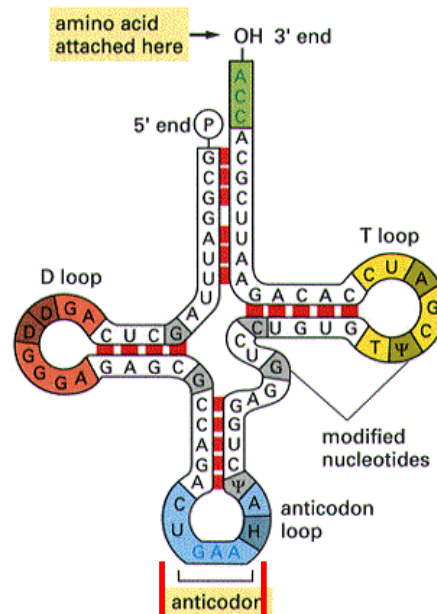


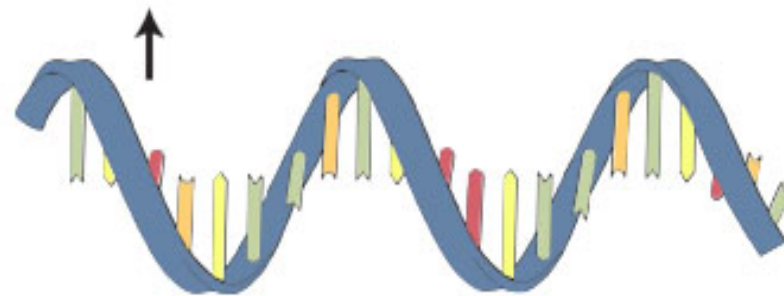
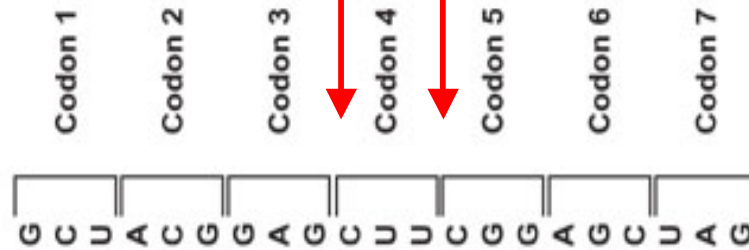
Traduzione e indirizzamento delle proteine

Traduzione

Traduzione:
mRNA -----> proteine



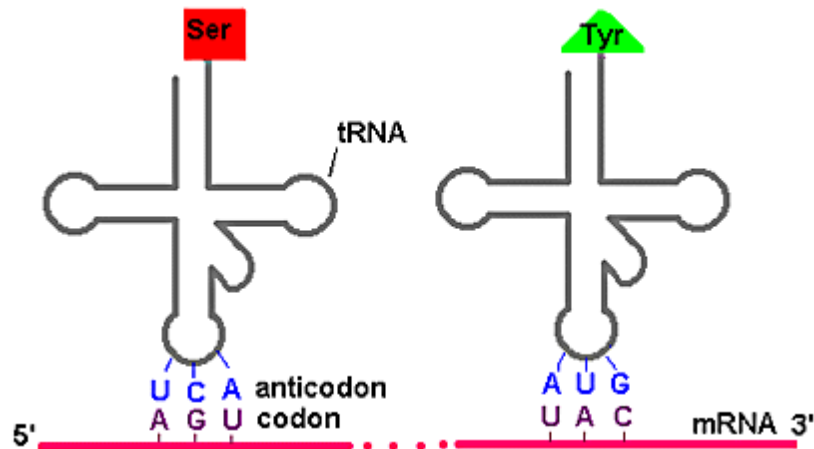
tRNA



mRNA
Ribonucleic acid

mRNA

Genetic code



		2nd base in codon					
		U	C	A	G		
1st base in codon	U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr STOP STOP	Cys Cys STOP Trp	U C A G	3rd base in codon
	C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg	U C A G	
	A	Ile Ile Ile Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg	U C A G	
	G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly	U C A G	

codone di inizio = AUG =Metionina =Met

	T			C			A			G		
T	TTT	Phe	F	TCT	Ser	S	TAT	Tyr	Y	TGT	Cys	C
	TTC	Phe	F	TCC	Ser	S	TAC	Tyr	Y	TGC	Cys	C
	TTA	Leu	L	TCA	Ser	S	TAA	stop	*	TGA	stop	*
	TTG	Leu	L	TCG	Ser	S	TAG	stop	*	TGG	Trp	W
C	CTT	Leu	L	CCT	Pro	P	CAT	His	H	CGT	Arg	R
	CTC	Leu	L	CCC	Pro	P	CAC	His	H	CGC	Arg	R
	CTA	Leu	L	CCA	Pro	P	CAA	Gln	Q	CGA	Arg	R
	CTG	Leu	L	CCG	Pro	P	CAG	Gln	Q	CGG	Arg	R
A	ATT	Ile	I	ACT	Thr	T	AAT	Asn	N	AGT	Ser	S
	ATC	Ile	I	ACC	Thr	T	AAC	Asn	N	AGC	Ser	S
	ATA	Ile	I	ACA	Thr	T	AAA	Lys	K	AGA	Arg	R
	ATG	Met	M	ACG	Thr	T	AAG	Lys	K	AGG	Arg	R
G	GTT	Val	V	GCT	Ala	A	GAT	Asp	D	GGT	Gly	G
	GTC	Val	V	GCC	Ala	A	GAC	Asp	D	GGC	Gly	G
	GTA	Val	V	GCA	Ala	A	GAA	Glu	E	GGA	Gly	G
	GTG	Val	V	GCG	Ala	A	GAG	Glu	E	GGG	Gly	G

GenBank Overview

http://www.ncbi.nlm.nih.gov/Genbank/index.html

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GenBank Overview

NCBI **GenBank Overview**

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International sequence databases exceed 100 gigabases

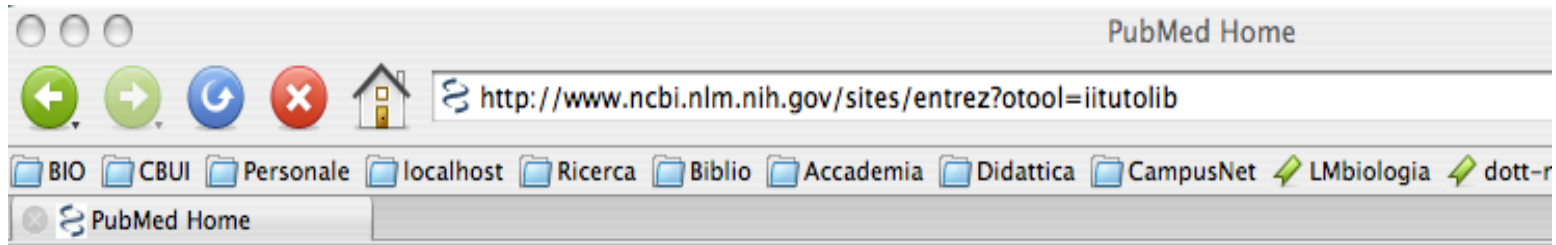
In August 2005, the INSDC announced the DNA sequence database exceeded 100 gigabases. GenBank is proud of its contributions toward this milestone. We thank all the scientists who have worked through the submission process at GenBank and made their sequence data available to the world. See the related [press release](#).

Growth of the International Nucleotide Sequence Database Collaboration

Date	GenBank (Billions)	EMBL (Billions)	DDBJ (Billions)	Total (Billions)
Aug-00	~1	~0	~0	~1
Aug-01	~5	~1	~0	~6
Aug-02	~15	~2	~0	~17
Aug-03	~30	~3	~0	~33
Aug-04	~55	~5	~0	~60
Aug-05	~85	~10	~0	~95

Base Pairs contributed by GenBank®— EMBL— DDBJ—

Come raggiungere le informazioni contenute nelle banche dati?



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and the National Institutes of Health

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News [Clinical Alert: Immunizations Are Discontinued in Two HIV Vaccine Trials](#)
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The screenshot shows the NCBI Nucleotide search interface. The search query is 'stathmin rat mRNA complete'. The results page displays 12 nucleotide sequences. A red arrow points to the third result, BC062234.

Search Results:

- Found 12 nucleotide sequences. CoreNucleotide [10] EST [1] GSS [1]
- Display: Summary | Show: 20 | Sort by: | Send to: |
- All: 10 | Bacteria: 0 | RefSeq: 0 | mRNA: 10
- Items 1 - 10 of 10 | One page.

Accession	Organism	Gene	Product	Links
1: BC087660	Rattus norvegicus	stathmin-like 2	mRNA (cDNA clone MGC:105372 IMAGE:7313867), complete cds gil56585173 gb BC087660.1 [56585173]	Order cDNA clone, Links
2: BC092646	Rattus norvegicus	stathmin-like 4	mRNA (cDNA clone MGC:109417 IMAGE:7319130), complete cds gil62204232 gb BC092646.1 [62204232]	Order cDNA clone, Links
3: BC062234	Rattus norvegicus	stathmin 1	mRNA (cDNA clone MGC:72884 IMAGE:6917958), complete cds gil38328241 gb BC062234.1 [38328241]	Order cDNA clone, Links
4: AF306458	Rattus norvegicus	SCG10 (Scg10)	mRNA, complete cds gil11228977 gb AF306458.1 AF306458[11228977]	Links
5: AY004290	Rattus norvegicus	scg10-like-protein	mRNA, complete cds gil9547314 gb AY004290.1 [9547314]	Links
6: AF026530	Rattus norvegicus	stathmin-like-protein splice variant RB3"	mRNA, complete cds gil4003298 gb AF026530.1 AF026530[4003298]	Links

NCBI Sequence Viewer v2.0

NCBI **Sequences** **Nucleotide** [Sign In](#) [Register](#)

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

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Display Show Send to Hide: sequence all but gene, CDS and mRNA features

Range: from to Reverse complemented strand Features:

1: BC062234. Reports *Rattus norvegicus*...[gi:38328241] [Order cDNA clone, Links](#)

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LOCUS BC062234 1138 bp mRNA linear ROD 20-OCT-2004
 DEFINITION *Rattus norvegicus* stathmin 1, mRNA (cDNA clone MGC:72884 IMAGE:6917958), complete cds.
 ACCESSION BC062234
 VERSION BC062234.1 GI:38328241
 KEYWORDS MGC.
 SOURCE *Rattus norvegicus* (Norway rat)
 ORGANISM [Rattus norvegicus](#)
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Rattus.
 REFERENCE 1 (bases 1 to 1138)
 AUTHORS Strausberg,R.L., Feingold,E.A., Grouse,L.H., Derge,J.G., Klausner,R.D., Collins,F.S., Wagner,L., Shenmen,C.M., Schuler,G.D., Altschul,S.F., Zeeberg,B., Buetow,K.H., Schaefer,C.F., Bhat,N.K., Hopkins,R.F., Jordan,H., Moore,T., Max,S.I., Wang,J., Hsieh,F., Diatchenko,L., Marusina,K., Farmer,A.A., Rubin,G.M., Hong,L., Stapleton,M., Soares,M.B., Bonaldo,M.F., Casavant,T.L., Scheetz,T.E., Brownstein,M.J., Usdin,T.B., Toshiyuki,S., Carninci,P., Prange,C., Raha,S.S., Loquellano,N.A., Peters,G.J., Abramson,R.D., Mullahy,S.J., Bosak,S.A., McEwan,P.J., McKernan,K.J., Malek,J.A., Gunaratne,P.H., Richards,S., Worley,K.C., Hale,S., Garcia,A.M., Gay,L.J., Hulyk,S.W., Villalon,D.K., Muzny,D.M., Sodergren,E.J., Lu,X., Gibbs,R.A., Fahey,J., Helton,E., Ketteman,M., Madan,A., Rodrigues,S., Sanchez,A., Whiting,M., Madan,A., Young,A.C., Shevchenko,Y., Bouffard,G.G., Blakesley,R.W., Touchman,J.W., Green,E.D., Dickson,M.C., Rodriguez,A.C., Grimwood,J., Schmutz,J., Myers,R.M., Butterfield,Y.S., Krzywinski,M.I., Skalska,U., Smailus,D.E., Schnerch,A., Schein,J.E., Jones,S.J. and Marra,M.A.
 TITLE Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences

numan and mouse cDNA sequences
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (26), 16899-16903 (2002)
 PUBMED [12477932](#)
 REFERENCE 2 (bases 1 to 1138)
 AUTHORS Director MGC Project.
 TITLE Direct Submission
 JOURNAL Submitted (13-NOV-2003) National Institutes of Health, Mammalian Gene Collection (MGC), Cancer Genomics Office, National Cancer Institute, 31 Center Drive, Room 11A03, Bethesda, MD 20892-2590, USA
 REMARK NIH-MGC Project URL: <http://mgc.nci.nih.gov>
 COMMENT Contact: MGC help desk
 Email: cgapbs-r@mail.nih.gov
 Tissue Procurement: John C. Marshall, M.D., Ph.D
 cDNA Library Preparation: CLONTECH Laboratories, Inc.
 cDNA Library Arrayed by: The I.M.A.G.E. Consortium (LLNL)
 DNA Sequencing by: Genome Sequence Centre, BC Cancer Agency, Vancouver, BC, Canada
info@bcgsc.bc.ca
 Steve Jones, Sarah Barber, Mabel Brown-John, Yaron Butterfield, Andy Chan, Steve S. Chand, William Chow, Alison Cloutier, Ruth Featherstone, Malachi Griffith, Obi Griffith, Ran Guin, Nancy Liao, Kim MacDonald, Amara Masson, Mike R. Mayo, Josh Moran, Ryan Morin, Teika Olson, Diana Palmquist, Anca Petrescu, Anna Liisa Prahbu, Parvaneh Saeedi, JR Santos, Angelique Schnerch, Ursula Skalska, Duane Smailus, Jeff Stott, Miranda Tsai, George Yang, Jacquie Schein, Asim Siddiqui, Rob Holt, Marco Marra.
 Clone distribution: MGC clone distribution information can be found through the I.M.A.G.E. Consortium/LLNL at: <http://image.llnl.gov>
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Sequenza
aminoacidica

