

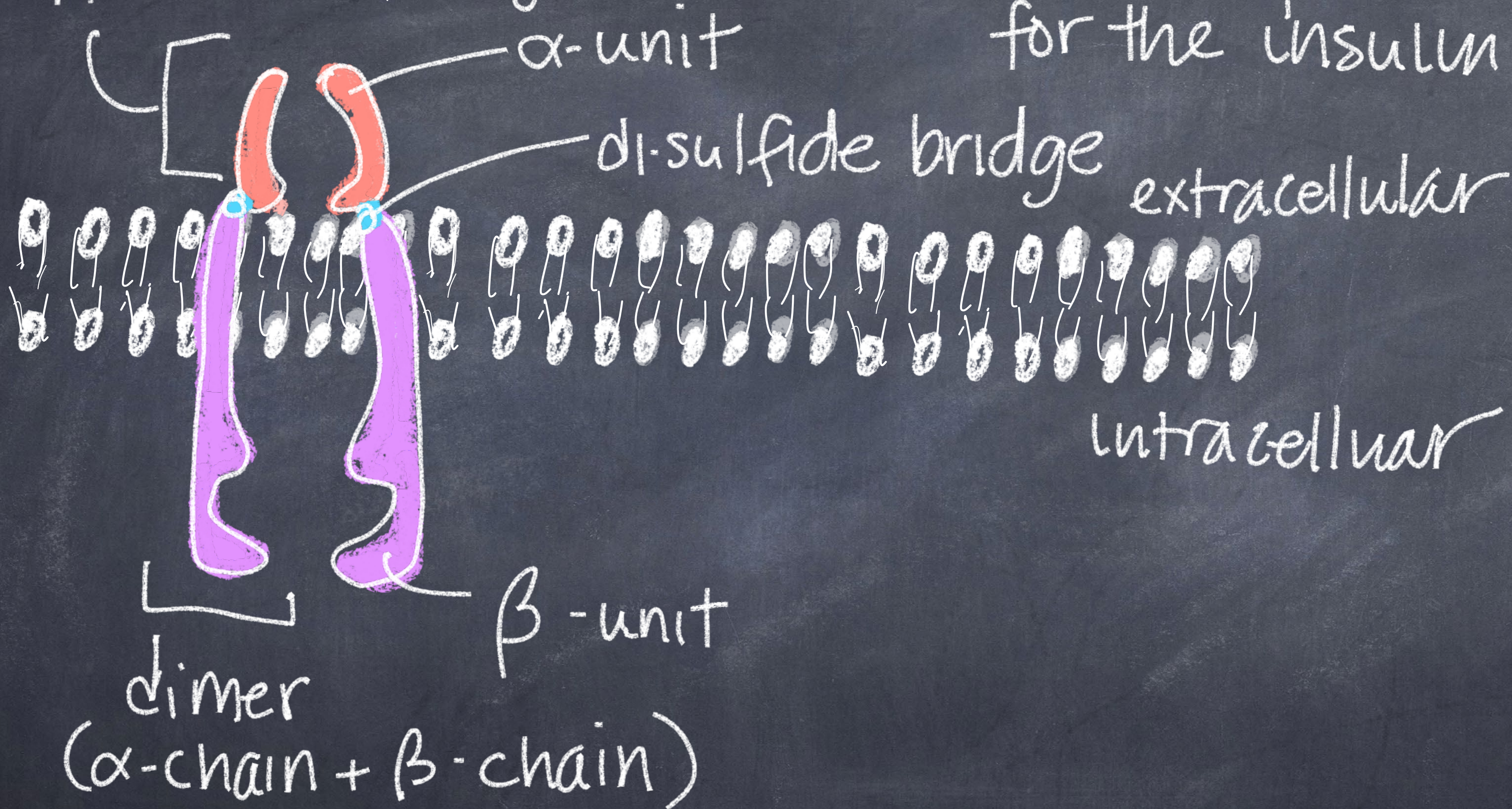
Insulin Signaling Pathway

Boyle - Metabolic Brain Disorders

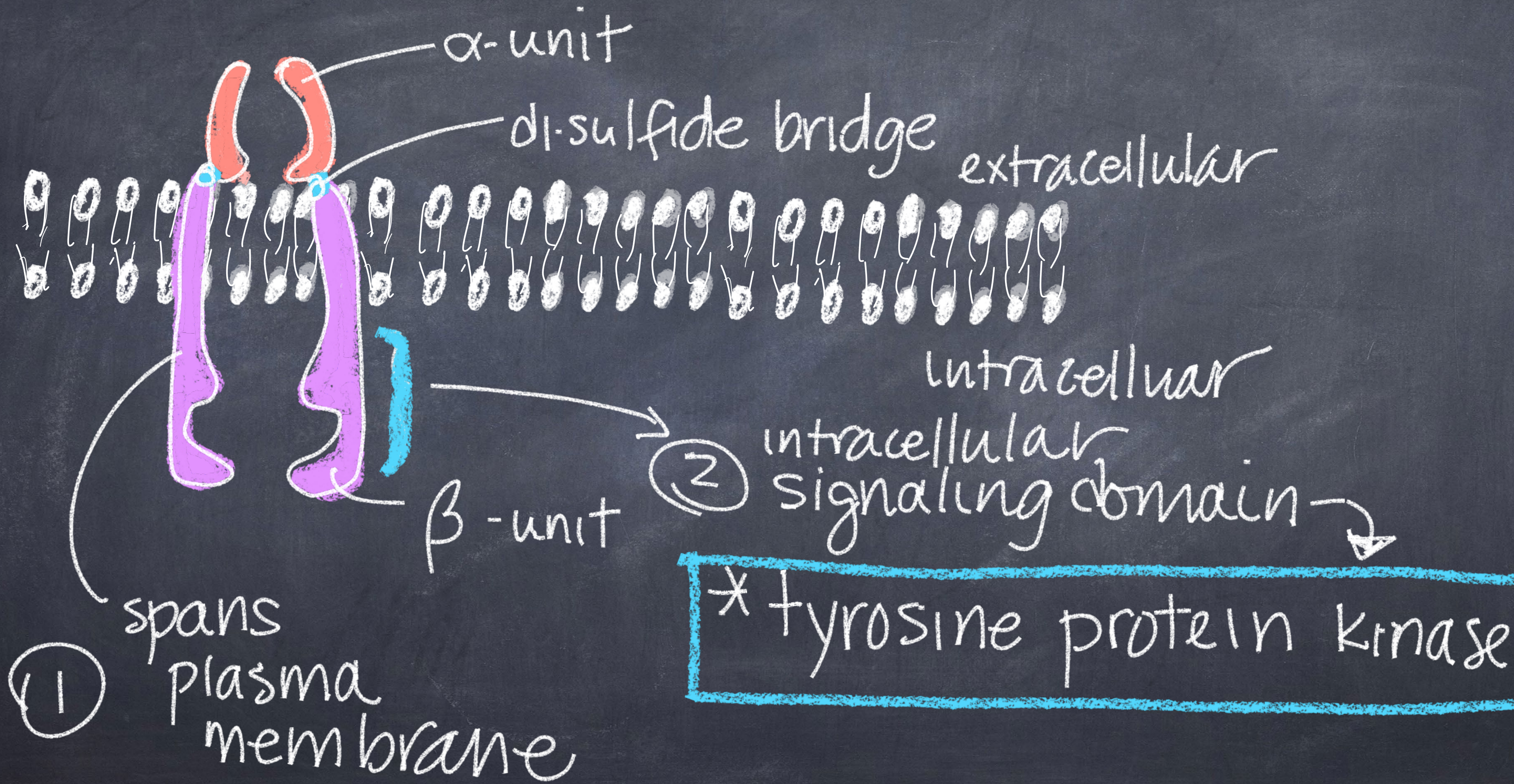
 IRS-1

extracellular region

2 α -units form a "pocket"
for the insulin



INSULIN RECEPTOR (IR)



