# Modulo B3

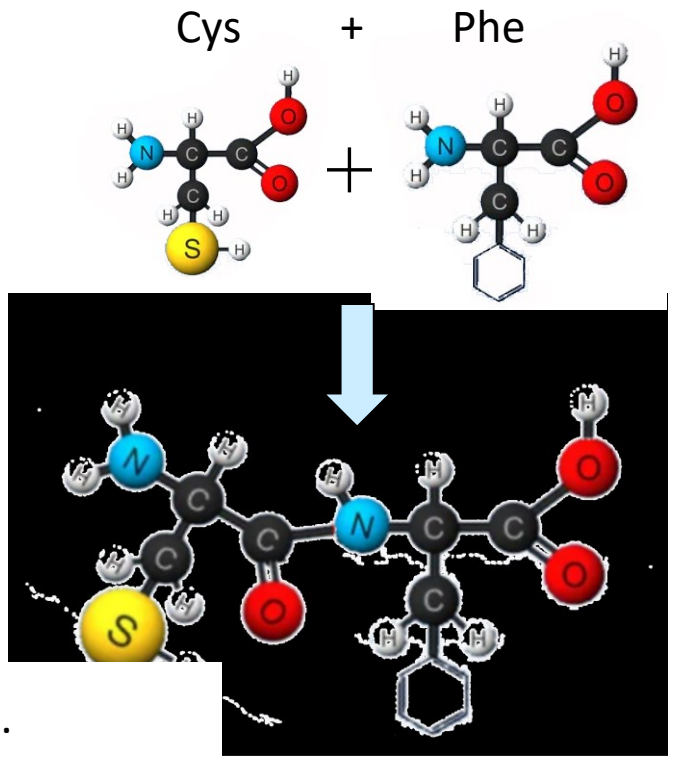
## Sintesi in fase solida di peptidi e proteine

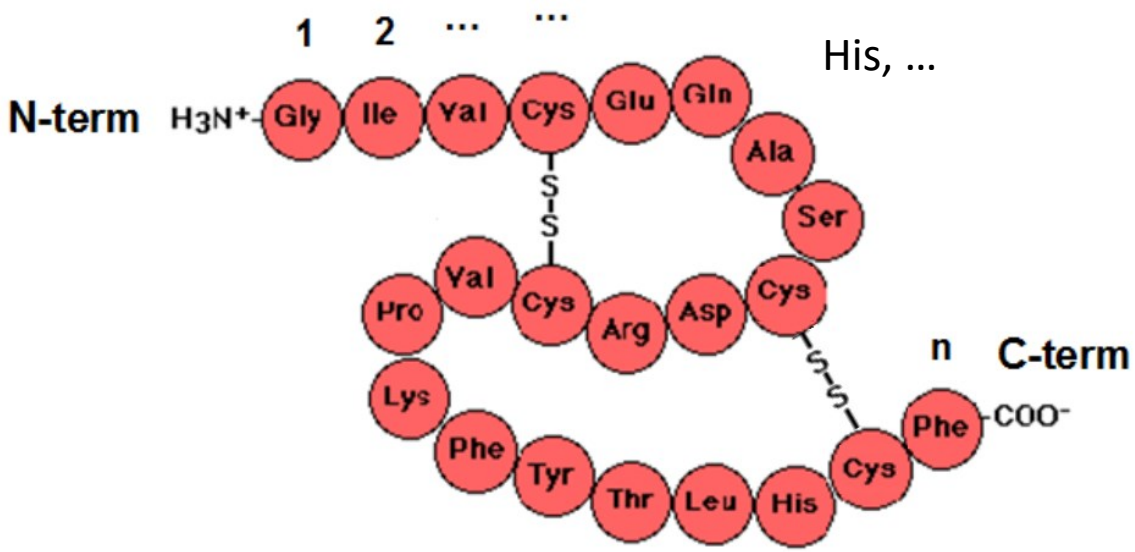
2023-24

# SPPS – Sintesi in fase solida di peptidi e proteine

**Protein production:**

- **Biochemical (extraction)**
- **Recombinant**
- **Chemical synthesis**
- **Semisynthesis**