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121 gagctggaga agcgtgcttc cggccaggct tttgagctga ttctcagccc tcgatcaaaa  
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Sequenza
nucleotidica

//

CDS 94..543

Codone di inizio: nucleotidi 94-96

N-term

5'

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C-term

Capping

```

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961 tgcgatccca attctgtccc aatctcacca gatgctactg tacttgaatg gtttaataaac
1021 tgcacagtgc tgttgaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa
1081 aaaaaaaaaa aaaaaaaaaa aaaaaagcaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa
    
```

Codone di STOP: nucleotidi 541-543

polyA

3'

Ribosomi e sintesi proteica



The Nobel Prize in Chemistry 2009

"for studies of the structure and function of the ribosome"



Photo: MRC Laboratory
of Molecular Biology

**Venkatraman
Ramakrishnan**

🕒 1/3 of the prize

United Kingdom

MRC Laboratory of
Molecular Biology
Cambridge, United
Kingdom



Credits: Michael
Marsland/Yale University

Thomas A. Steitz

🕒 1/3 of the prize

USA

Yale University
New Haven, CT,
USA; Howard
Hughes Medical
Institute



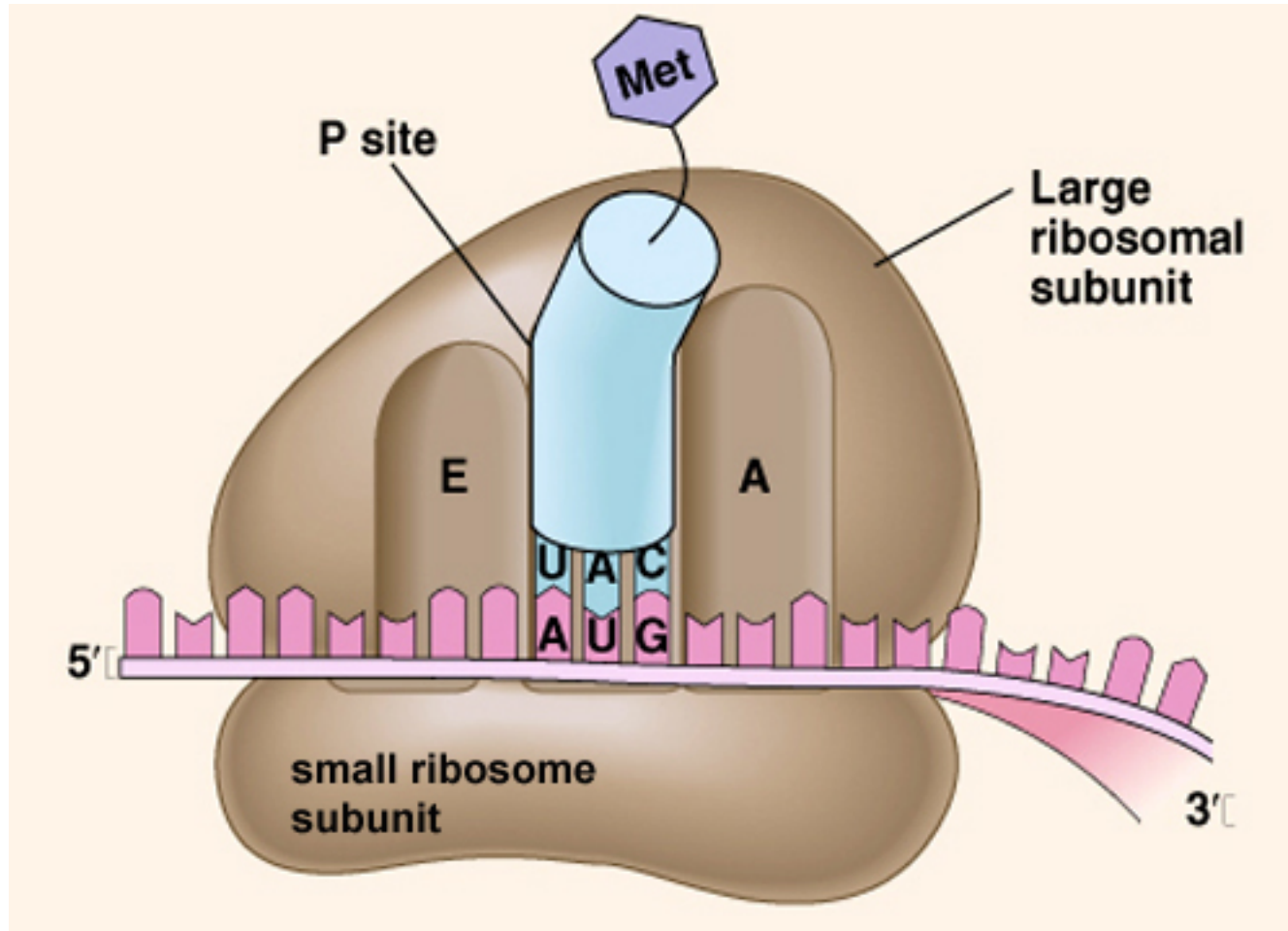
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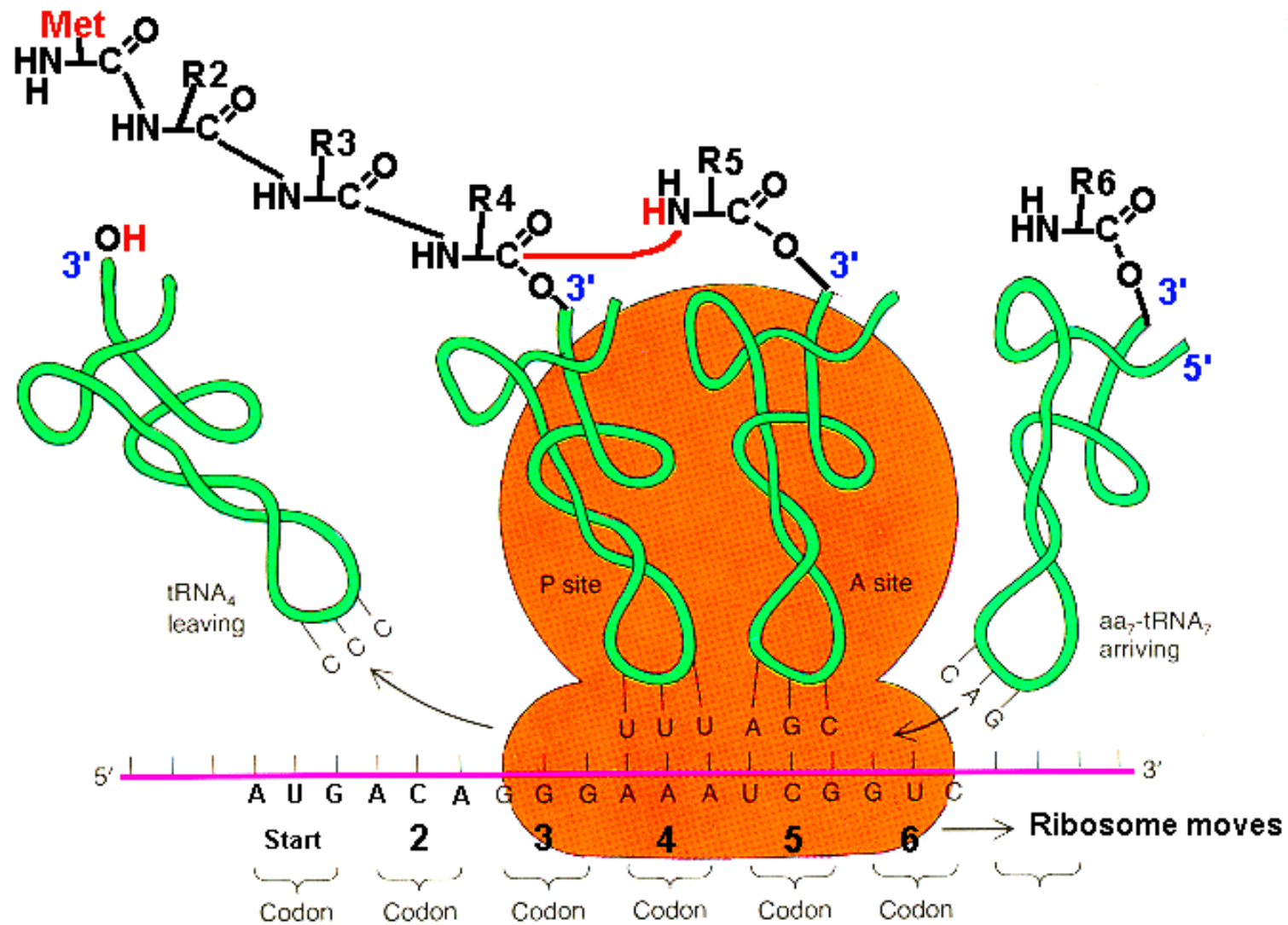
Ada E. Yonath

🕒 1/3 of the prize

Israel

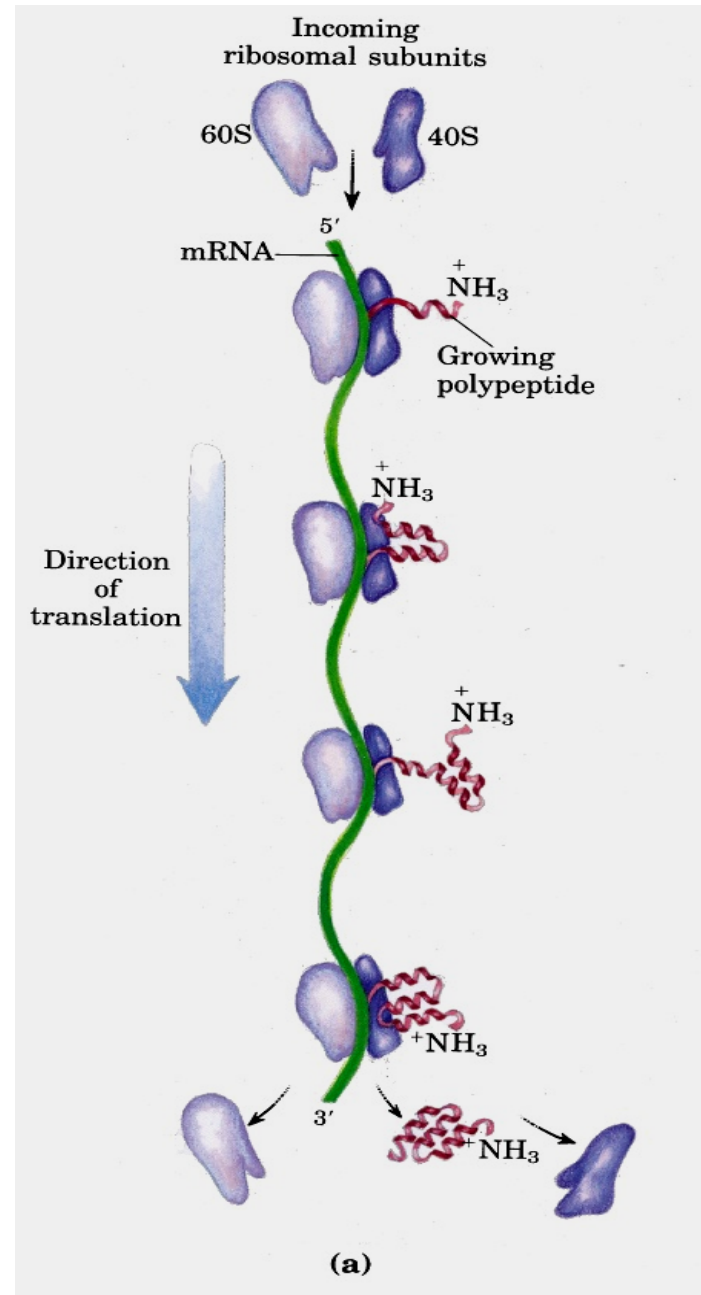
Weizmann Institute
of Science
Rehovot, Israel





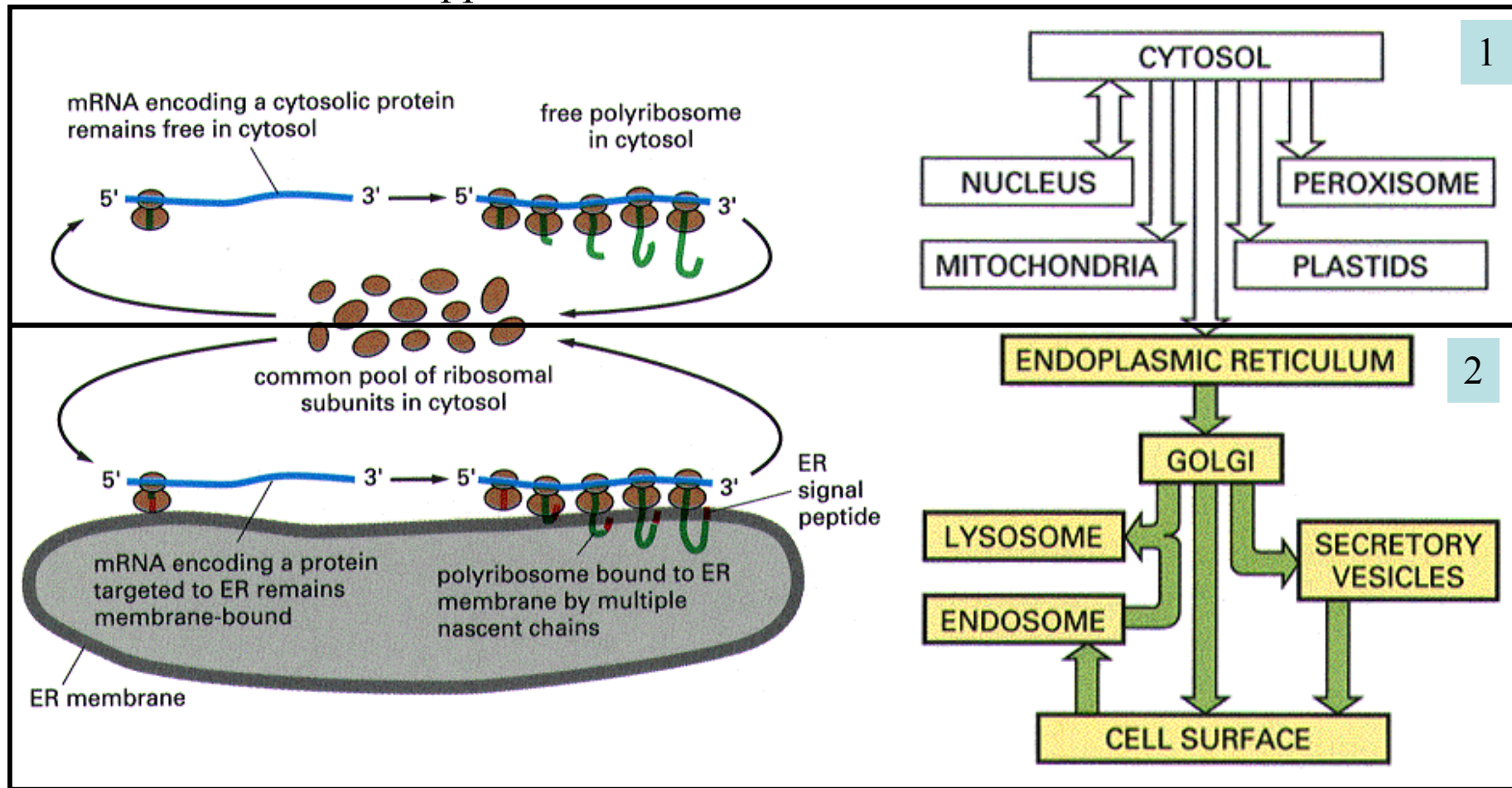
Modified from Griffiths et al., AN INTRODUCTION TO GENETIC ANALYSIS, 6th Ed., W.H. Freeman & Co., 1996.