Recall: tyrosine protein kinase

① is an enzyme, the Ⓟ

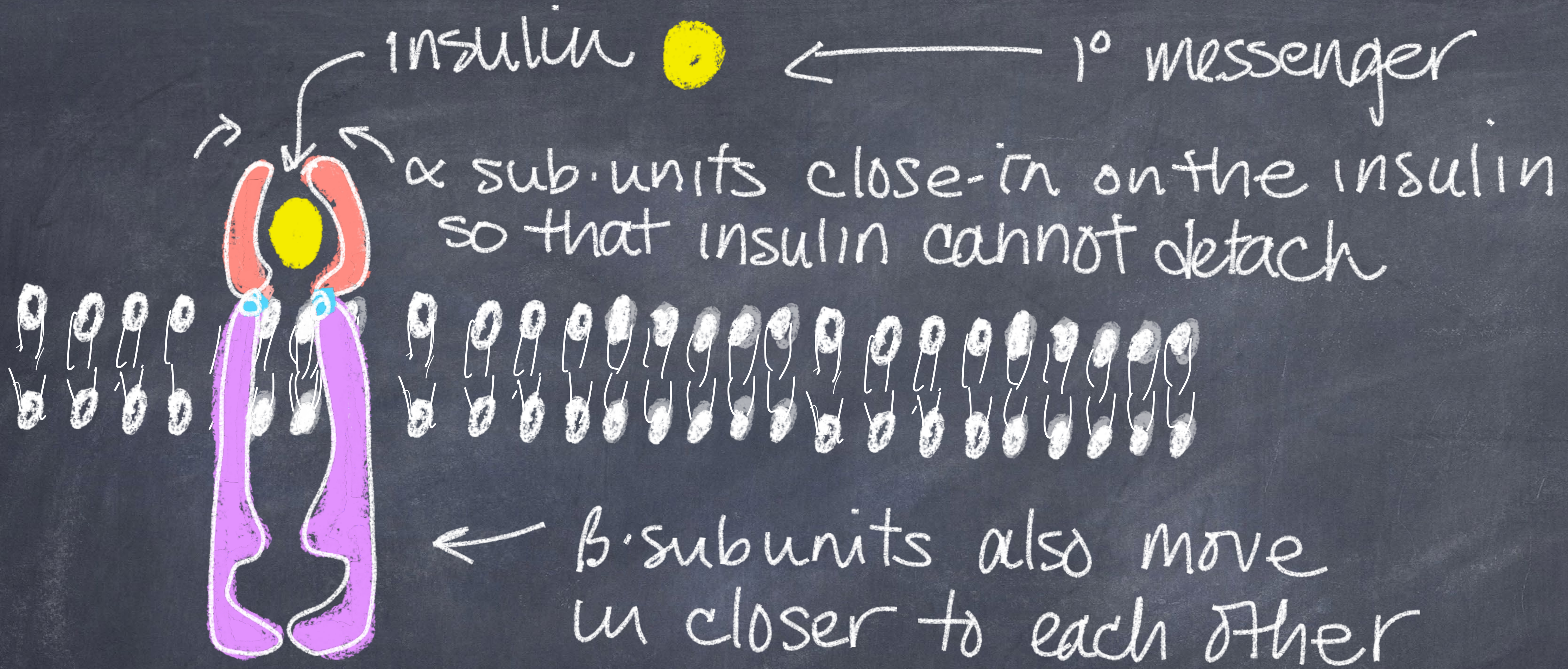
tyrosine
amino
acids



note:

