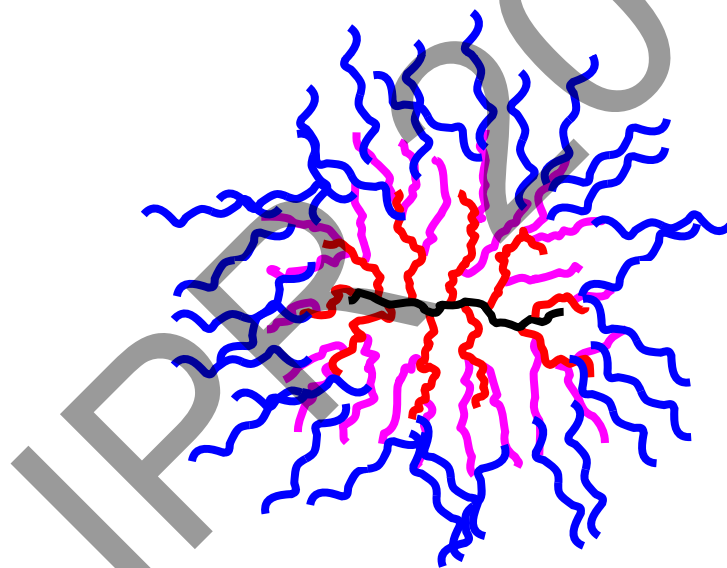



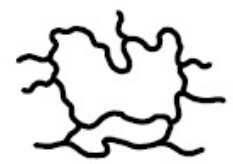


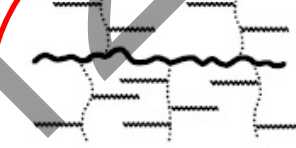
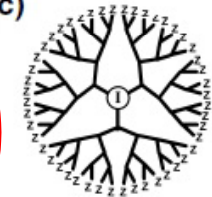
ARBORESCENT POLYMERS BASED ON AMINO ACIDS