La sintesi proteica inizia nel citoplasma con l'aggancio della piccola subunità ribosomiale all'estremità 5' dell'mRNA. In corrispondenza del codone di inizio "AUG" si aggancia la grande subunità ribosomiale. Il primo a.a. al N-terminale è dunque una metionina (Met) e la sintesi proteica prosegue con la lettura dell'mRNA nella direzione 5'--->3'. A questo punto, se i primi a.a. sintetizzati corrispondono al "peptide segnale" allora la sintesi potrà proseguire soltanto in corrispondenza della membrana del RER. Negli altri casi il ribosoma rimane "libero" e la sintesi prosegue fino allo stop codon.



Indirizzamento delle proteine

E' la proteina nascente a determinare se il ribosoma che catalizza la sua sintesi deve rimanere libero oppure essere associato alla membrana del RER.



Proteine che hanno destinazione finale in un compartimento dell'elenco **1** sono sintetizzate da ribosomi liberi mentre proteine che hanno destinazione finale in un compartimento dell'elenco **2** guidano il ribosoma che le traduce verso il RER.

La sequenza delle proteine determina non soltanto le loro regolazioni e funzioni ma anche la loro localizzazione.



L'informazione sulla localizzazione finale delle proteine è contenuta nella loro sequenza amminoacidica

Esempi di sequenze di localizzazione:

Importazione nel nucleo (NLS) -Pro-Pro-Lys-Lys-Lys-Arg-Lys-Val-

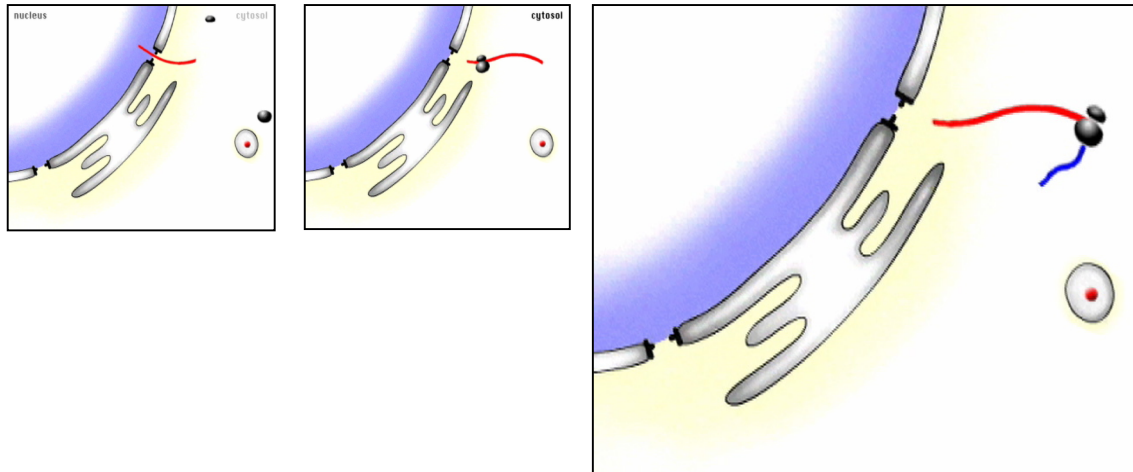
Exportazione dal nucleo (NES) -leu-Ala-Leu-Lys-Leu-Ala-Gly-Leu_Asp_Ile-

Importazione nel RER (peptide segnale): H2N-Met-Met-Ser-Phe-Val-Ser-Leu-
Leu-Leu-Val-Gly-Ile-Leu-Phe-
Trp-Ala-Thr-Glu-Ala-Glu-Gln-
Leu-Thr-Lys-Cys-Glu-Val-Phe-Gln-

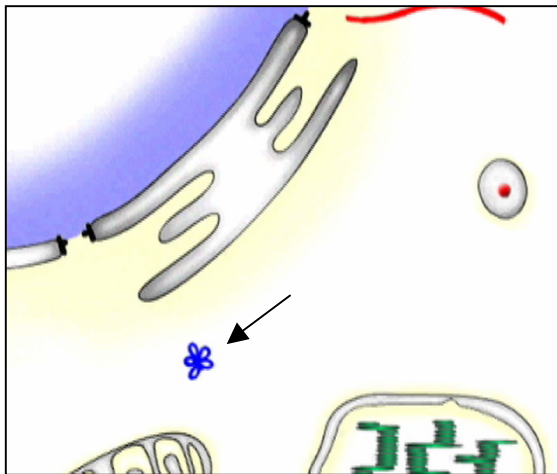
Ritorno al RER -Lys-Asp-Glu-Leu-COOH

Importazione nella matrice del mitocondrio H2N-Met-Leu-Ser-Leu-Arg-Gln-Ser-
Ile-Arg-Phe-Phe-Lys-Pro-Ala-
Thr-Arg-Thr-Leu-Cys-Ser-Ser-
Arg-Tyr-Leu-Leu-

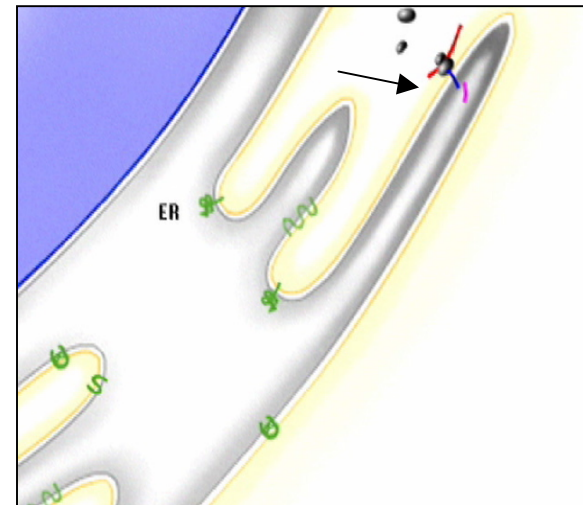
Importazione nei perossisomi (PTS1) -Ser-Lys-Leu-COOH

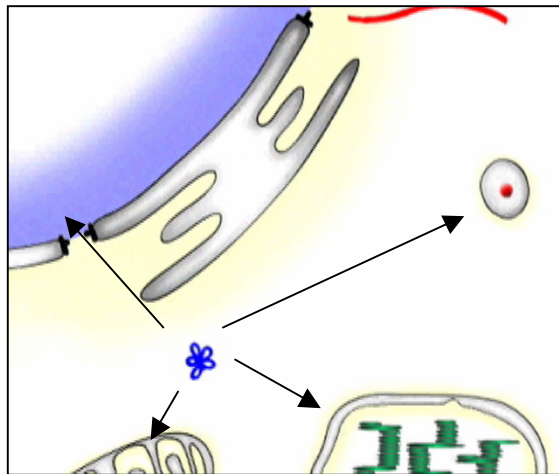
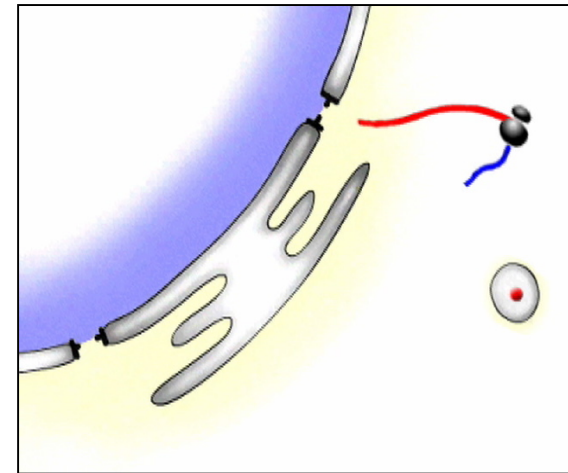
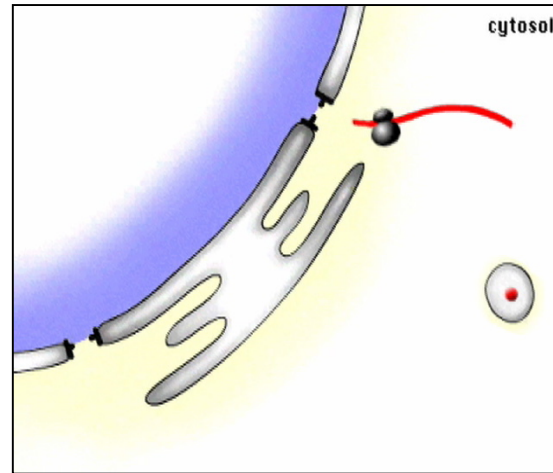
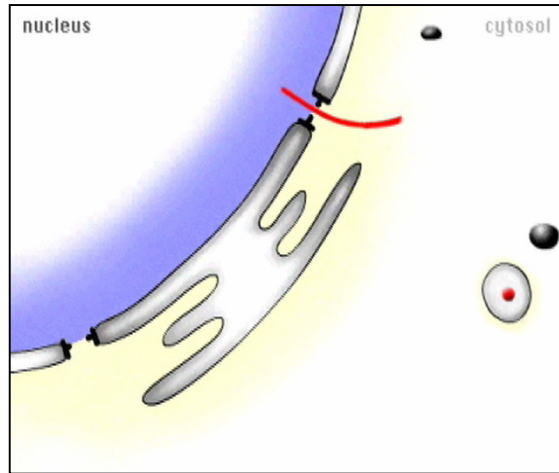


Assenza di peptide segnale
(traslocazione post-traduzionale)

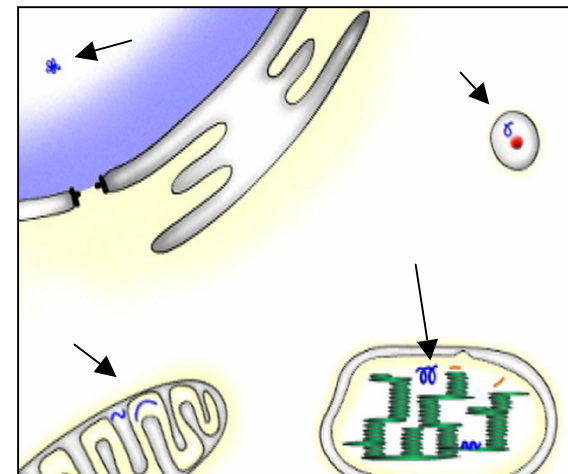


Peptide segnale ---> RER
(traslocazione co-traduzionale)



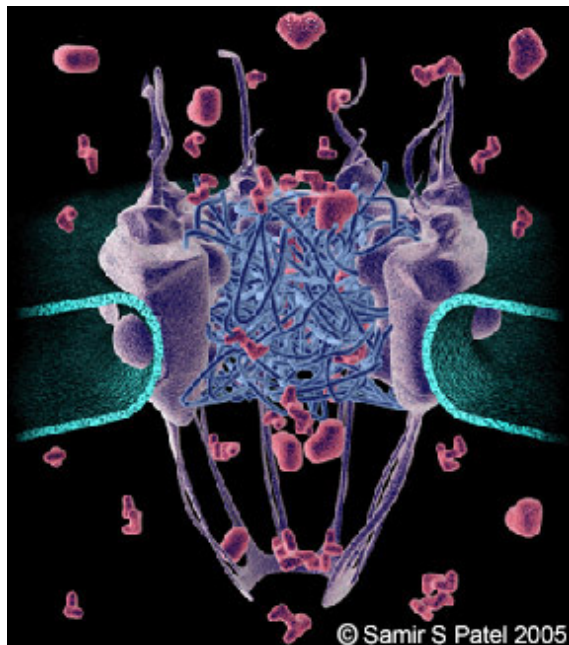


Proteine con sequenze di localizzazione nucleare oppure sequenze di localizzazione mitocondriale oppure sequenze di localizzazione perossisomiale oppure sequenze di localizzazione cloroplastica (cellule vegetali).