* the protein kinase
is found in the structure

* tyrosine protein kinase

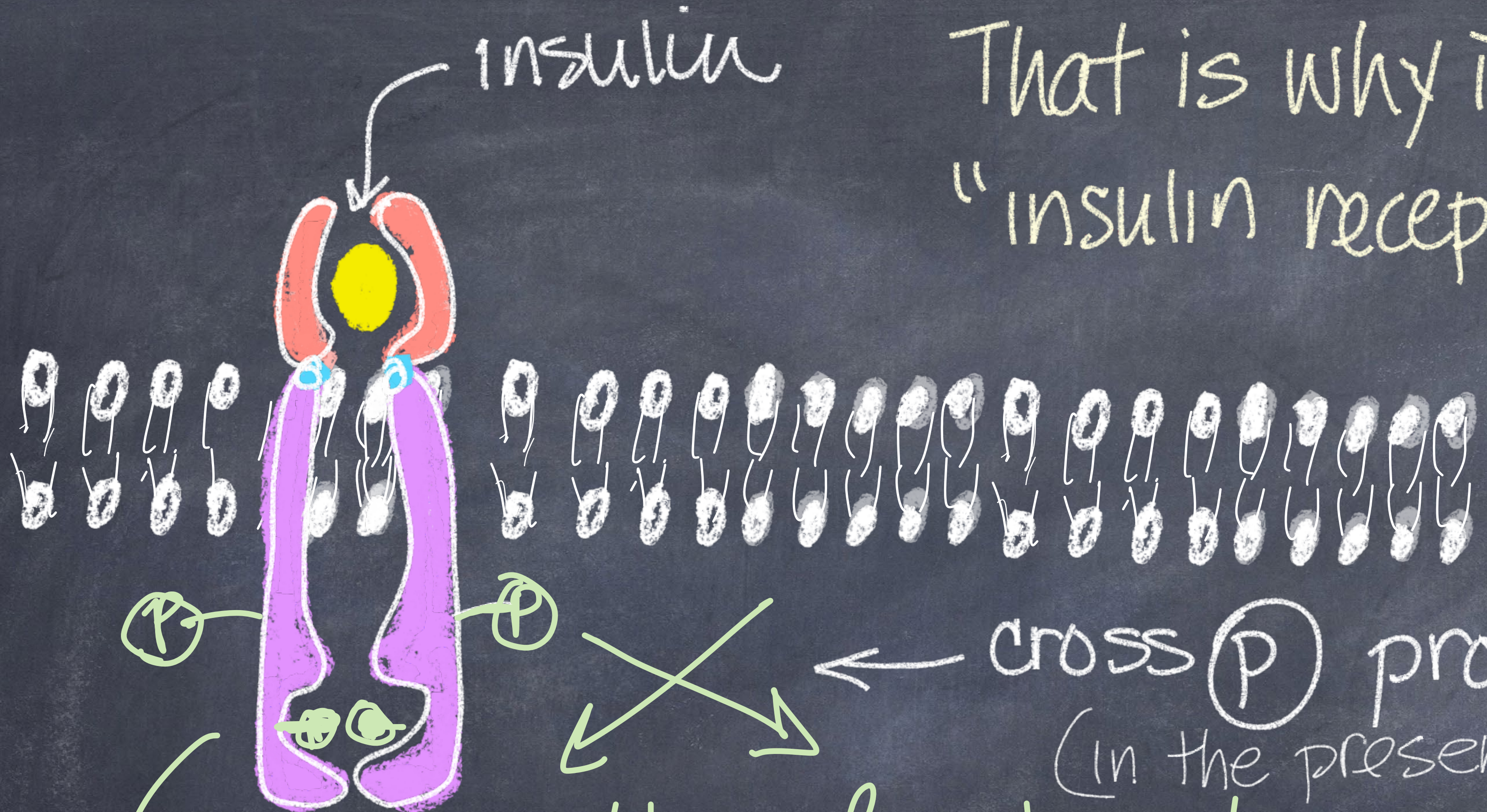


insulin ● ← 1^o messenger

α sub-units close-in on the insulin so that insulin cannot detach

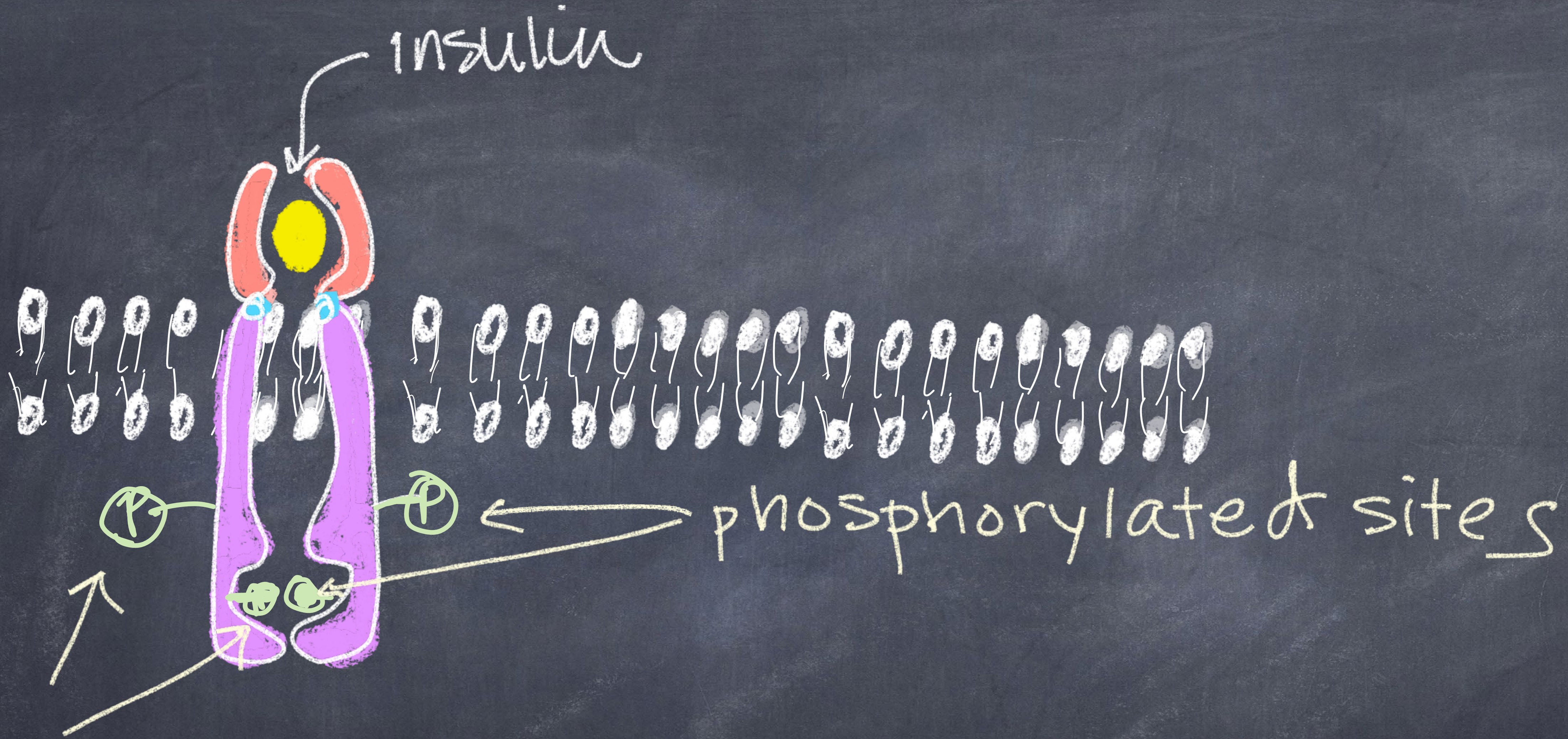
← β-subunits also move in closer to each other

That is why it is called
"insulin receptor protein
kinase"

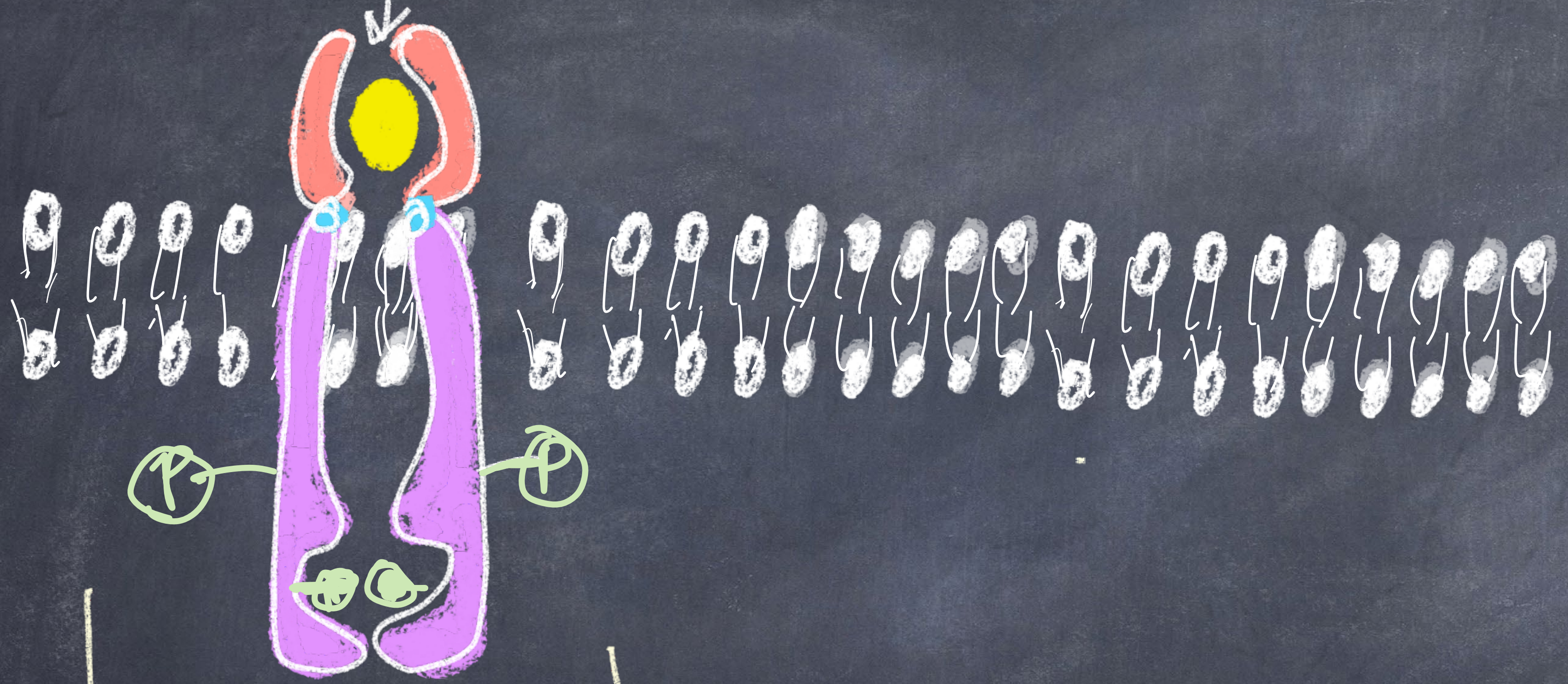


cross (P) process
(in the presence of ATP)

