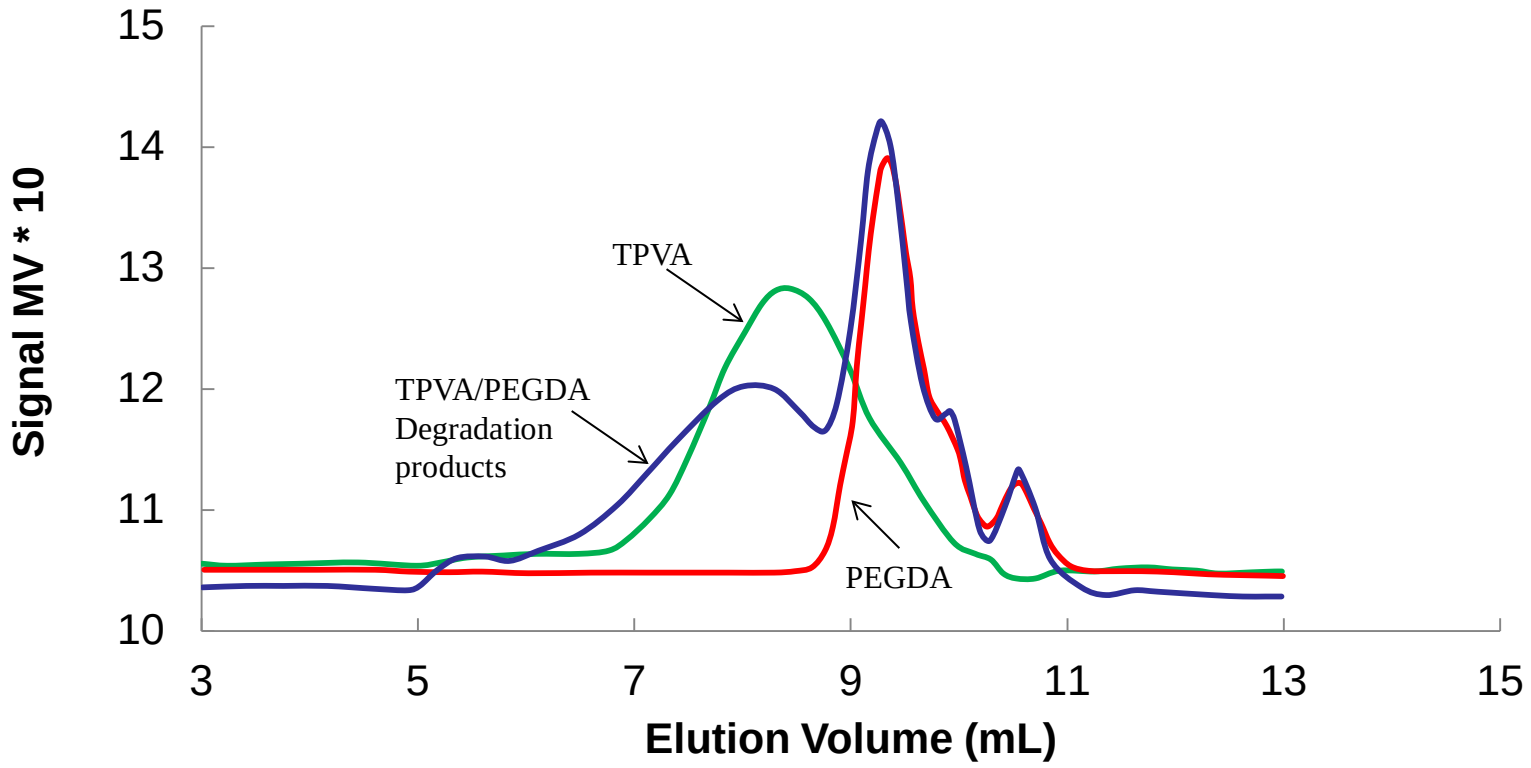
# *Degradation of TPVA Hydrogel*

- The use of the mercaptopropionic and acrylate results in hydrolysable ester bonds within the crosslinks