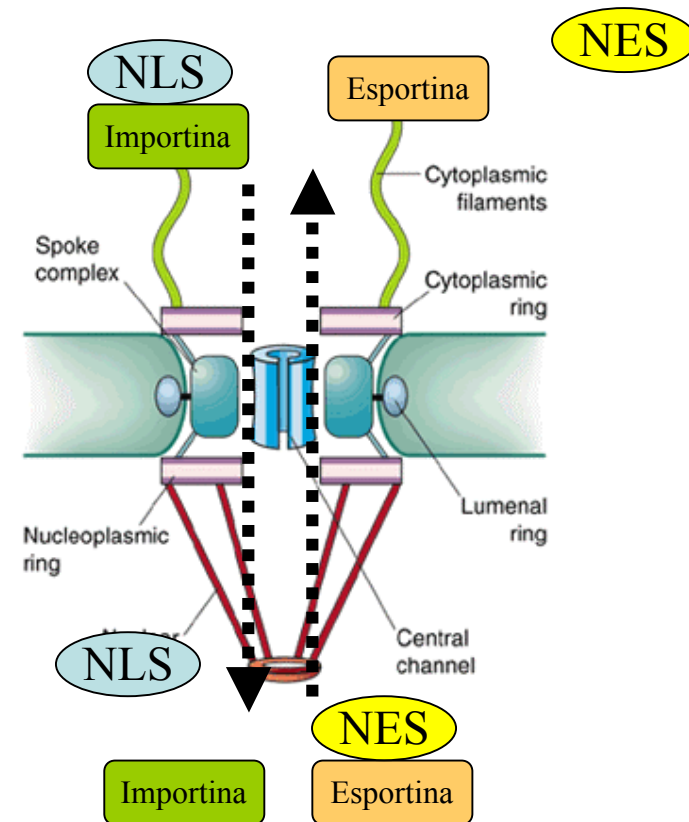
Sequenza di localizzazione nucleare (NLS):

Proteine di trasporto tipo “importine” accompagnano le proteine che possiedono una sequenza “NLS” nel passaggio dal citoplasma al nucleoplasma attraverso i pori nucleari.



citosol

nucleo



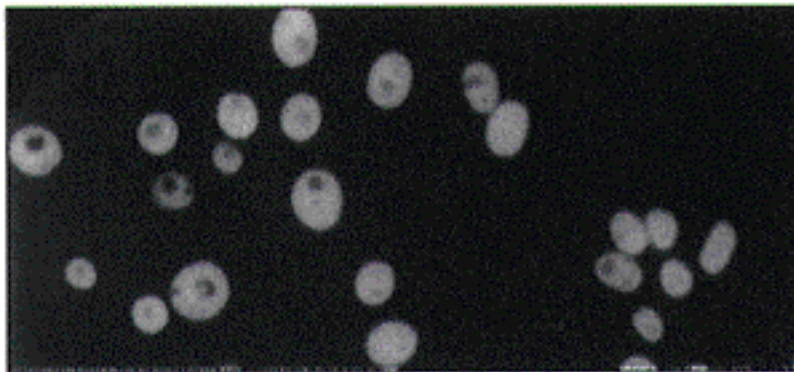
Se la sequenza NLS è mutata, la proteina non viene più trasportata dal citoplasma al nucleoplasma.

(A): sequenza NLS corretta: la proteina ha una localizzazione nucleare

(B): stessa proteina messa in evidenza in (A) ma con una mutazione puntiforme nella sequenza NLS (a.a. treonina in sostituzione della seconda lisina della sequenza NLS): la localizzazione è chiaramente citoplasmatica e non più nucleare perché la proteina mutata non è più riconosciuta dall'importina.

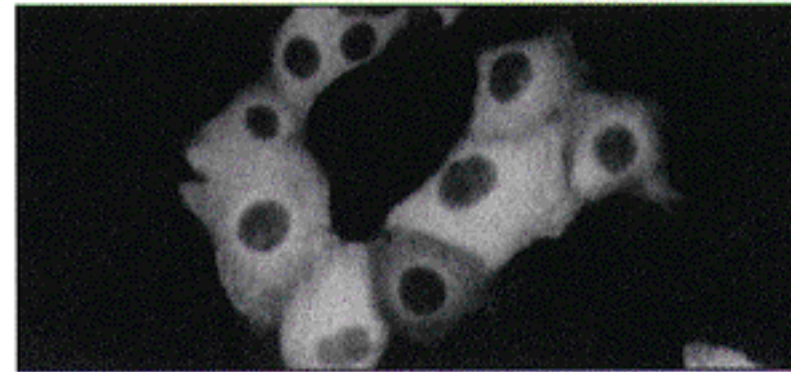
(A) LOCALIZATION OF T-ANTIGEN CONTAINING WILD-TYPE NUCLEAR IMPORT SIGNAL

Pro — Pro — Lys — Lys — Lys — Arg — Lys — Val —



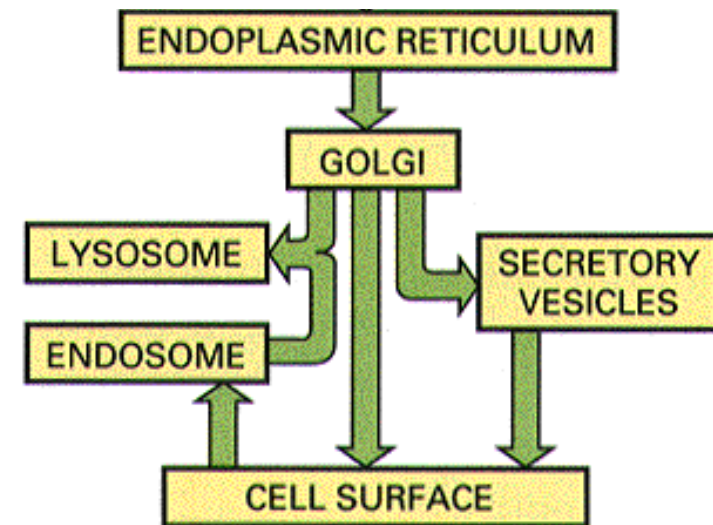
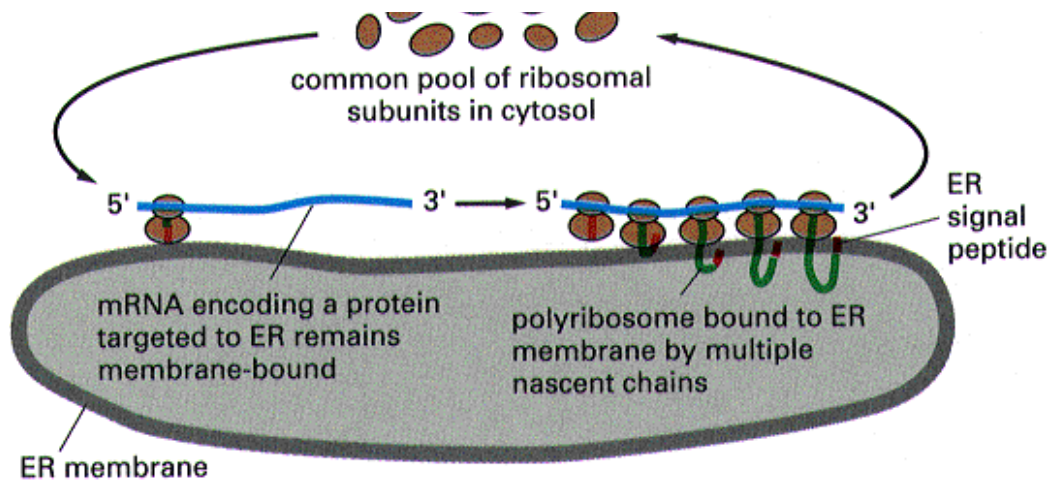
(B) LOCALIZATION OF T-ANTIGEN CONTAINING A MUTATED NUCLEAR IMPORT SIGNAL

Pro — Pro — Lys — Thr — Lys — Arg — Lys — Val —

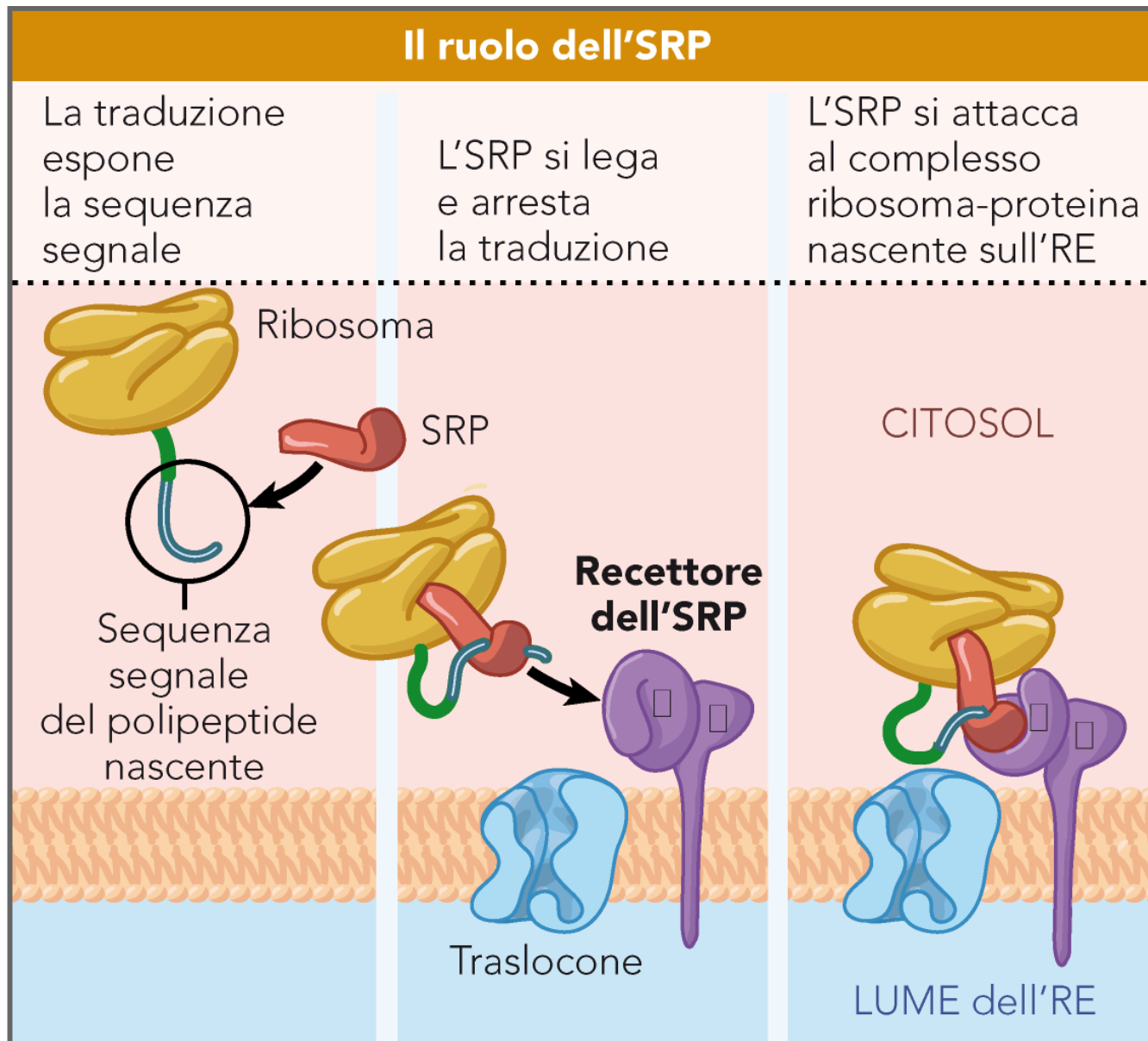


indirizzamento delle proteine della via secretoria

Con alcune eccezioni, le sequenze delle proteine della via “secretoria” iniziano con al N-terminale il peptide segnale



Nota: anche se chiamata genericamente via “secretoria”, proteine di questa via possono avere come localizzazione finale uno qualsiasi dei compartimenti elencati ed essere solubili, associate a membrane oppure transmembrana.



Function of Signal Peptide

Import into ER

Example of Signal Peptide

$^+$ H₃N-Met-Met-Ser-Phe-Val-Ser- **Leu-Leu-Leu-Val**
Gly-Ile-Leu-Phe-Trp-Ala -Thr-Glu-Ala-Glu-
Gln-Leu-Thr-Lys-Cys-Glu-Val-Phe-Gln-

1- La sintesi del polipeptide inizia su di un ribosoma libero nel citosol

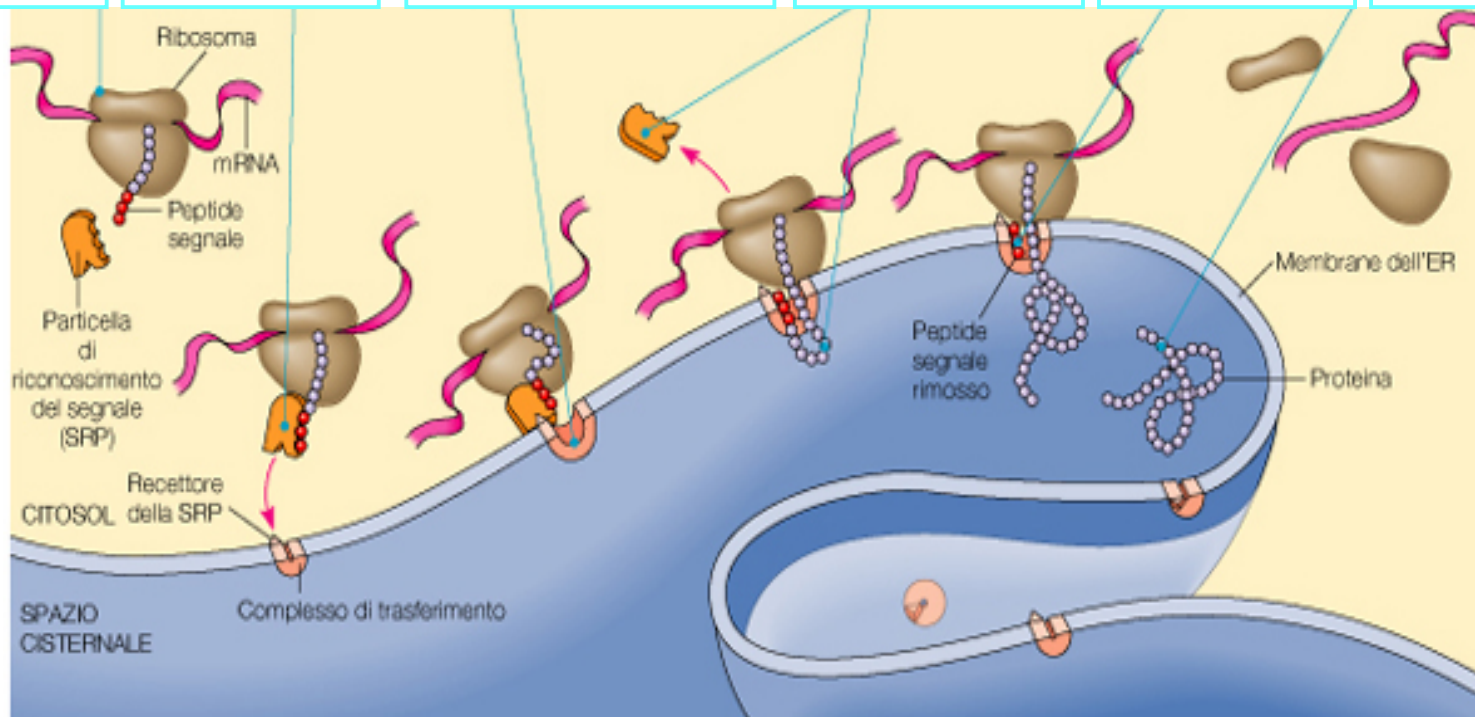
2- la proteina SRP si lega al peptide segnale e blocca temporaneamente la sintesi proteica