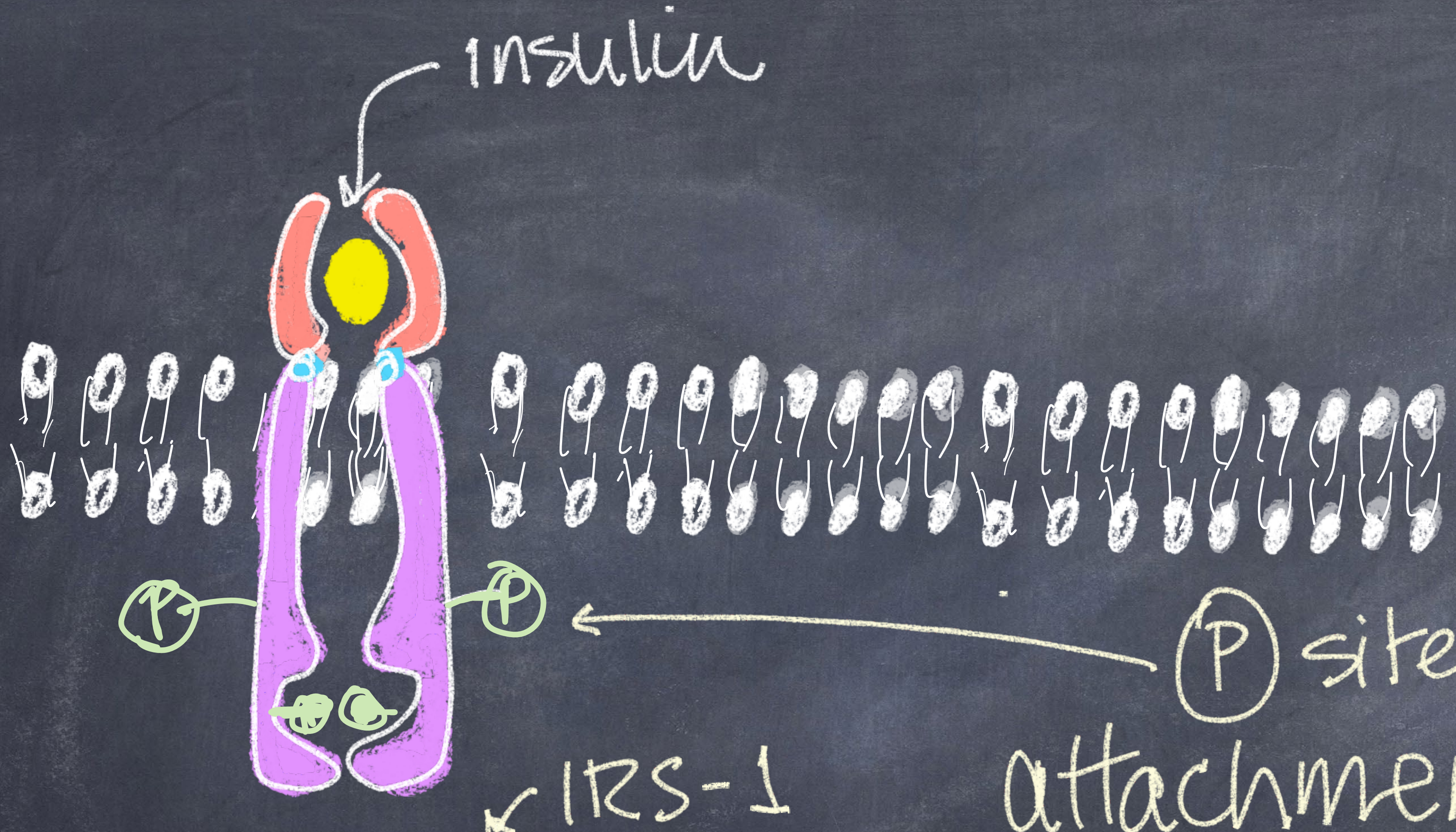
as the β -subunits move closer
together one subunit activates
the other subunit.



insulin



activated.

