

*Pancreas cell*

❖ ~ 70% of current pharmaceuticals target membrane proteins

❖ ~ 30 - 40% of the genes of an organism code for membrane proteins

❖ ~ 110 structures of membrane proteins; whereas over 30,000 structures of globular proteins in the RSCB Protein Data Bank

Topography Mapping:  
Proteolytic Cleavage  
Chemical Labeling  
Sequence Prediction  
Accessibility Measurements

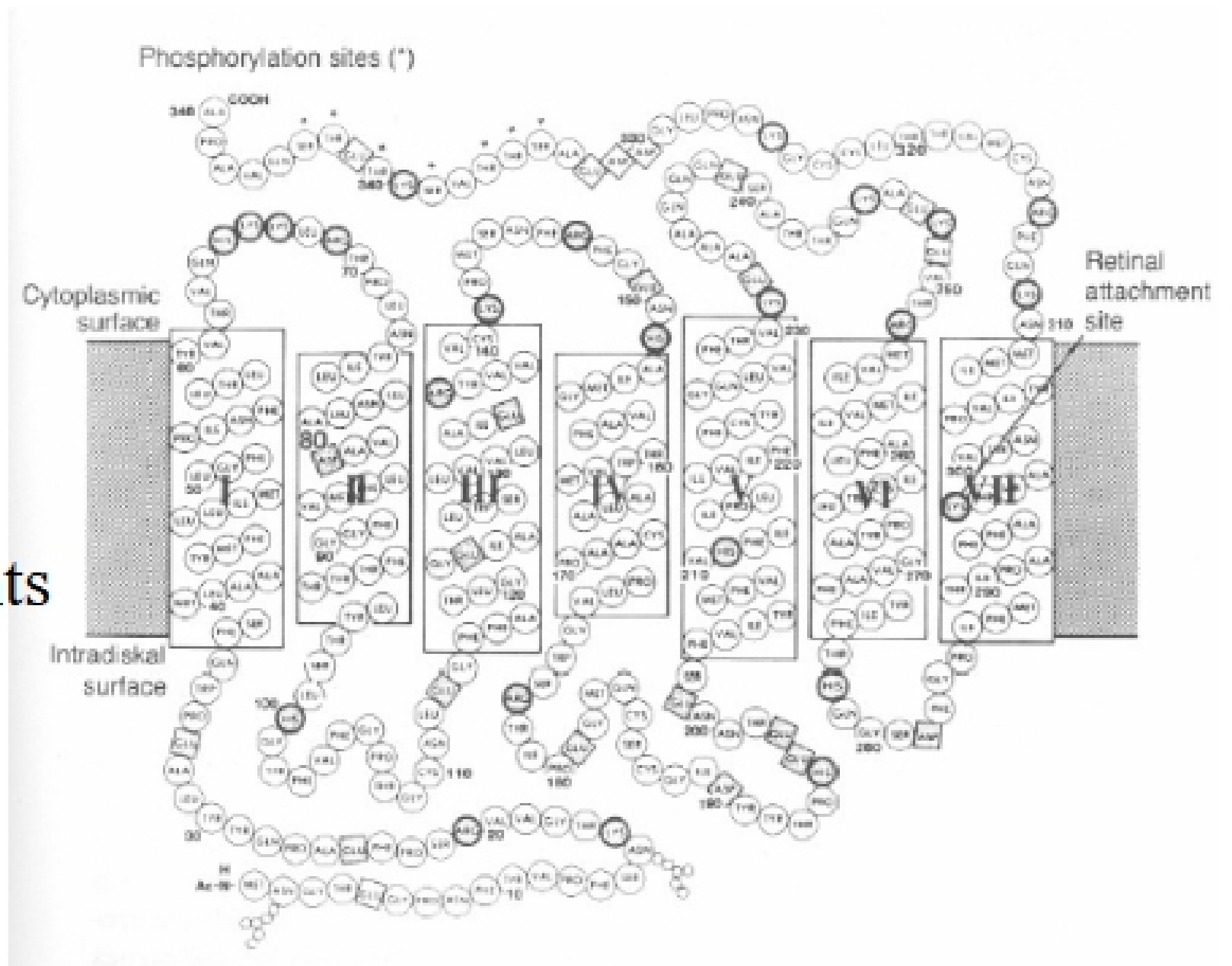

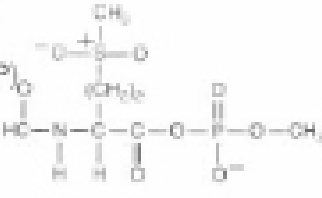
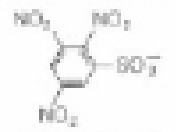



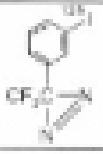

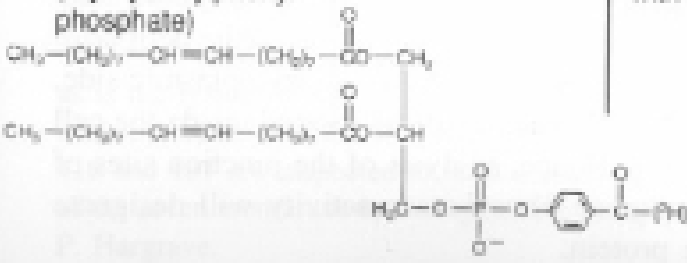


Figure 4.1. Topographic model of bovine rhodopsin indicating the seven transmembrane helices. Phosphorylation sites (asterisks) and N-linked glycosylation sites are indicated, as is the lysine in helix 7 which is the retinal attachment site. The aspartate in helix 2 is suspected to function as a counterion for the Schiff base formed by retinal. Cysteines 110 and 187 are suspected to form a disulfide bond. Note the presence of proline in five of the seven membrane-spanning helices. Adapted from ref. 593a. Kindly provided by Dr. P. Hargrave.

Table 4.1. Some reagents used to probe the topography of membrane proteins.

Reagent	Target	Reference
(1) Diazotized sulfanilic acid (DSA, DABS) 	Surface-accessible amino groups, tyrosine, histidine, cysteine.	1182
(2) Formyl-methionyl sulfone methyl-phosphate (FMMP) 	Surface-accessible protein or phospholipid amino groups	145
(3) Trinitrobenzene sulfonic acid (TNBS) 	Surface-accessible protein or phospholipid amino groups	1332, 1251
(4) Isethionylacetimidate (IAI) 	Surface-accessible protein or phospholipid amino groups	1059
(5) N-(4-Azido-2-nitrophenyl)-2-aminethane sulfonate (NAP-Taurine) 	Non-specific label for surface-accessible groups. Photoactivated to reactive nitrene.	1182
(6) 1-azido-4-[ <sup>125</sup> I]iodobenzene (AIB) 	Non-specific label for membrane-buried groups. Forms reactive nitrene.	296
(7) 3-(trifluoromethyl)-3-m-[ <sup>125</sup> I]iodophenyl diazine (TID) 	Non-specific label for membrane-buried groups. Forms reactive carbene.	962, 157, 653, 1116
(8) 1-palmitoyl-2-[10-[4-(trifluoromethyl diazirnyl)phenyl]-[9- <sup>3</sup> H] 8-oxaundecanoyl]-sn-glycero-3-phosphocholine (PTPC) 	Non-specific label for membrane-buried groups. Forms reactive carbene.	158 (also see similar labels, 1421)
(9) 1,2-dioleoylglycerol-3-(4-[ <sup>3</sup> H]formylphenyl-phosphate) 	Protein amino groups in contact with lipid polar headgroups.	957 see also 6, 170