3- SRP si lega ad un recettore posto sulla membrana del RE. Tale recettore fa parte del complesso di trasferimento o traslocone che forma un poro sulla membrana del RE e lega il peptide segnale

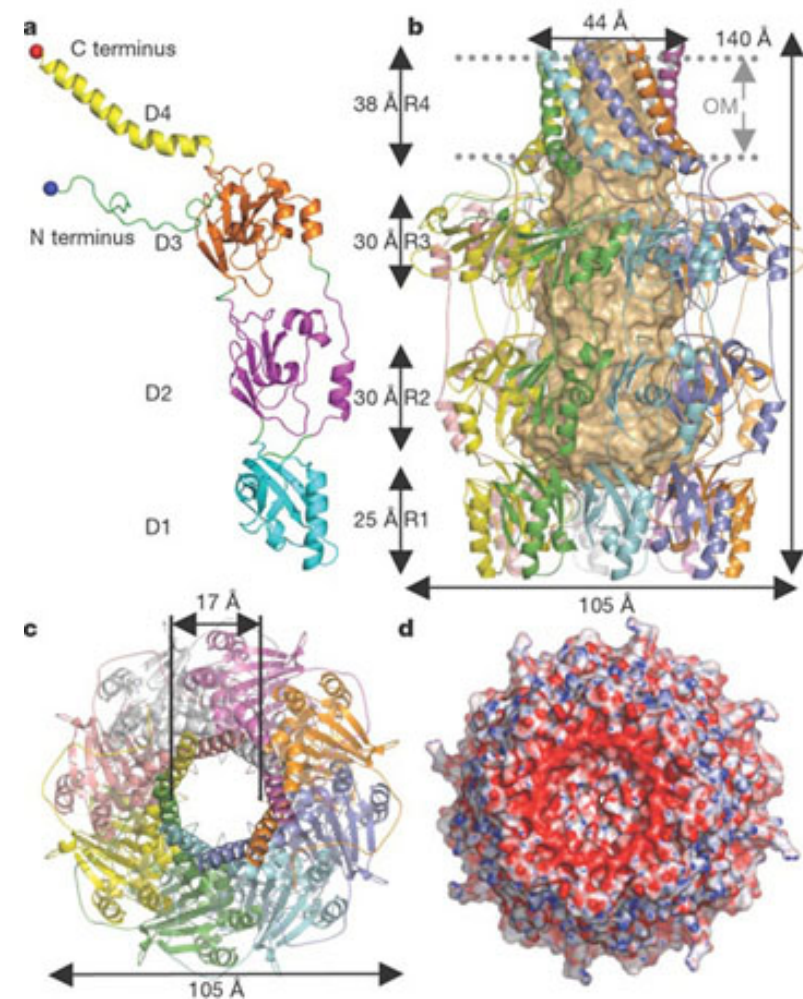
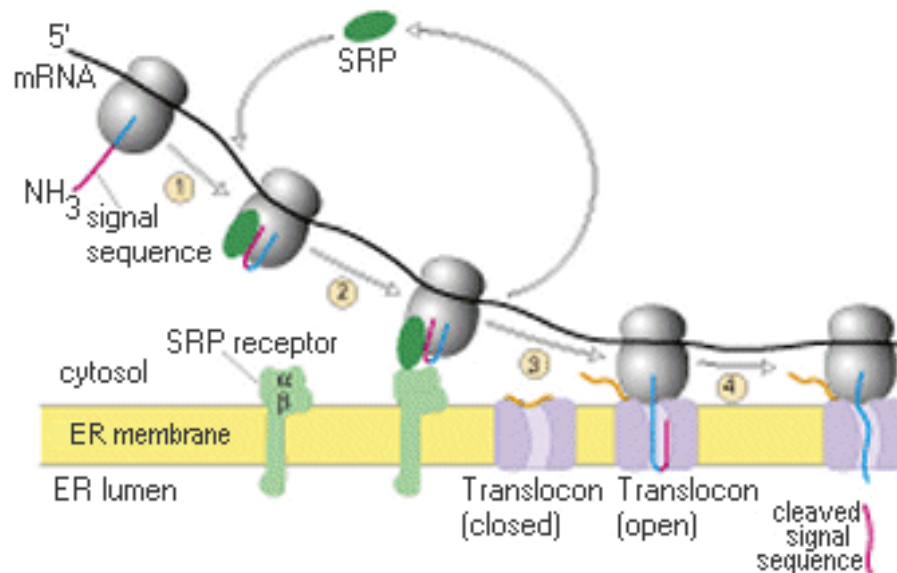
4- SRP abbandona il complesso, la sintesi proteica riprende. La proteina nascente attraversa contemporaneamente

5- un enzima idrolitico rimuove il peptide segnale della proteina

6- In assenza di altro segnale, raggiunto il codone di stop, il ribosoma si sgancia dall'mRNA e la proteina è localizzata nel lume del RER

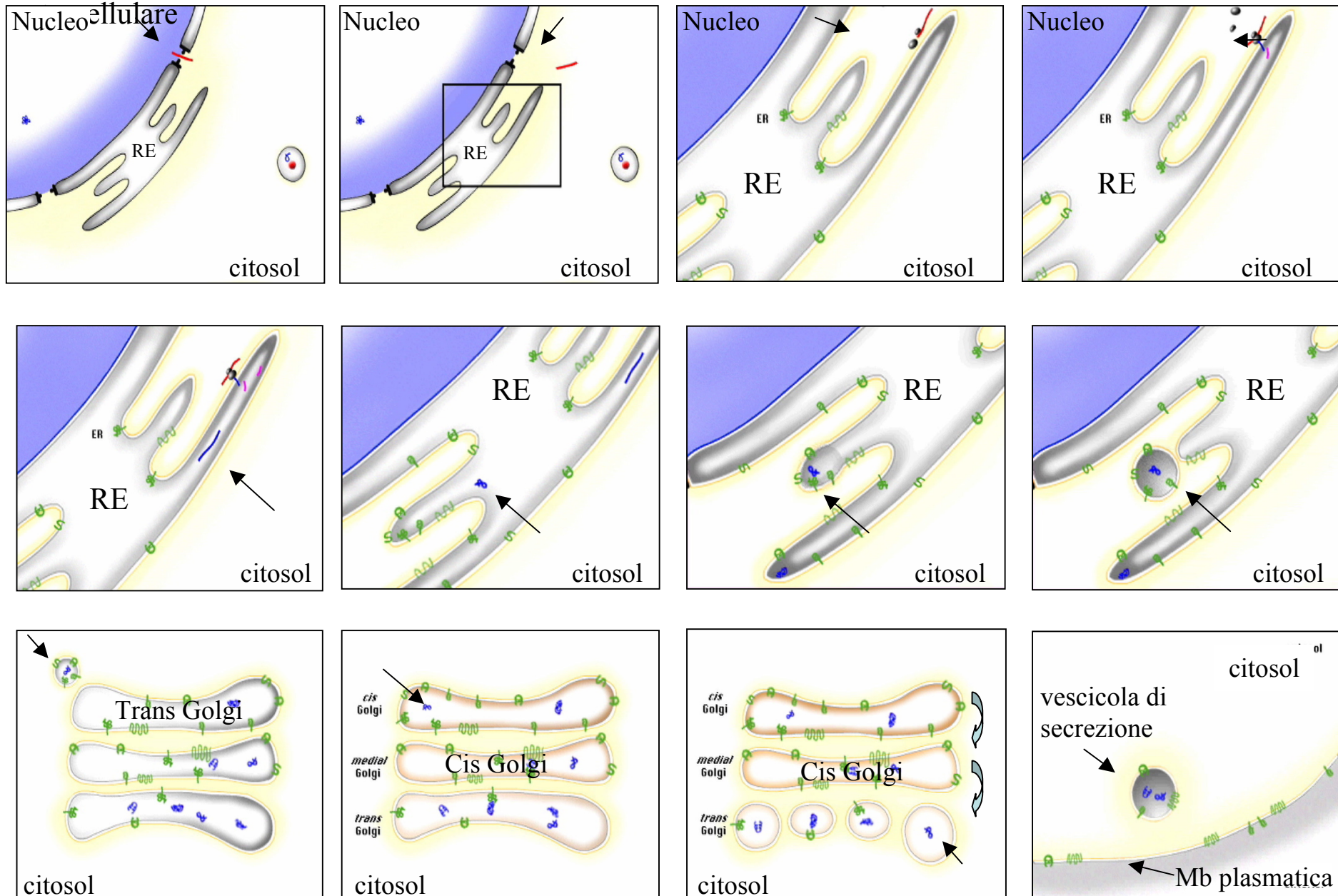


Le proteine SRP sono riciclate

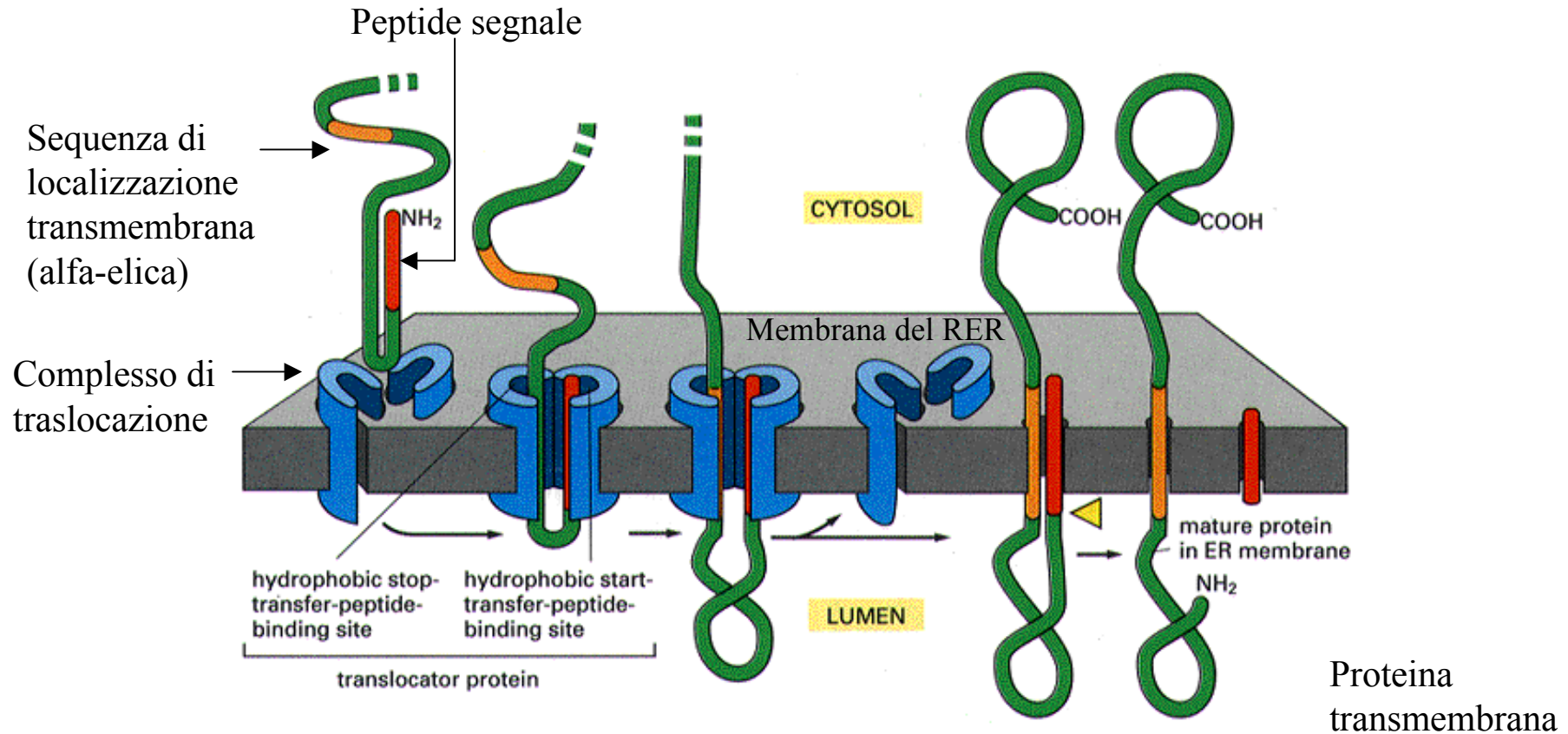


Il traslocone è un poro proteico tappato sul versante del lume del RE che si apre soltanto dopo interazione con un ribosoma.