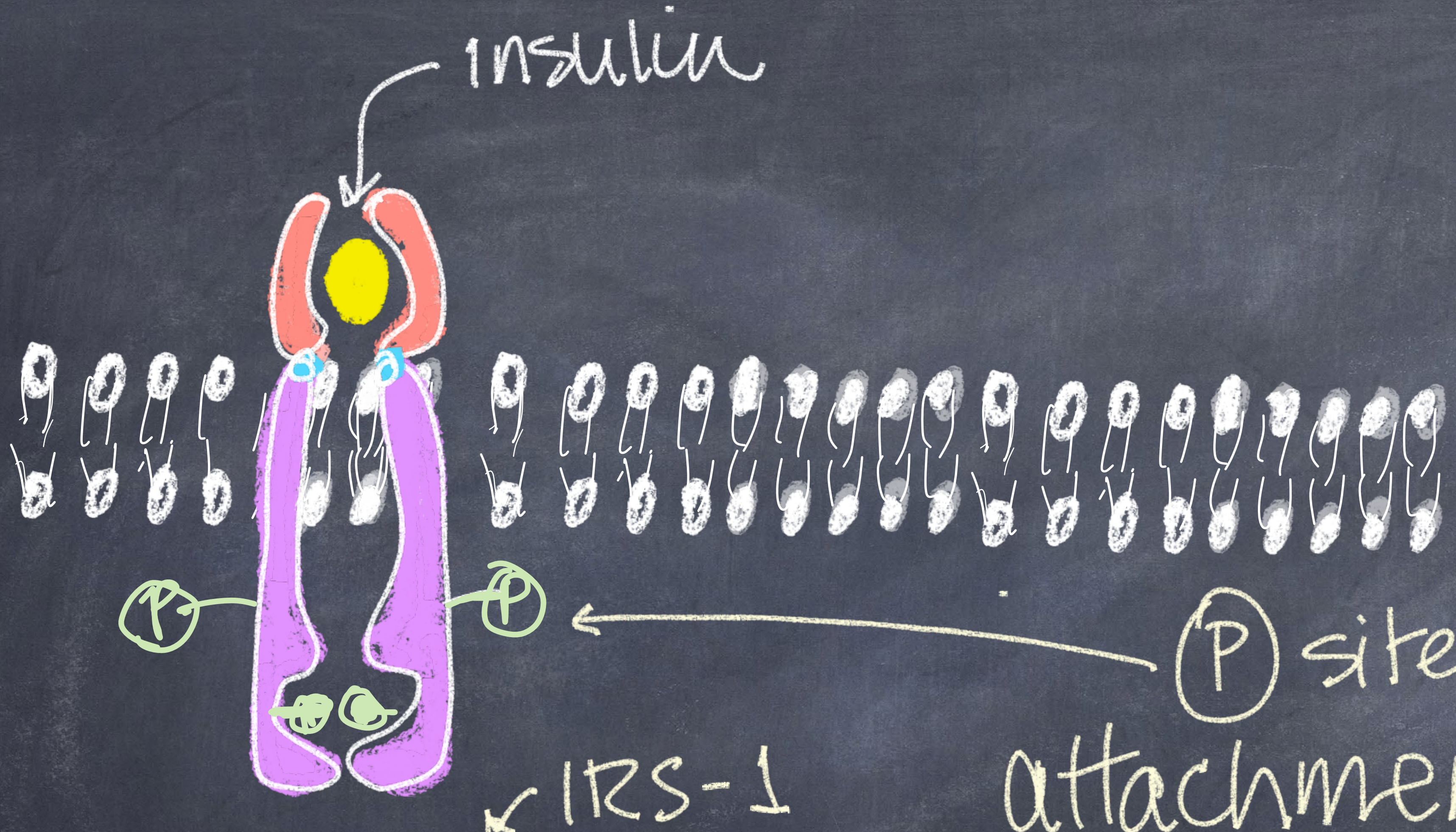


insulin

IRS-1

P sites act as attachment sites for other proteins
→ e.g. IRS-1

Insulin Receptor Substrate

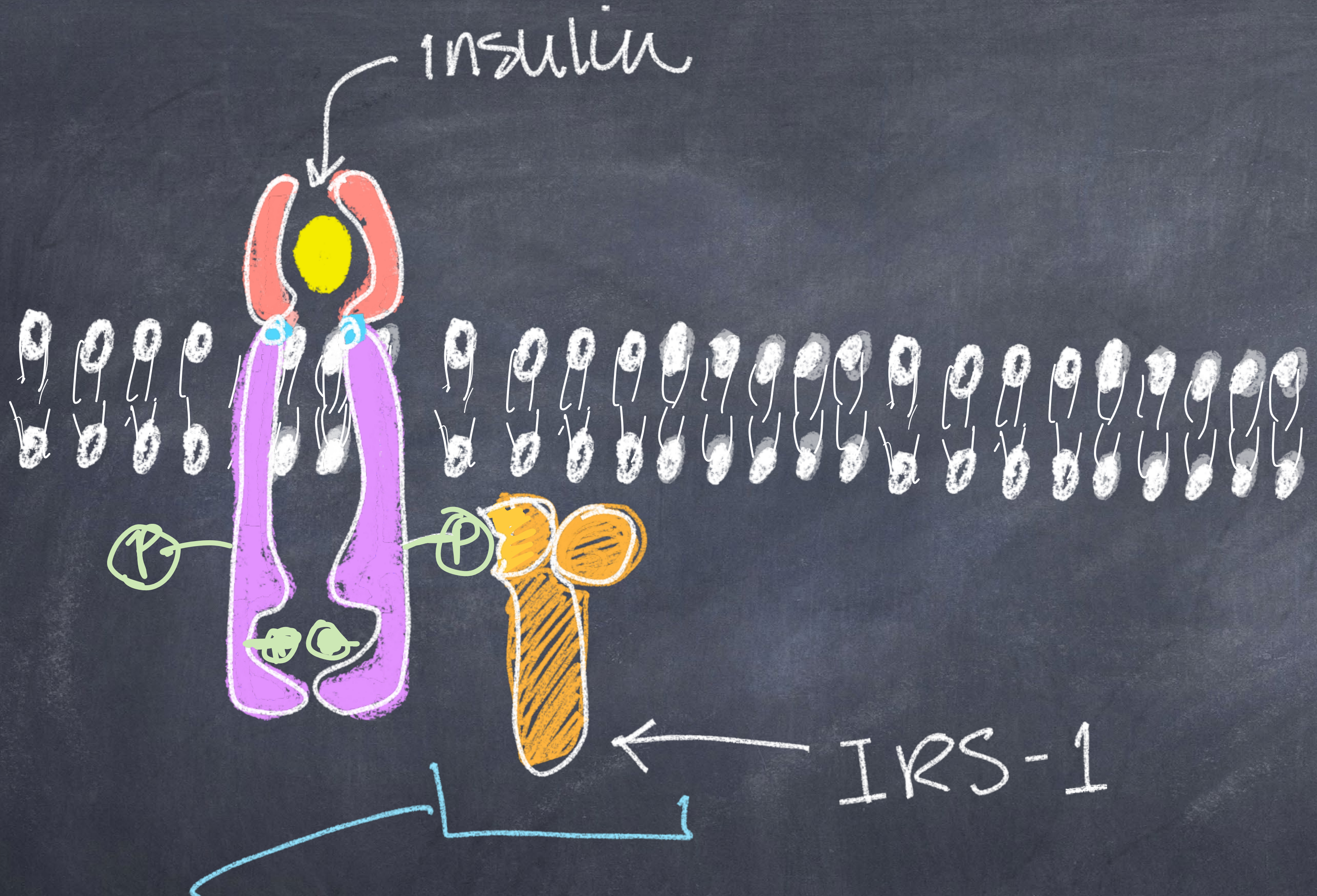


insulin

IRS-1

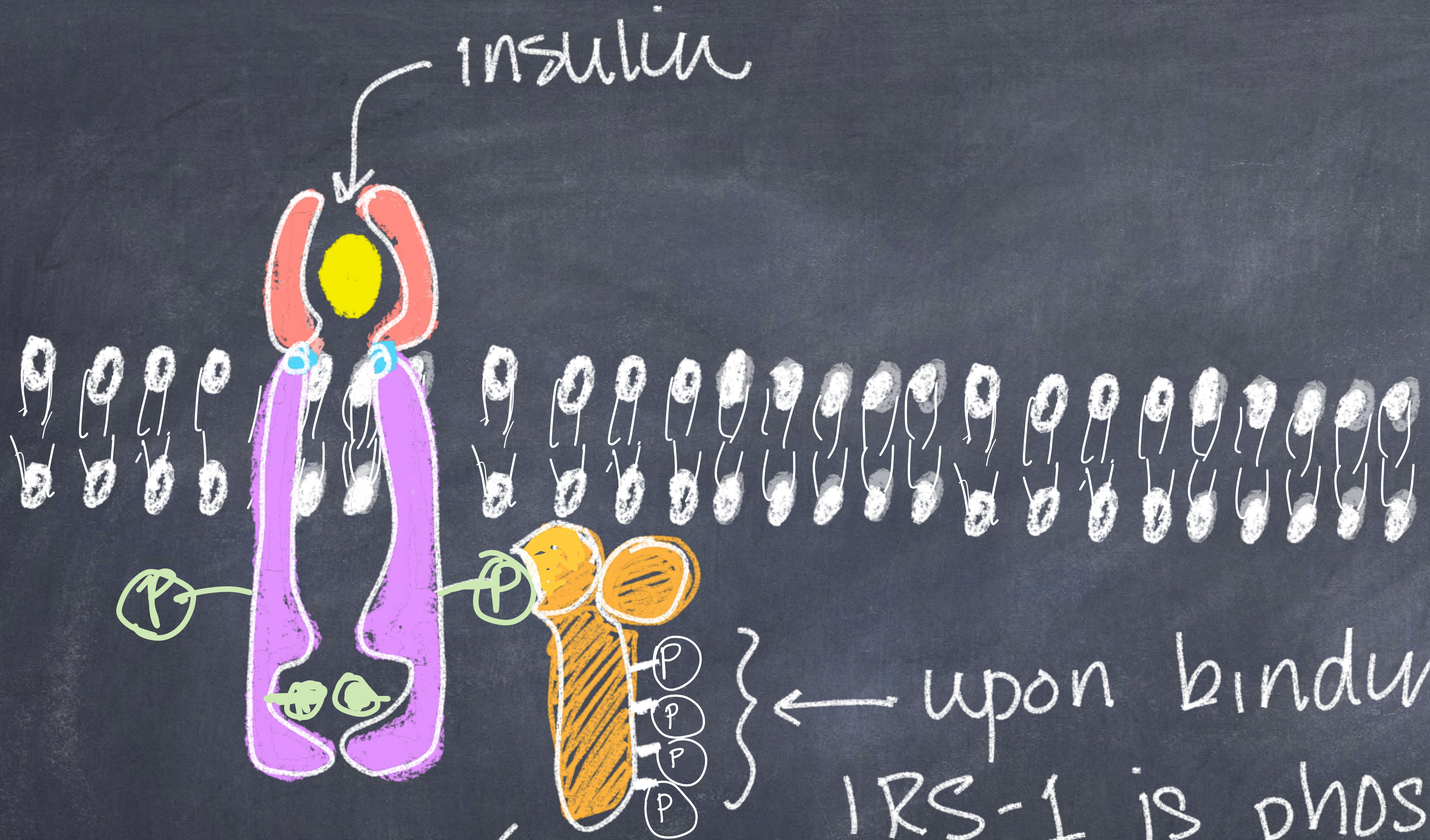
(P) sites act as attachment sites for other proteins
→ e.g. IRS-1