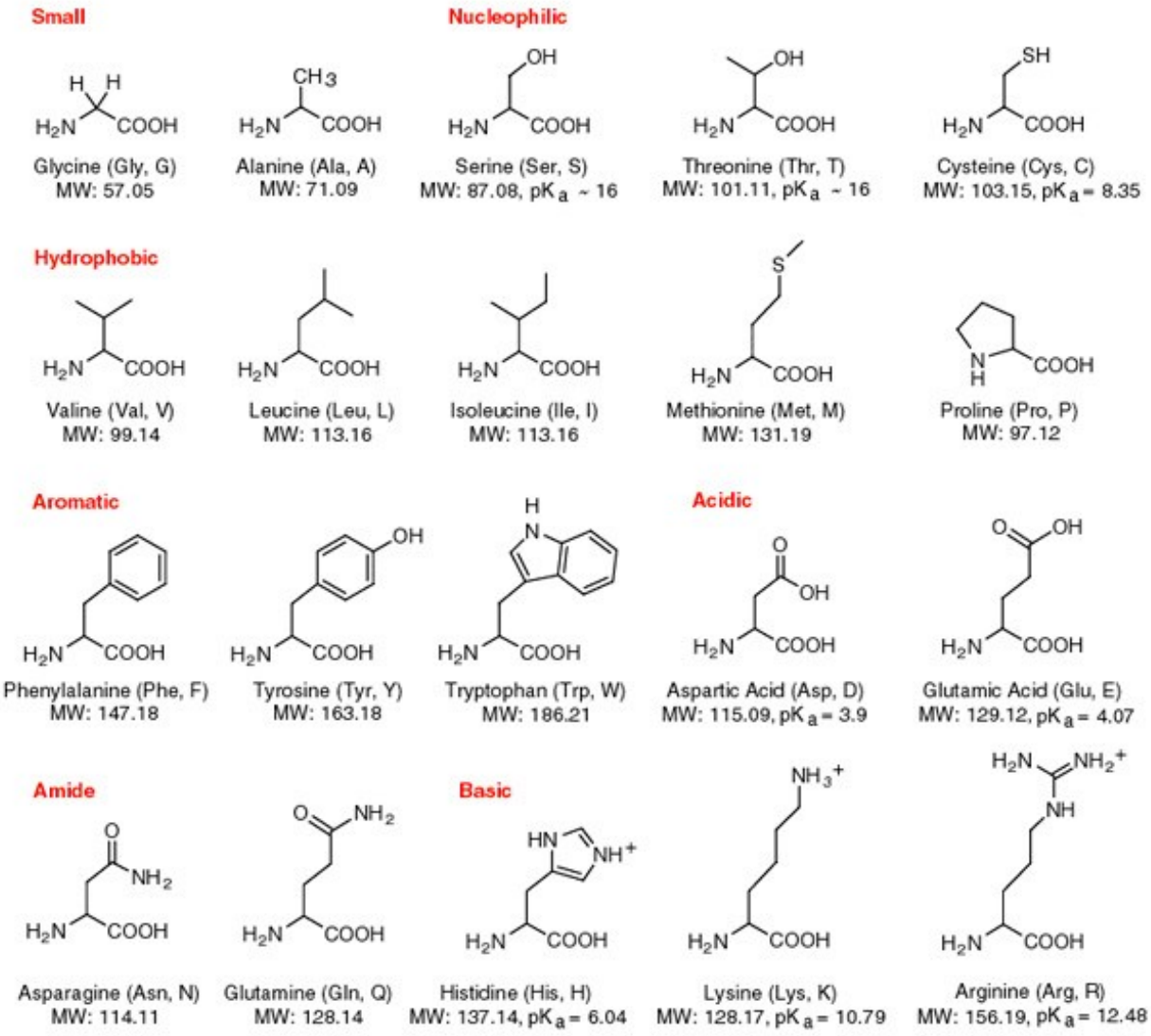



His, …

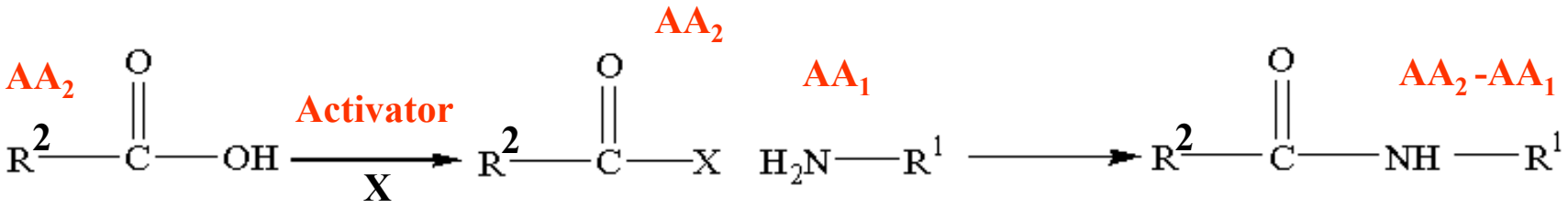
$NH_2$-Cys-Phe-COOH

# Caratteristiche degli amminoacidi



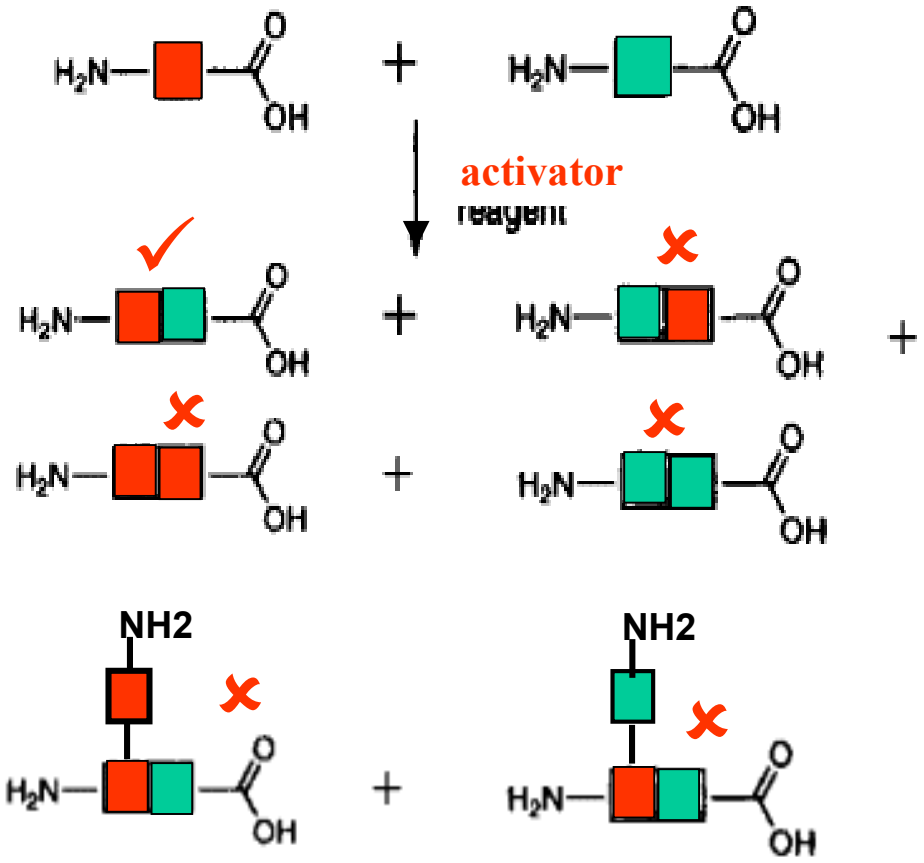

Amino acids have different reactive groups: $\alpha$-ammino, $\alpha$-carboxyl
side-chain ammino, amido, carboxyl, hydroxyl, sulphydril, guanidino, imidazole, indole