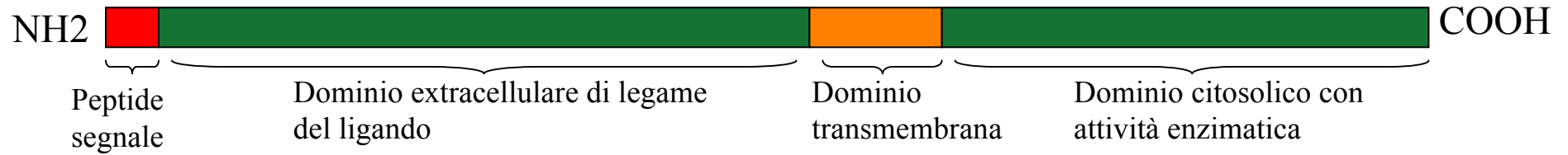
indirizzamento di una proteina di secrezione: RE --> Golgi --> vescicola di secrezione --> spazio



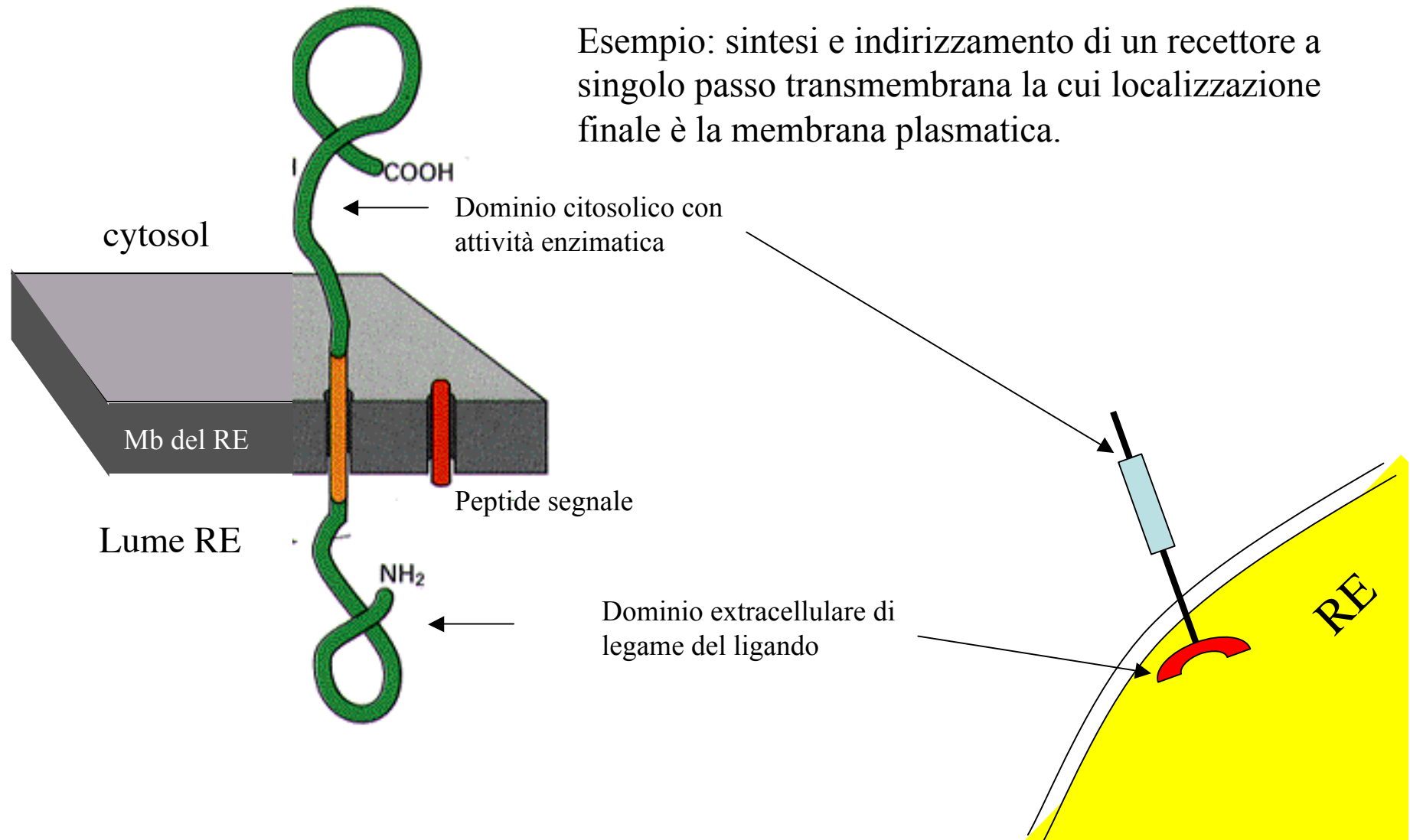
Proteine transmembrana: Inserimento co-traduzionale nel doppio strato fosfolipidico

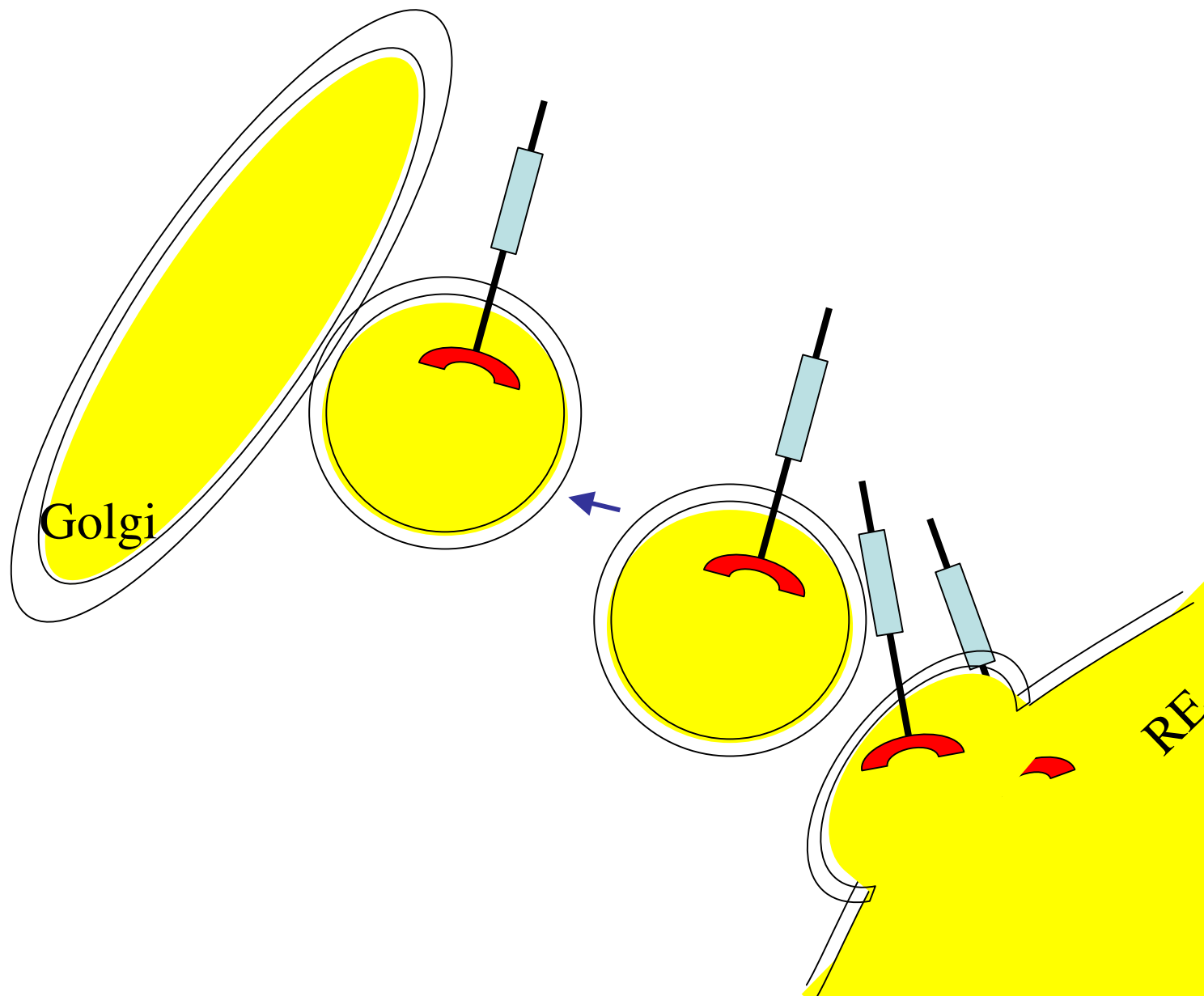


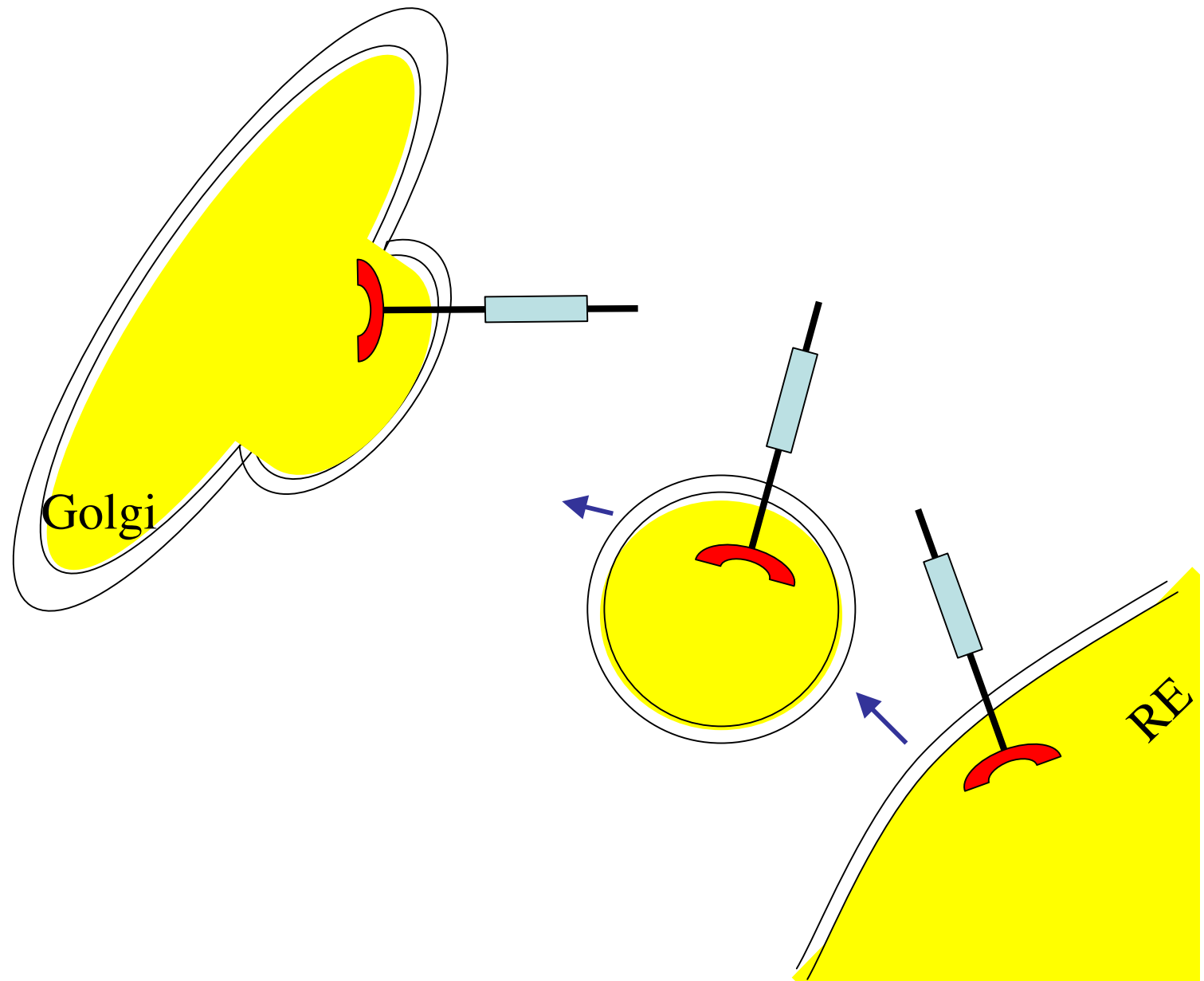
Nota: in questo schema per semplicità non sono più stati rappresentati mRNA e ribosoma.