Insulin Receptor Substrate



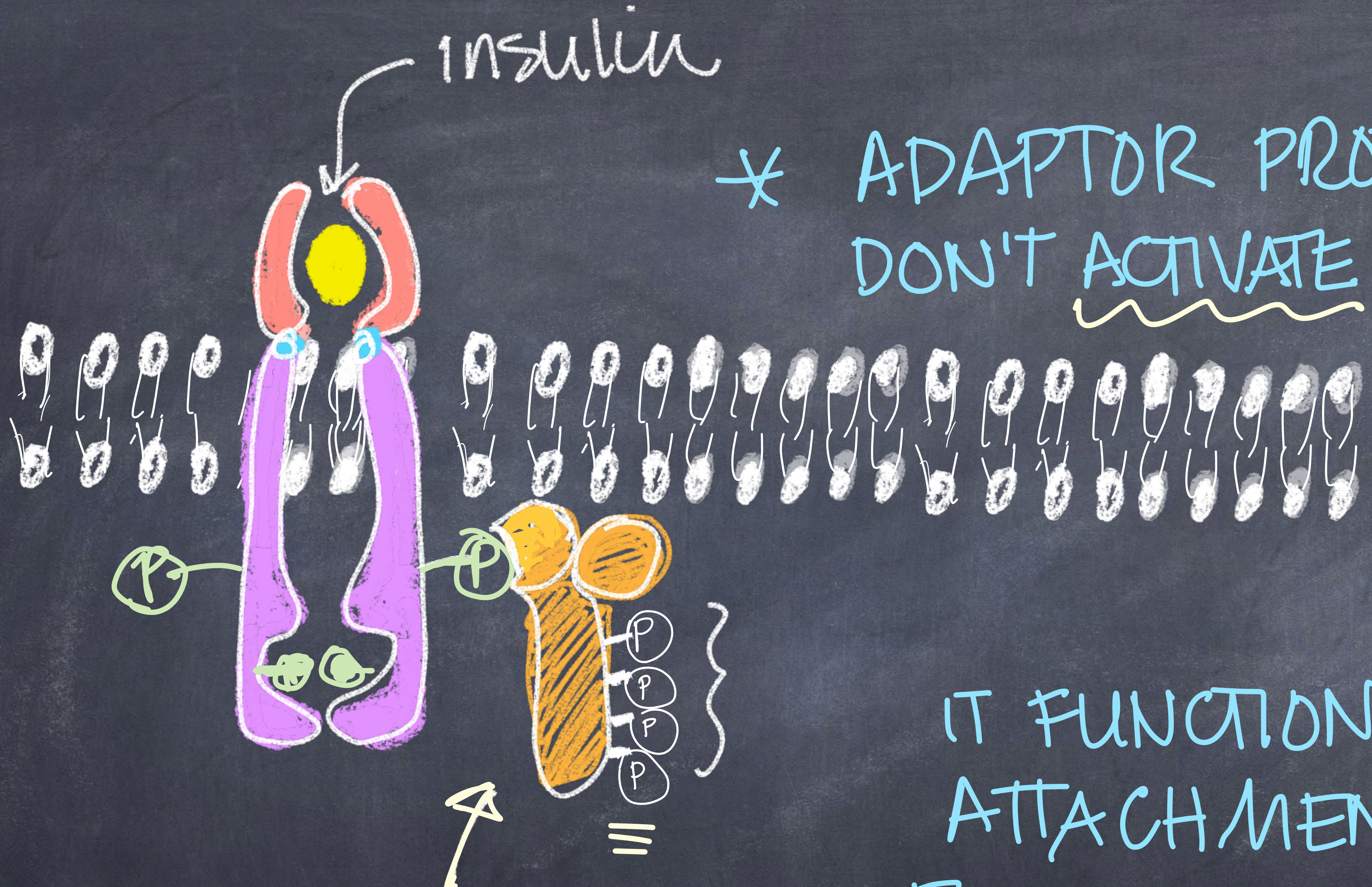
IRS molecules are called adaptor proteins

IRS = insulin receptor substrate



IRS-1

upon binding,
IRS-1 is phosphorylated
by the insulin receptor kinase

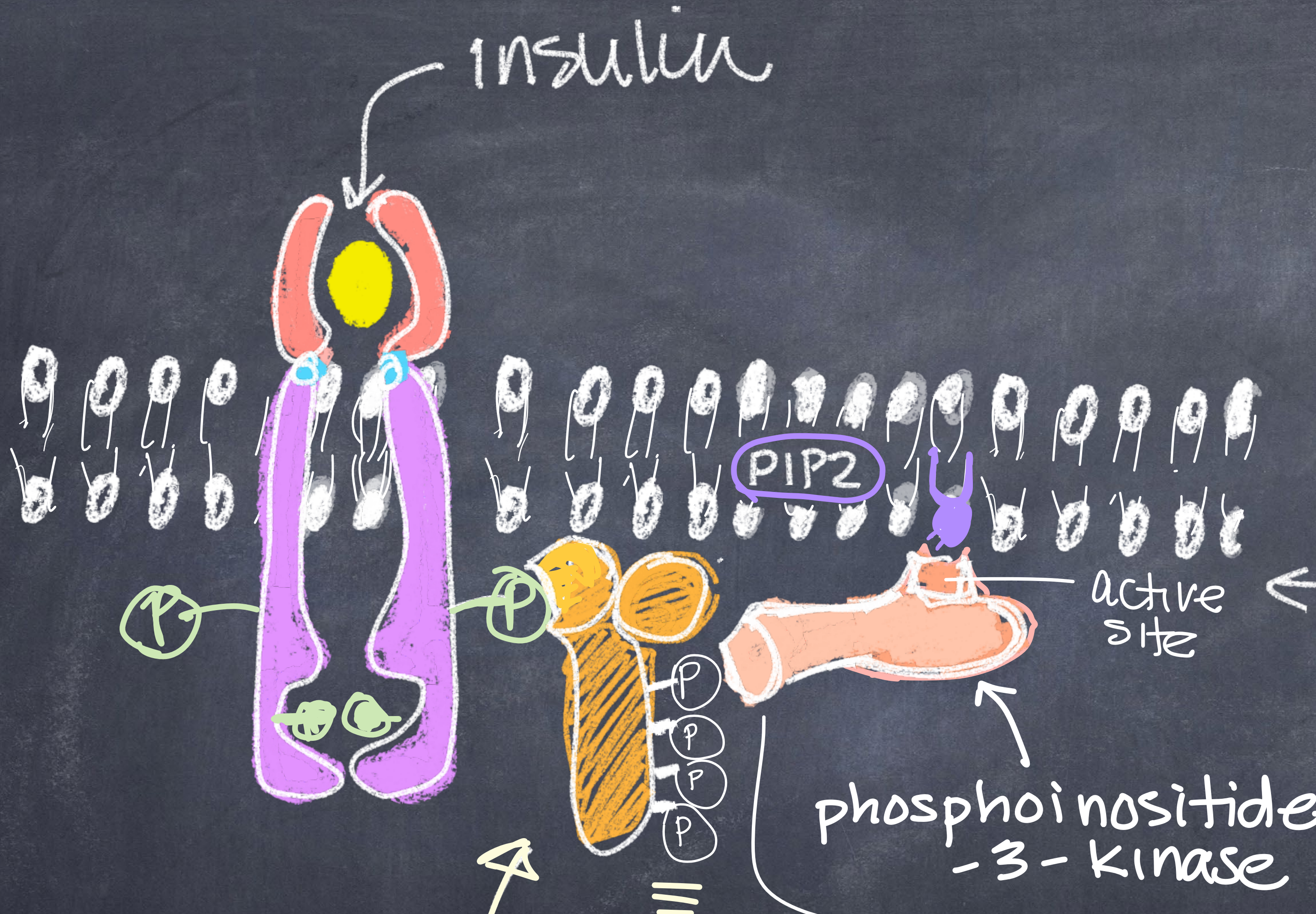


insulin

* ADAPTOR PROTEINS
DON'T ACTIVATE SOMETHING
IN THE
PATHWAY.