# Sintesi peptidica



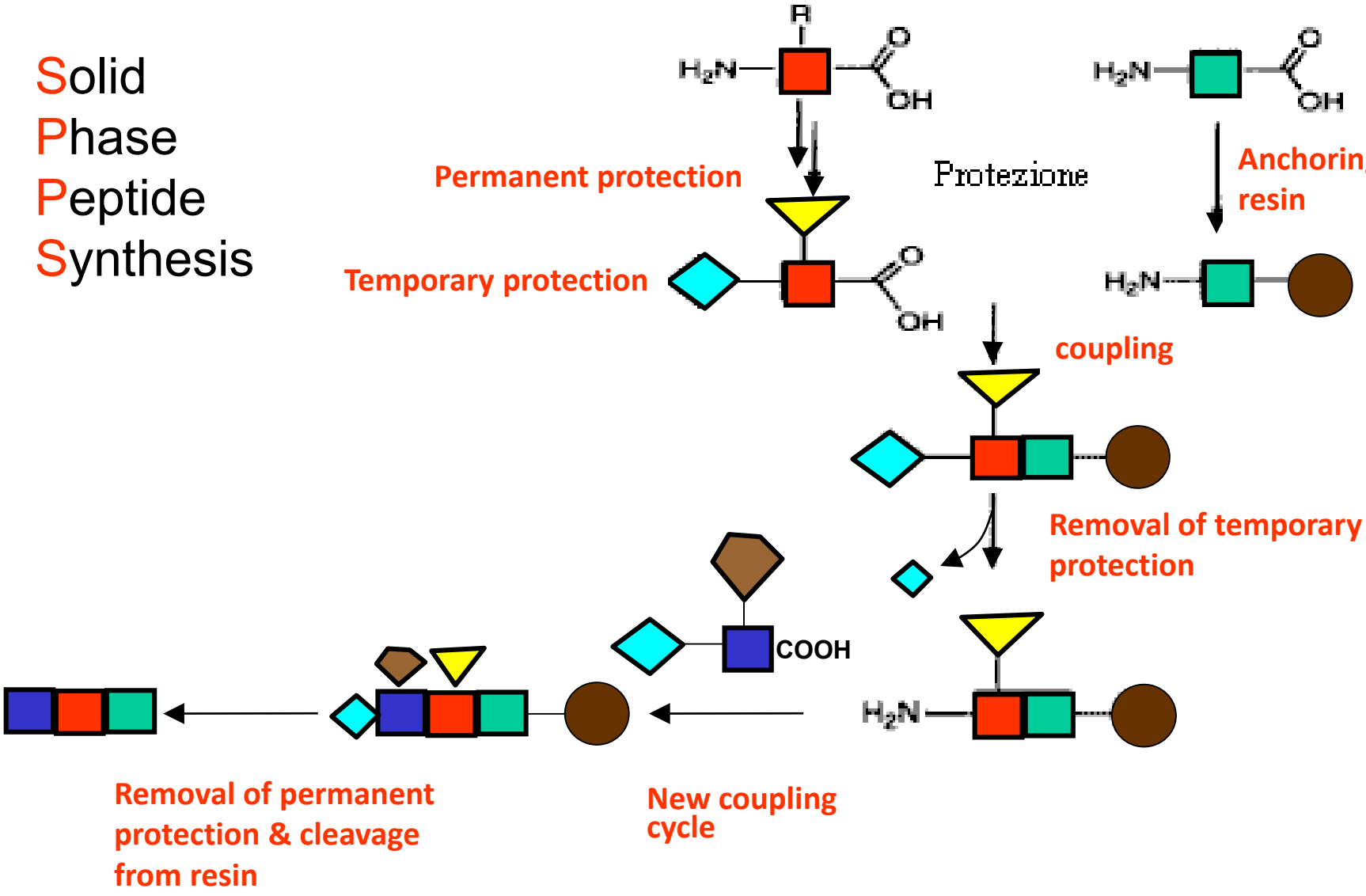

Solution synthesis without protection

Problem with side products

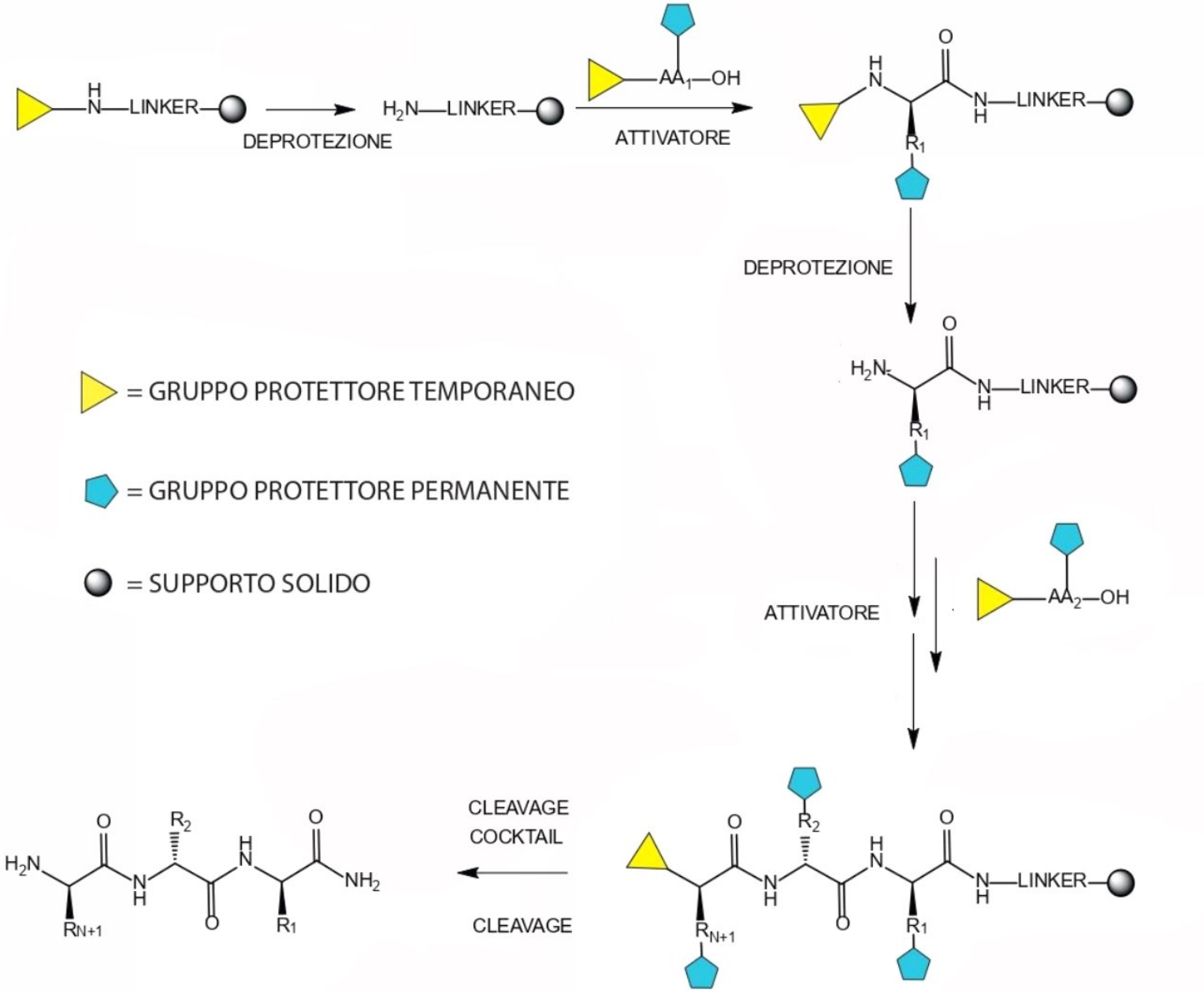


# SPPS – Solid Phase Peptide Synthesis

Solid
Phase
Peptide
Synthesis



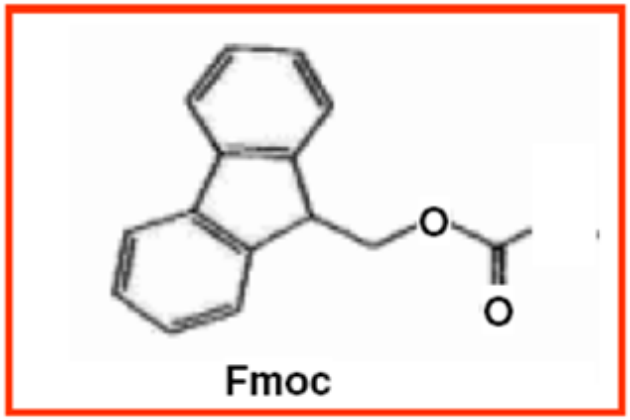