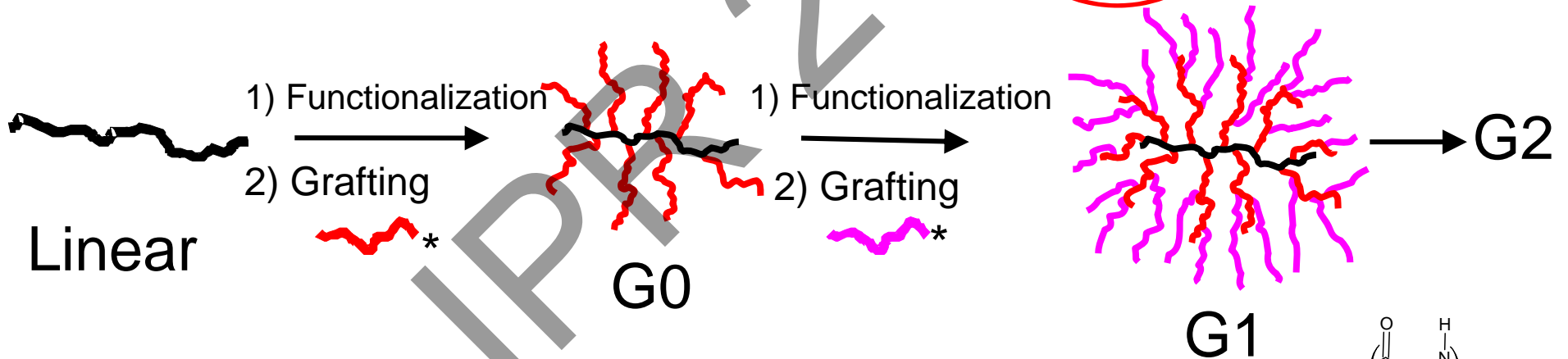


Greg Whitton, Mario Gauthier

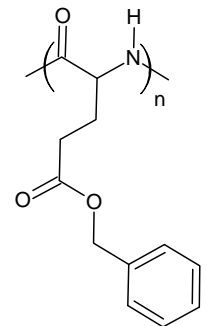
IPR Symposium, May 2, 2012

ARBORESCENT POLYMERS

I. Linear	II. Cross-linked	III. Branched	IV. Dendritic		
			(a)  Random Hyperbranched	(b)  Dendrigrafts	(c)  Dendrimers

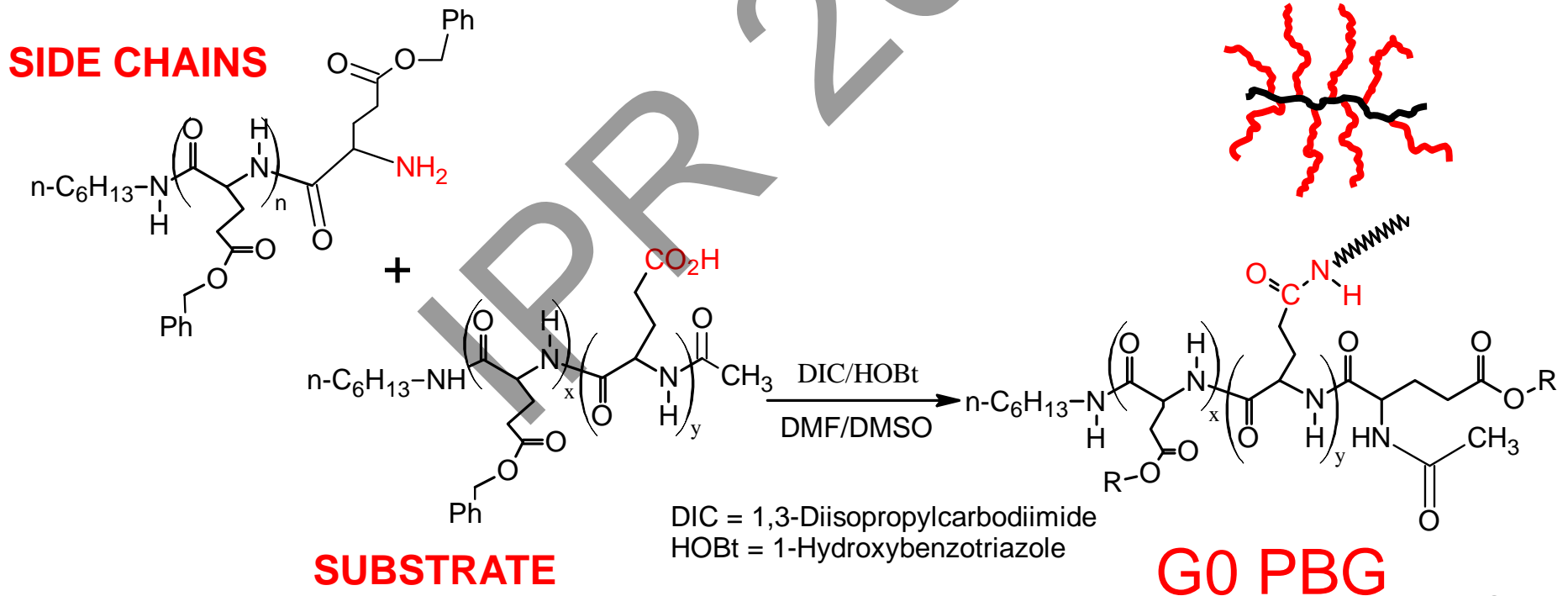


- ➔ Static structure (stable, no CMC)
- ➔ Biocompatibility: Amino acid derivatives
- ➔ Water solubility: Polyglycidol, PEG, PHEA, PGA



GRAFTING

- Substrate coupling with side chains
 - Grafting sites activated using carbodiimide techniques
 - DIC/HOBt
 - Stoichiometry varied to maximize coupling efficiency



ARBORESCENT PBG (CORE)