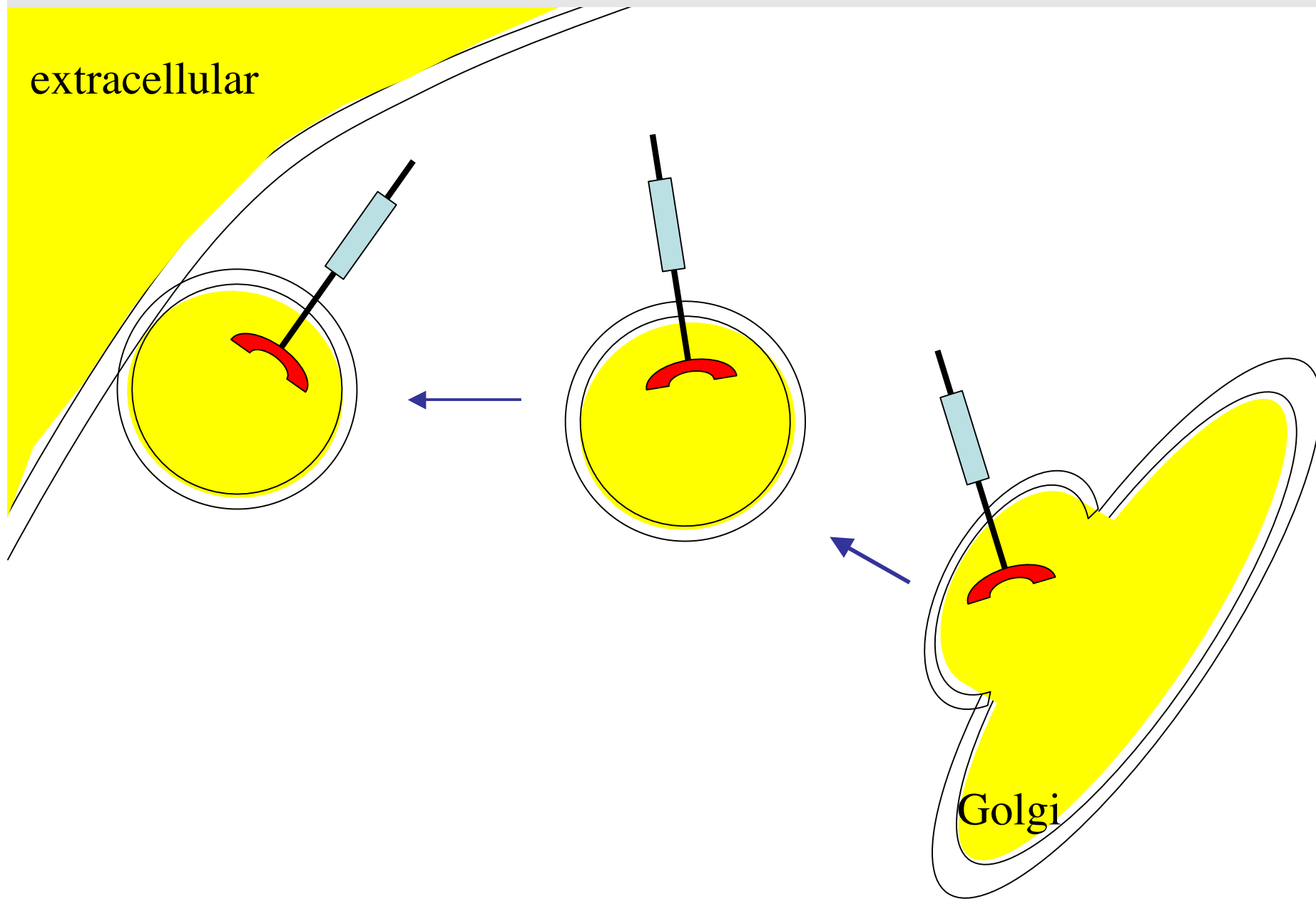


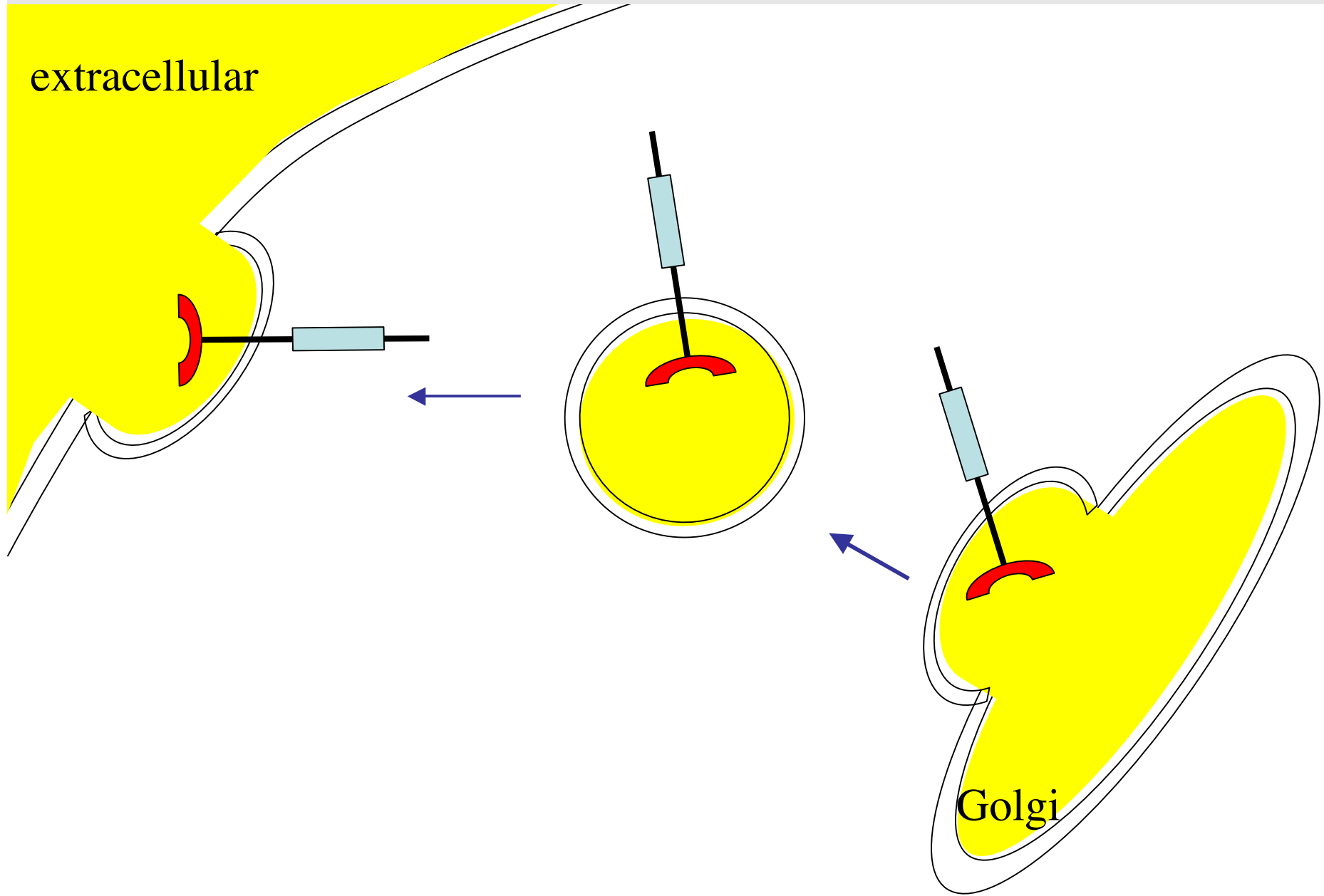
Esempio: sintesi e indirizzamento di un recettore a singolo passo transmembrana la cui localizzazione finale è la membrana plasmatica.