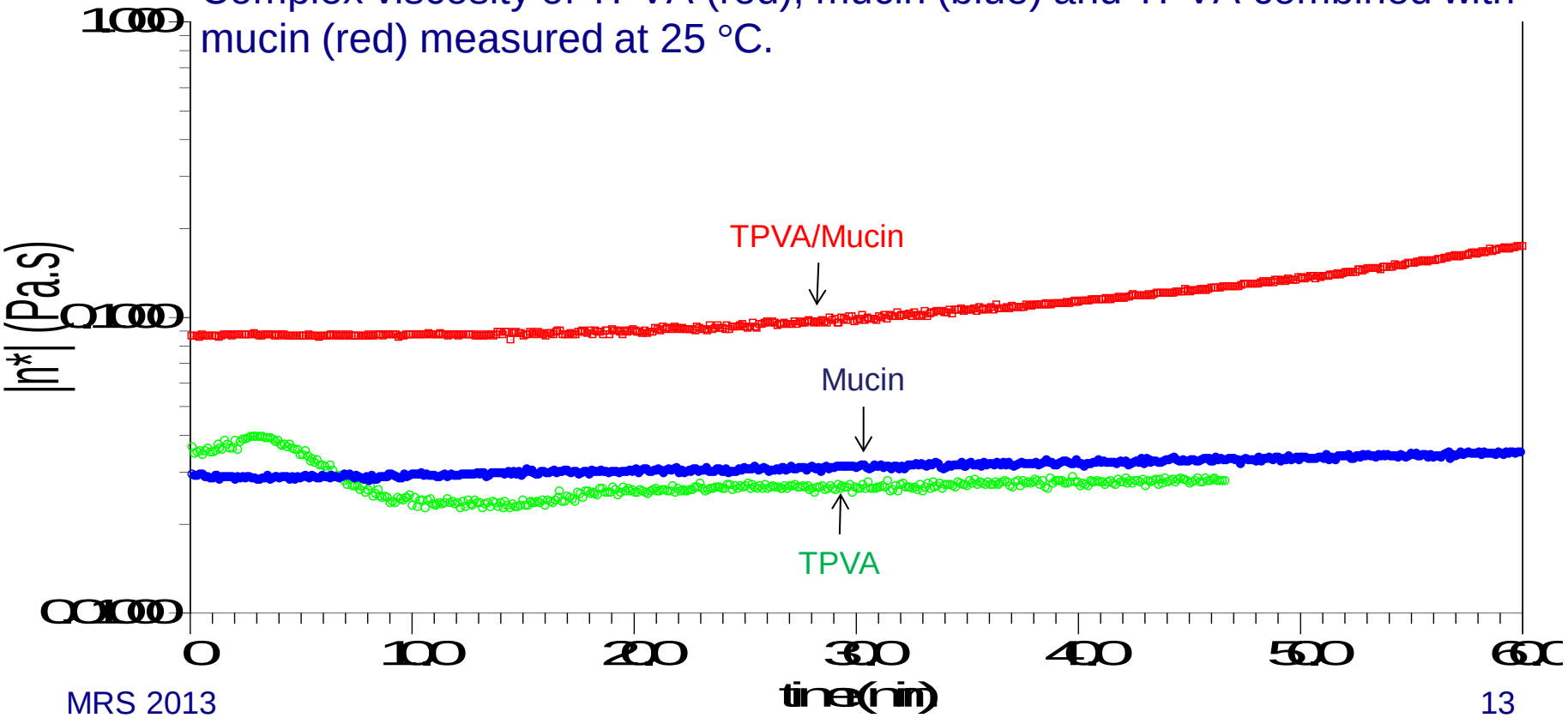
# *TPVA Degradation Products by GPC Analysis*

- Cleaving of ester bonds yields species with TPVA and PEGDA molecular weights



# *TPVA Mucoadhesive Properties*

- Thiol groups known to be mucoadhesive
- Mixing of TPVA with mucin and tracking rheology response proves molecular interactions
  - Complex viscosity of TPVA (red), mucin (blue) and TPVA combined with mucin (red) measured at 25 °C.



# *Features and applications of TPVA/PEGDA Hydrogels*

- TPVA/PEGDA hydrogels formed through Michael-Type addition reaction
  - physiological conditions from low viscosity TPVA and PEGDA
  - well suited for in situ applications
- Hydrolysable ester bonds in crosslinks
  - inherited biodegradability
  - degradation results in formation PVA and PEGDA
  - products are biocompatible and low molecular weight to allow for easy elimination by passing through kidneys
- Unreacted thiol groups,
  - not used in crosslinking reactions result in mucoadhesive properties
- Potential applications
  - percutaneous, temporary tissue bulking and scaffolding