Characteristics of Arborescent PBG for Successive Generations

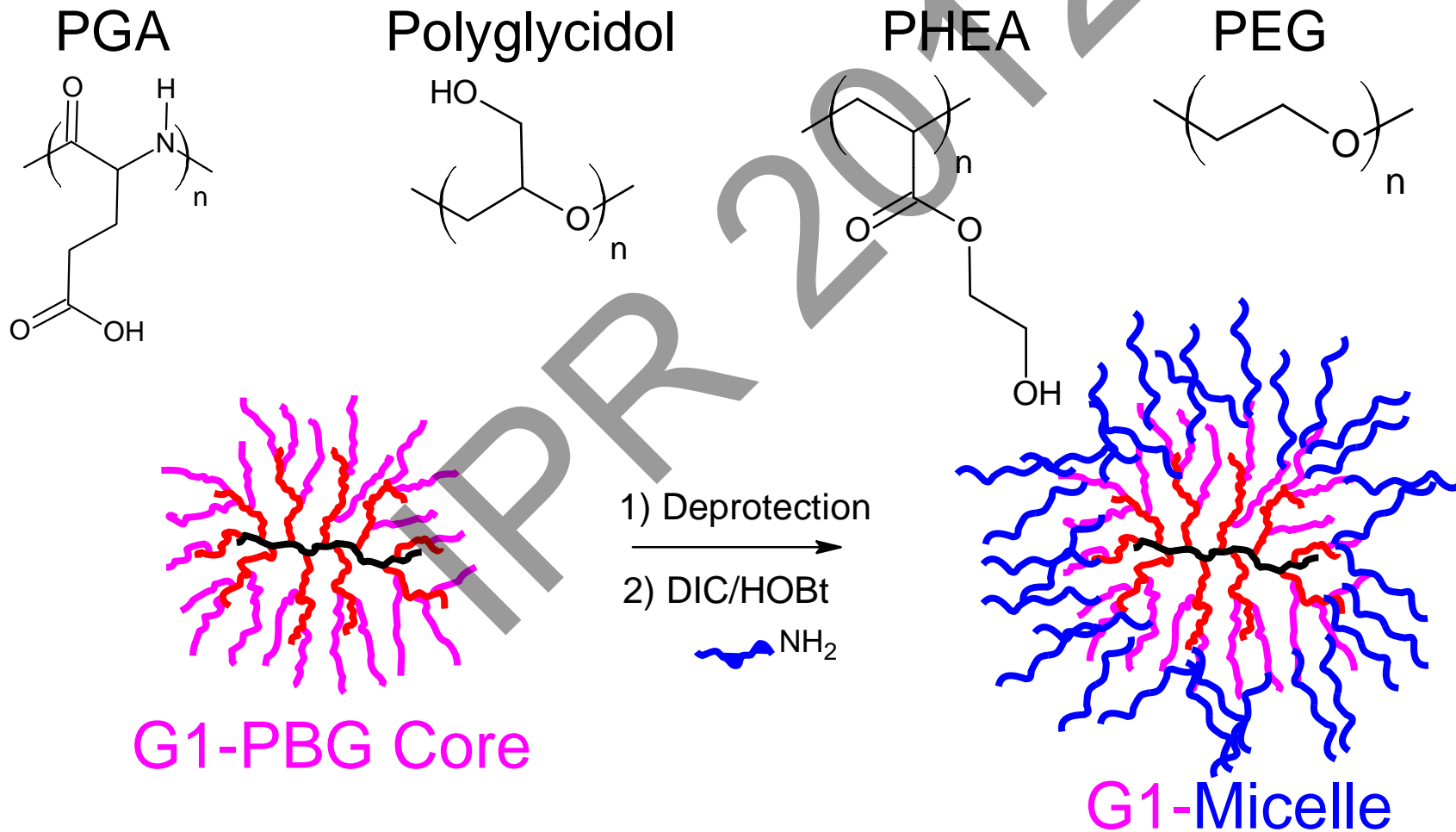
Sample #	M_n Side chains	MALLS		Grafting Yield (%)	Branching Functionality
		M_n	M_w/M_n		
G0	5,700	66,000	1.04	43	10
G1	4,300	235,000	1.05	63	43
G2	4,300	1,100,000	1.06	30	201
G3	4,300	3,300,000	1.07	35	512

Hydrodynamic Diameter of Arborescent PBG (nm)

	DMF		DMSO	
	1 st order	2 nd order	1 st order	2 nd order
G1	10.7	8.4	15.7	14.1
G2	13.1	12.1	21.3	20.1
G3	24.5	23.5	34.5	32.5