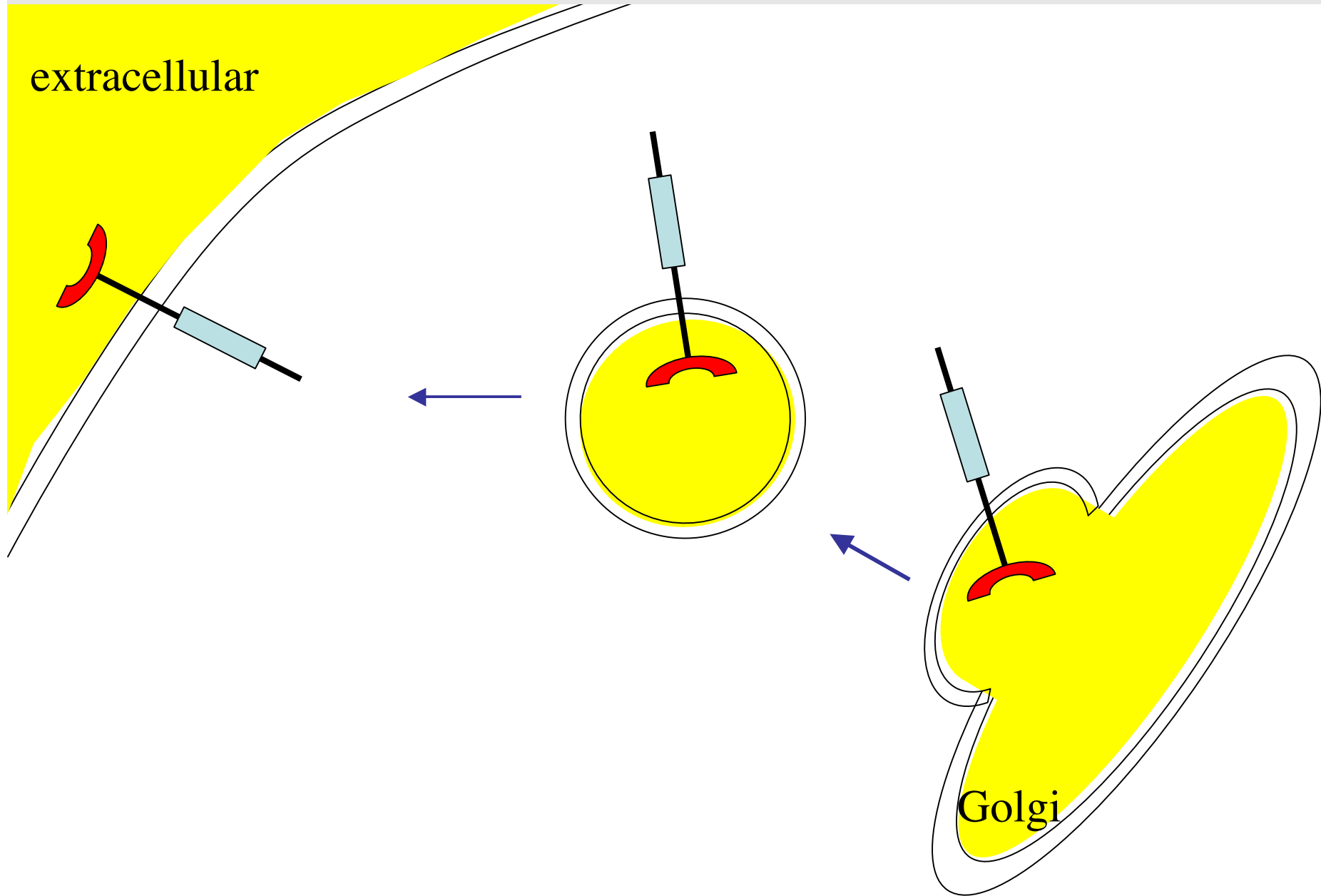




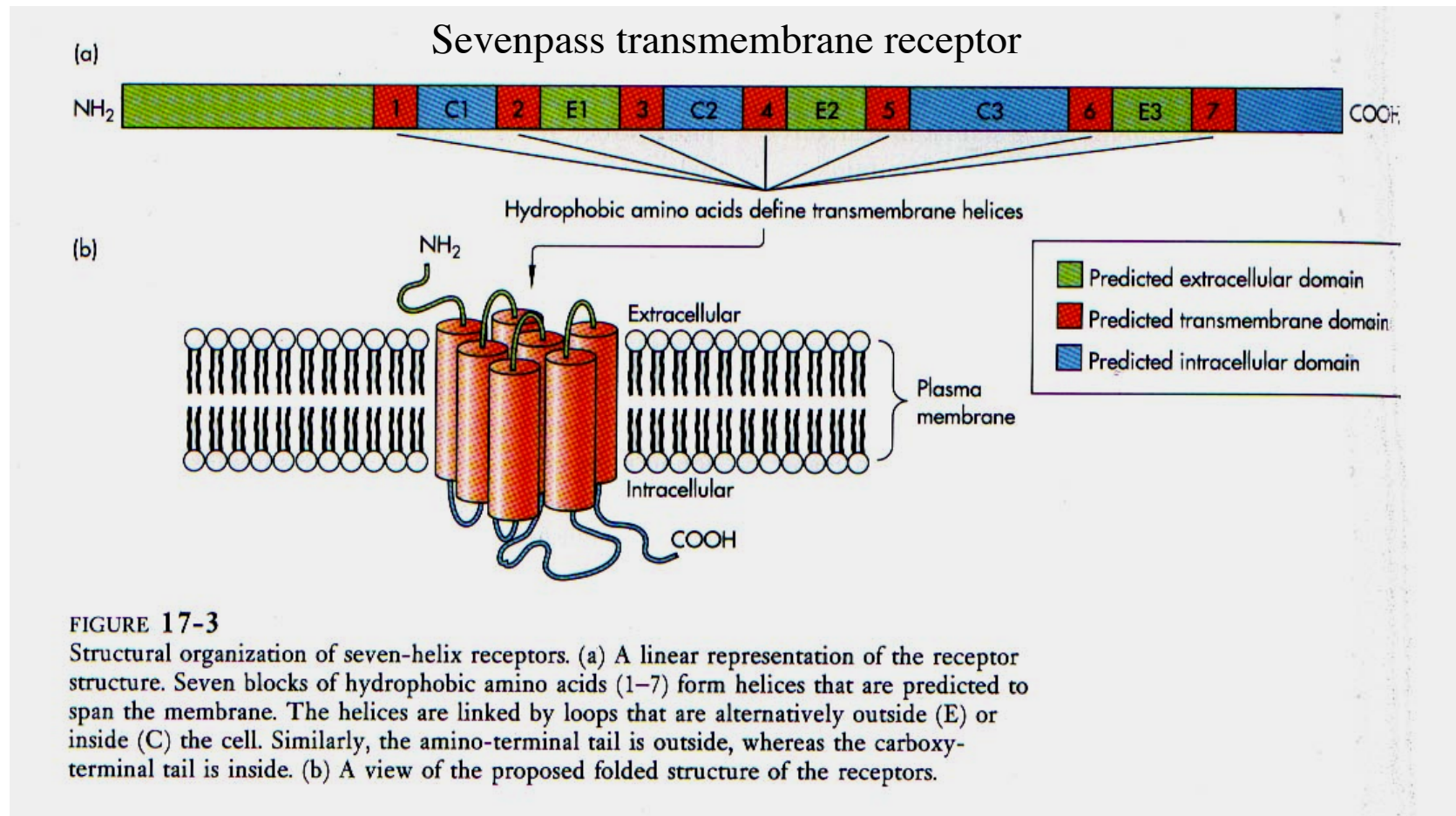




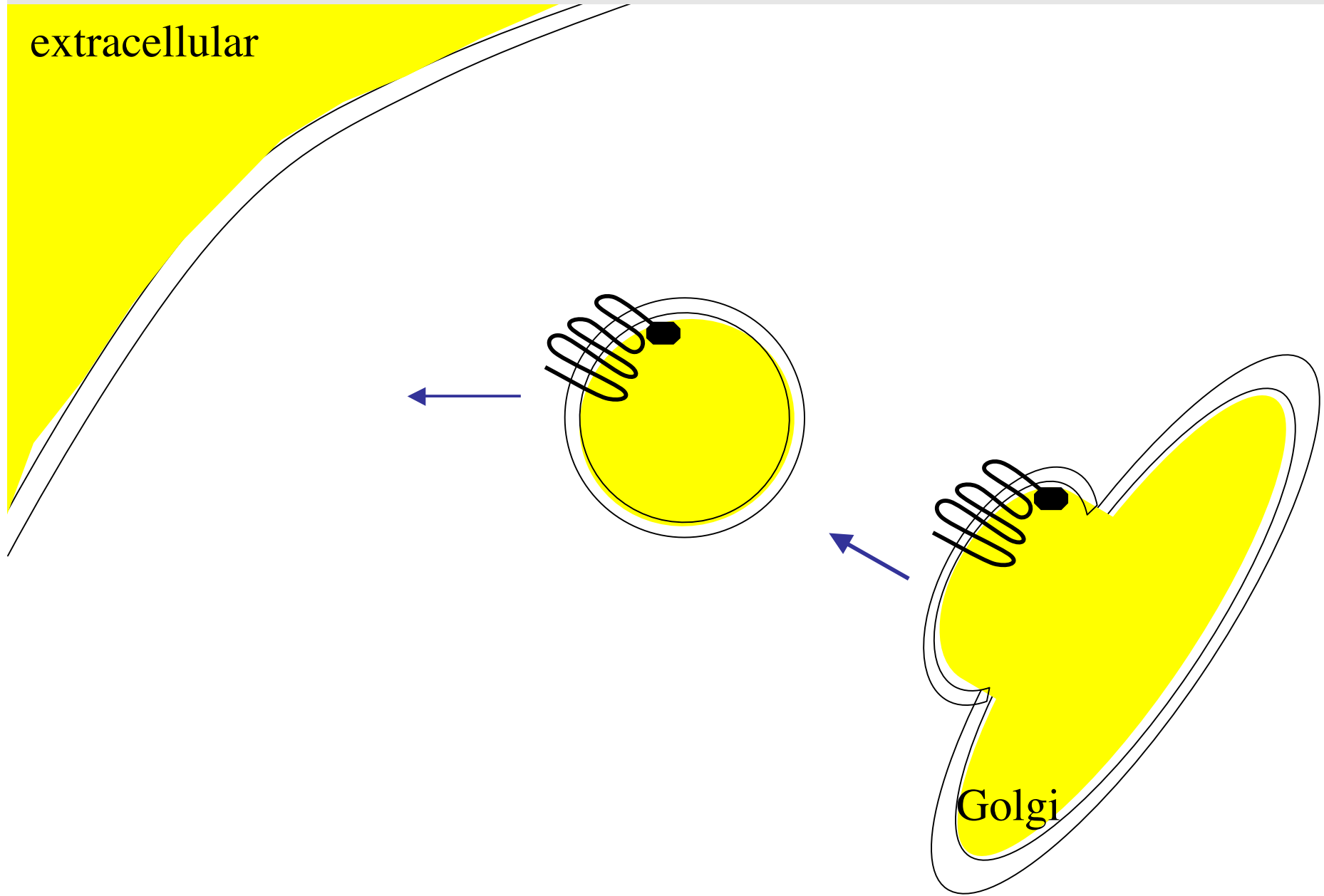


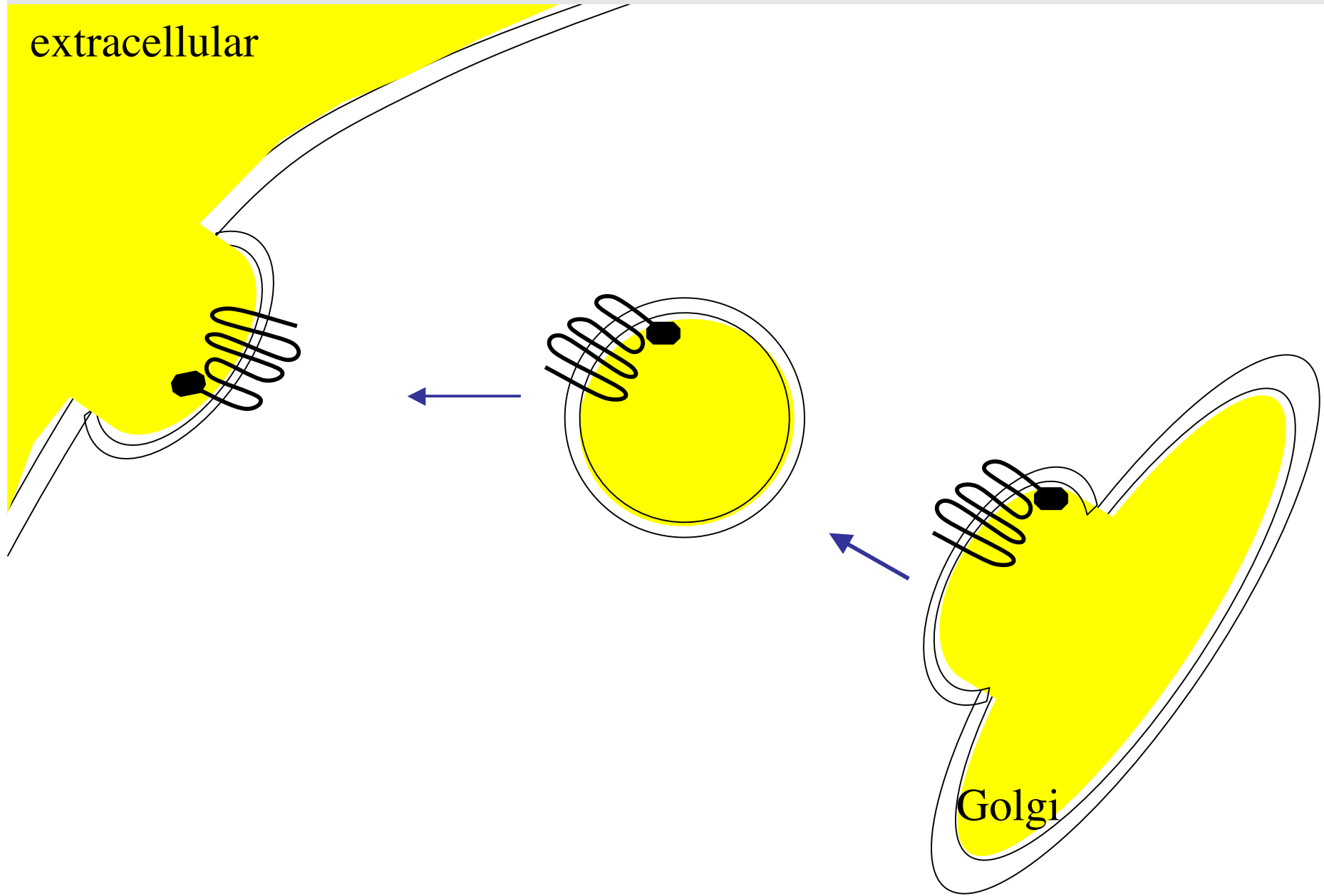


Spiegare la sintesi e lo indirizzamento del recettore metabotropico al glutamato?

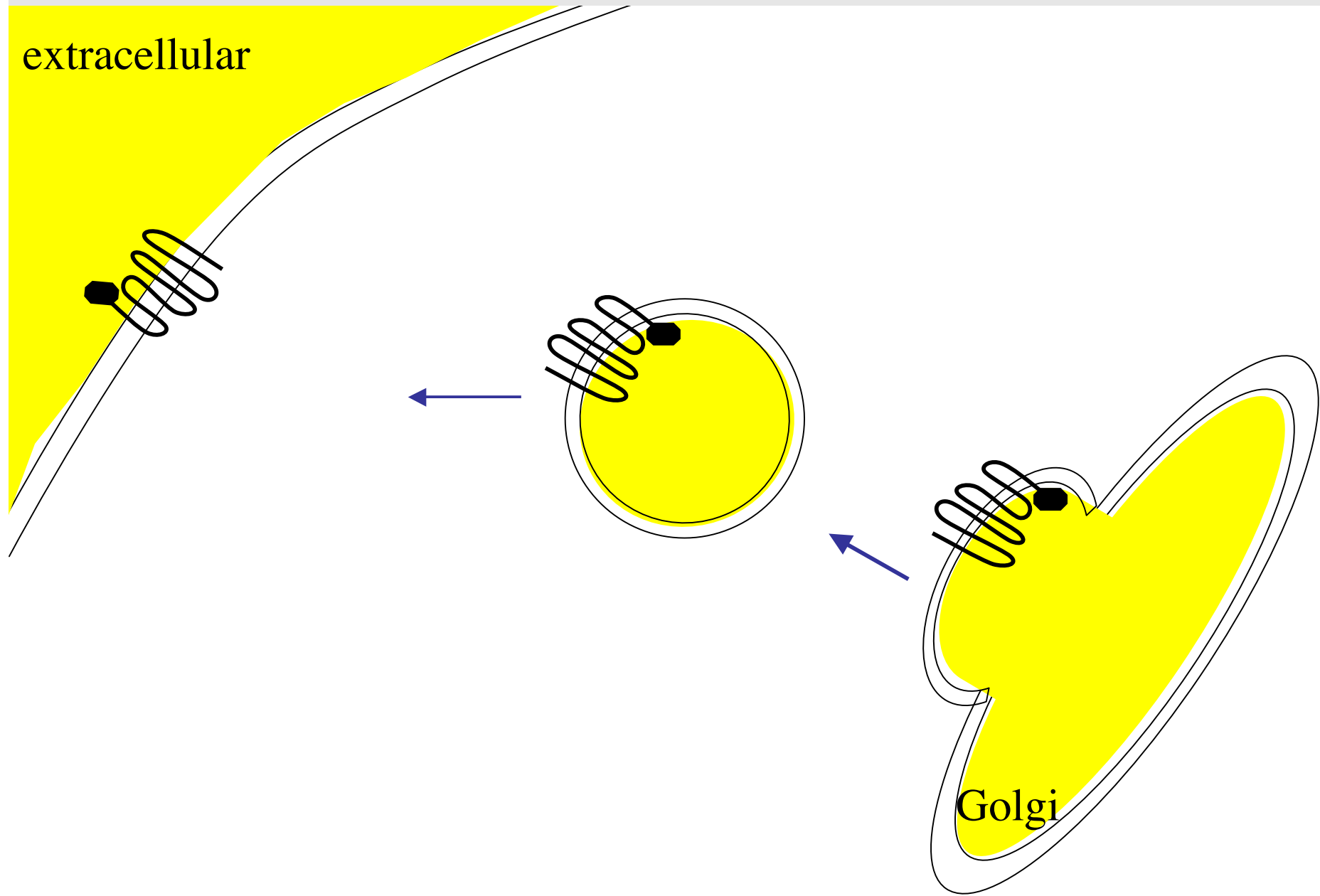


extracellular



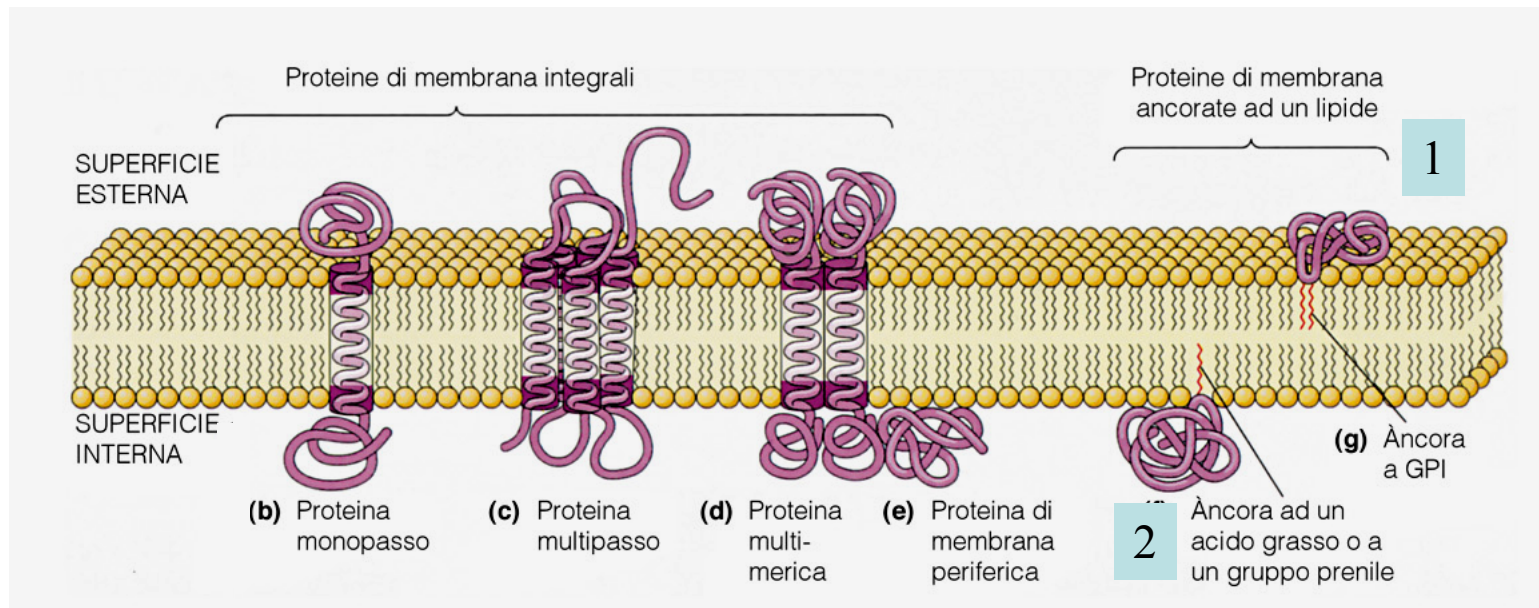


extracellular



Proteine di membrana (ma non transmembrana) ancorate a lipidi

- 1 Proteine extracellulari ancorate a lipidi sono sintetizzate da ribosomi associati al RE, traslocate in modo co-traduzionale nel lume del RER, agganciate a GPI, trasportate da vescicole attraverso il Golgi fino alla membrana plasmatica



- 2 Proteine intracellulari (citoplasmatiche) ancorate a lipidi sono sintetizzate da ribosomi liberi, ancorate alla membrana del RE sul lato citoplasmatico e trasportate fino alla membrana plasmatica associate a vescicole (vedi diapo successiva)