PHOSPHORYLATED
IRS-1

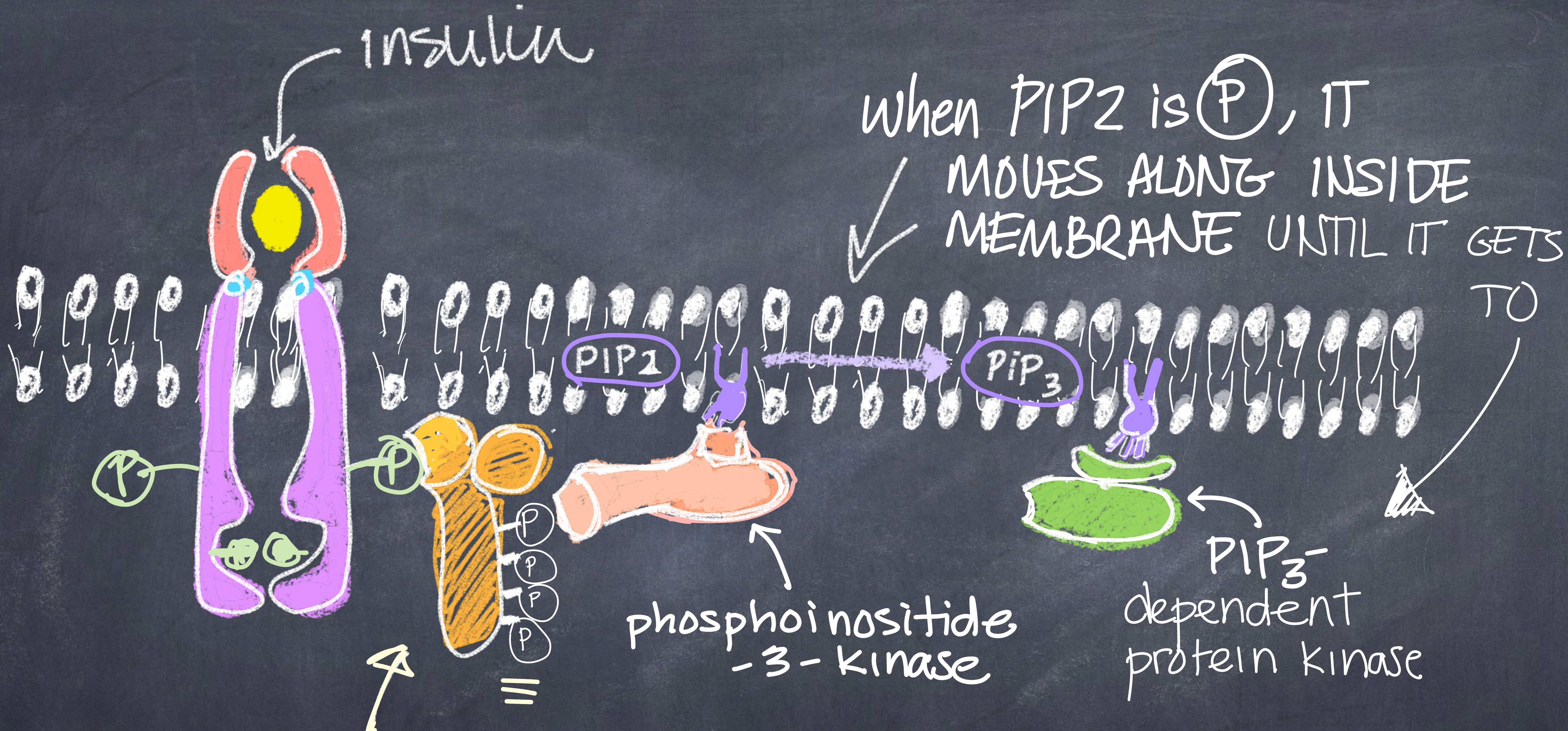
IT FUNCTIONS AS AN
ATTACHMENT POINTS
FOR OTHER ENZYMES
& PROTEINS IN PATHWAY.