MICELLES

Last Grafting Cycle: hydrophilic biocompatible components

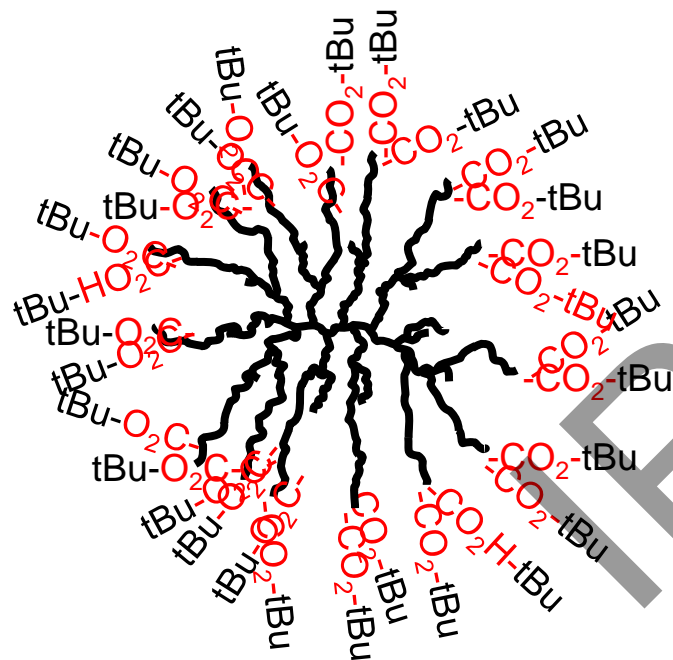
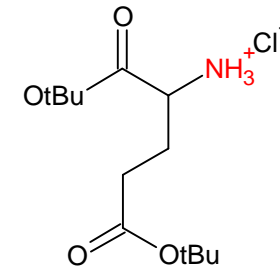


MICELLES: RANDOM GRAFTING

	MALLS		Grafting Yield (%)	Wt % PBG	Hydrodynamic Diameter	
	M_n	M_w/M_n			1 st order	2 nd order
					THF (nm)	
G1R35-GlyAc8	606,000	1.10	17*	39	29.2	25.6
G2R34-GlyAc8	1,780,000	1.11	44	62	26.8	25.0
G1R35-GlyAc25	1,800,000	1.08	48	13	47.1	45.3
G2R26-GlyAc25	3,740,000	1.07	29	29	70.0	66.6
					DMF (nm)	
G1R35-PEO5	1,000,000	1.07	33	18	22.5	13.3
G2R26-PEO5	3,470,000	1.05	43	28	46.3	36.8
G3R34-PEO5	3,810,000	1.04	24	75	--	--
					PBS Buffer (nm)	
G1R38-PGA1.2	--	1.17	22	38	217	208
G2R26-PGA1.2	--	1.22	32	46	120	98
G3R34-PGA1.2	--	1.17	18	39	--	--

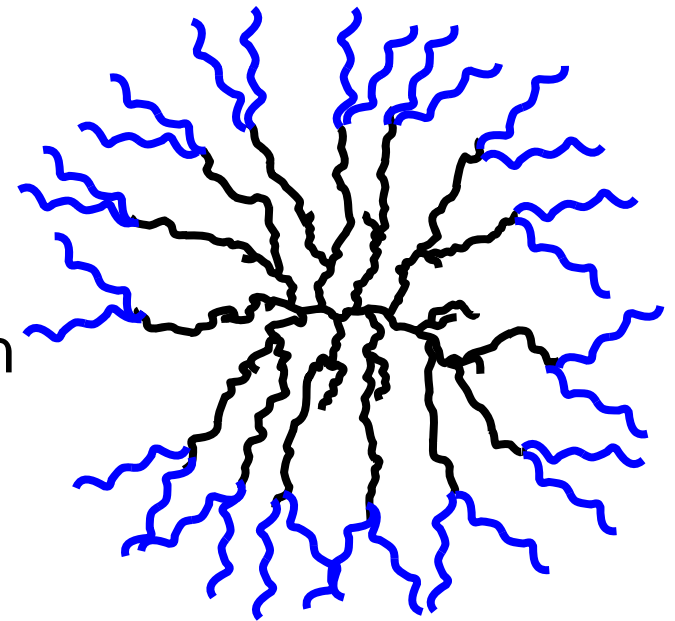
MICELLES: CHAIN-END ADDITION

- Last PBG grafting cycle: Side chains with H-Glu(OtBu)-OtBu initiator
- Functionalize ONLY chain ends



1) TFA

2) Grafting reaction



Hydrophilic Shell

MICELLES: CHAIN-END ADDITION

	MALLS		Grafting Yield (%)	Wt % PBG	Hydrodynamic Diameter (nm)	
	M_n	M_w/M_n			1 st order	2 nd order
					THF	
G1E9-GlyAc8	609,000	1.08	44	39	22.9	18.8
G3E11-GlyAc8	6,800,000	1.04	46	49	42.3	39.6
					PBS	
G2E10-PGA2	--	--	40	59	47	43

IPR 2012

Questions?