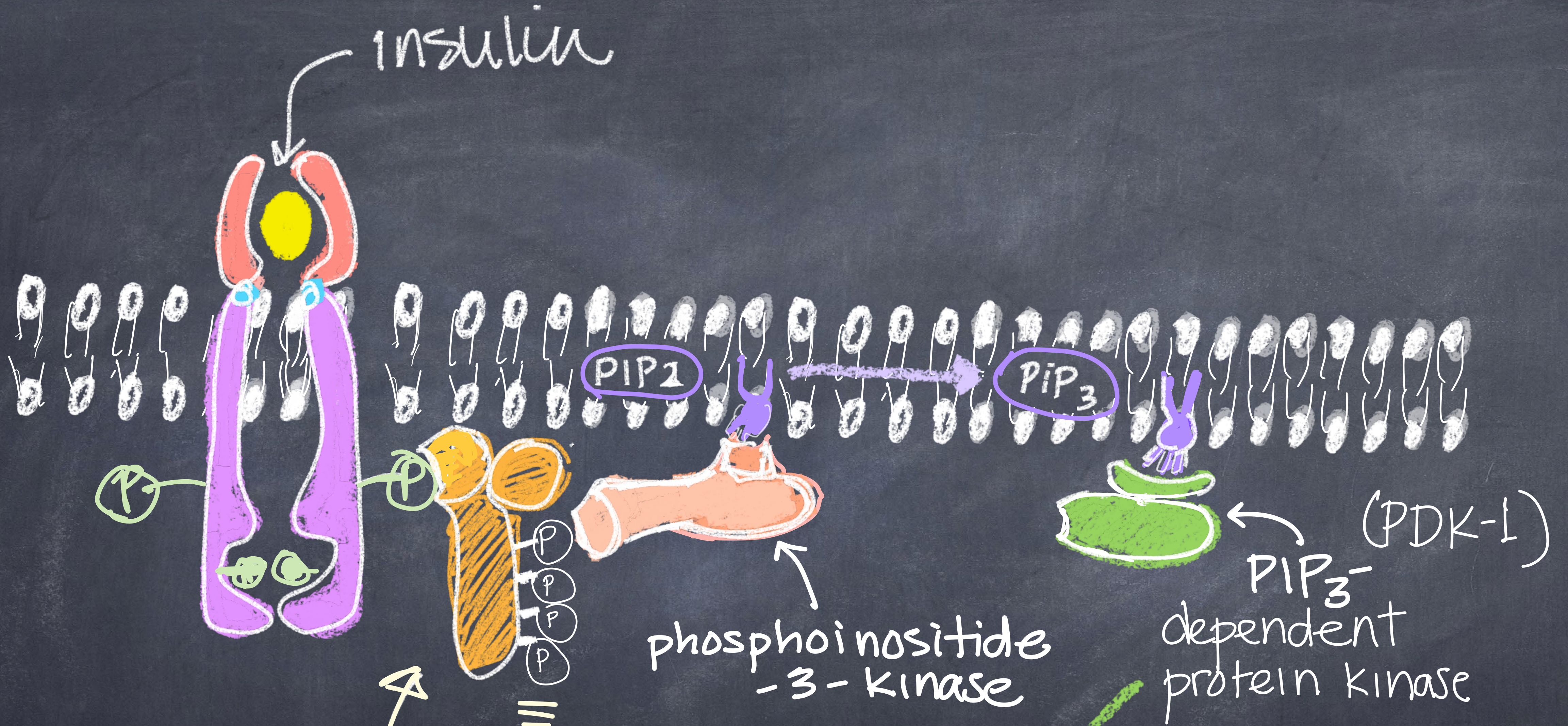
phosphorylates
 $PIP2 \Rightarrow PIP3$

PHOSPHORYLATED
 IRS-1

note this is a lipid kinase
 regulatory region



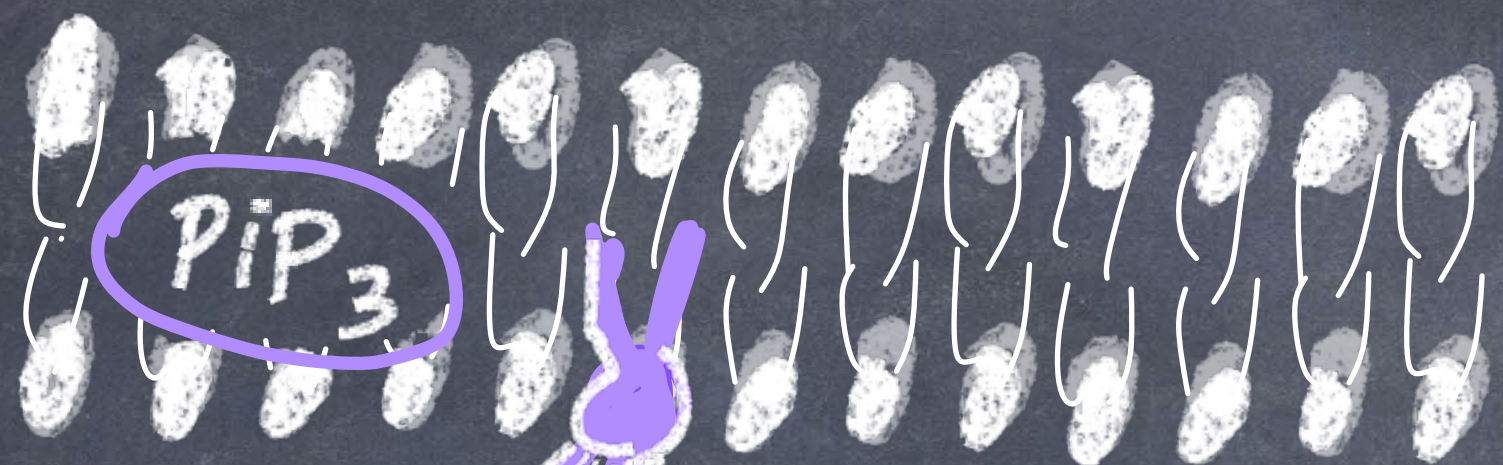
PHOSPHORYLATED
IRS-1



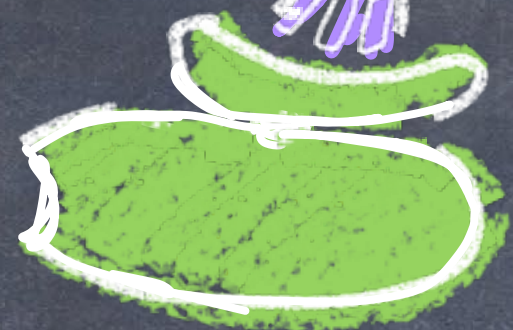
PHOSPHORYLATED
IRS-1

once PDK-1 is
activated then it
activates PKB/AKT-1

Akt-1 = protein kinase B



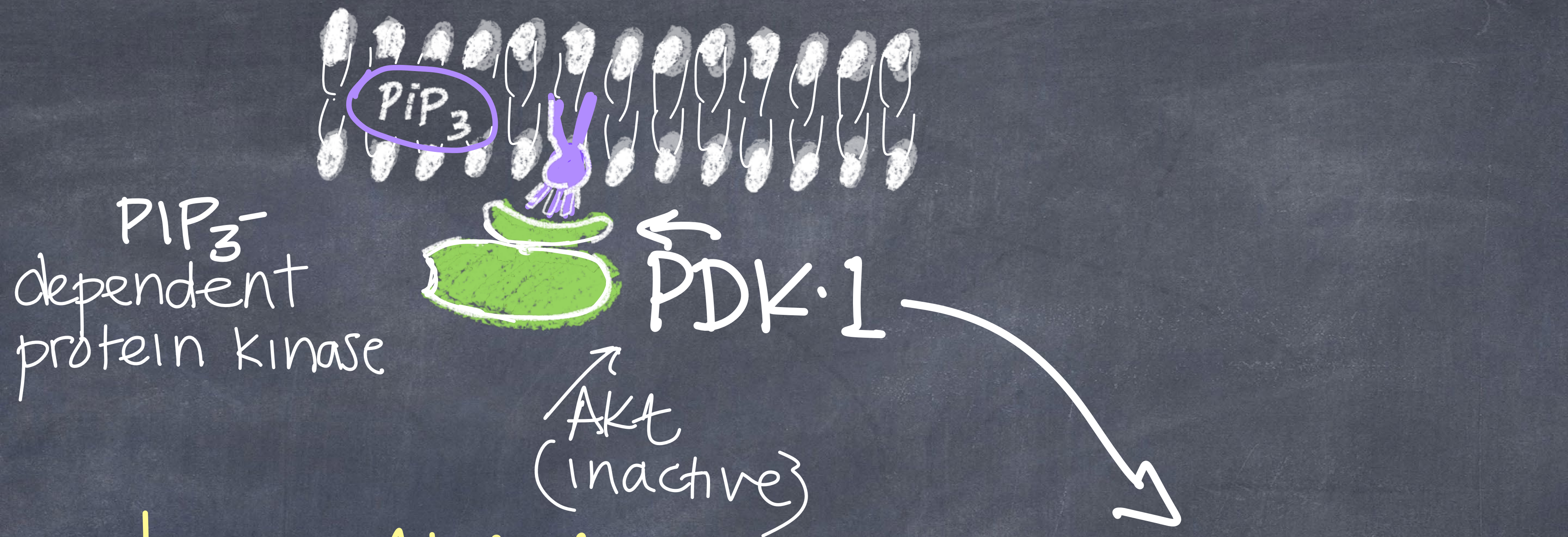
PIP₃-dependent protein kinase



PDK-1

Activated Akt-1

Akt-1 (inactive)

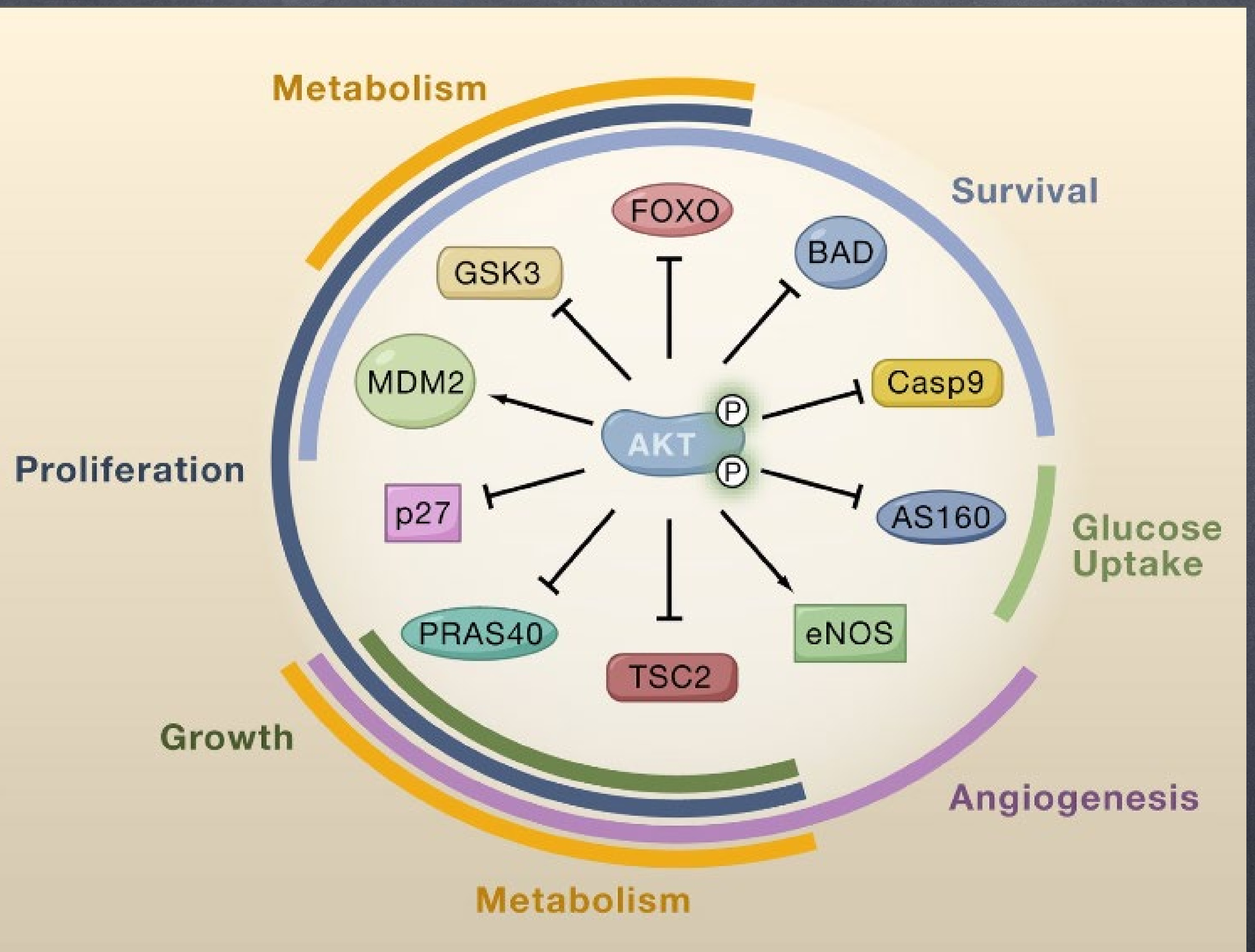


PDK-1 activates Akt-1
(protein kinase B).

* This kinase is not membrane-bound
& can diffuse all around the cell.

Activated
Akt-1

Akt is involved in so many critical functions.



AKT 1 is a big deal - b/c

① IT STIMULATES THE
MOVEMENT OF GLUCOSE
MEMBRANE TRANSPORTERS TO
CELL MEMBRANE

② phosphorylates enzymes

that synthesize
glycogen from glucose.