# SPPS – Solid Phase Peptide Synthesis (cont.)



# Proteizione – temporanea e permanente

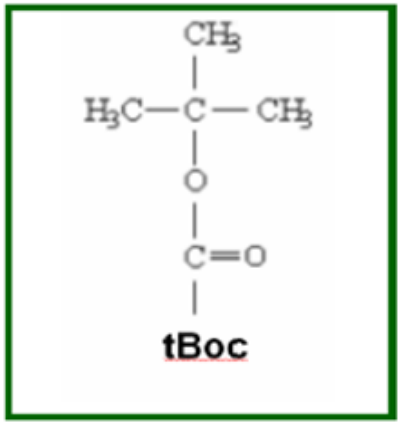
## Protezione temporanea sul gruppo α-amminico

Fluorenilmetossicarbonile




labile in base
(20% piperidina)

*tert*Butossicarbonile

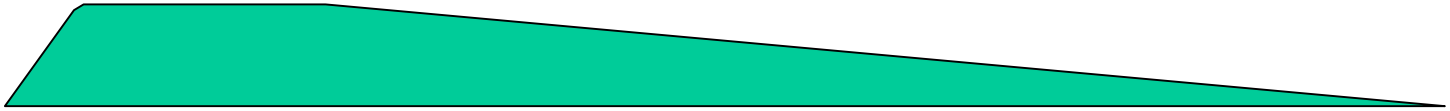



labile in acido
(TFA)

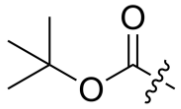
## Legame alla resina e protezione permanente sulle catene laterali

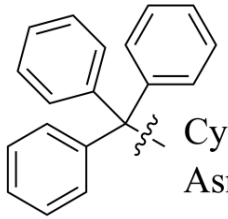
- Labile in acido (TFA)
- Ortogonale

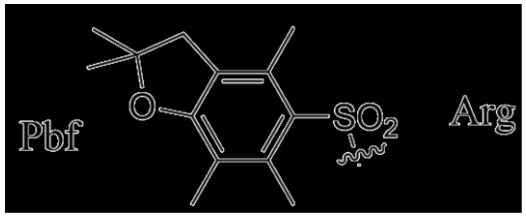
- Labile in acido molto forte (HF)
- Parzialmente ortogonale



*t*Bu  Ser, Thr, Tyr
Asp, Glu

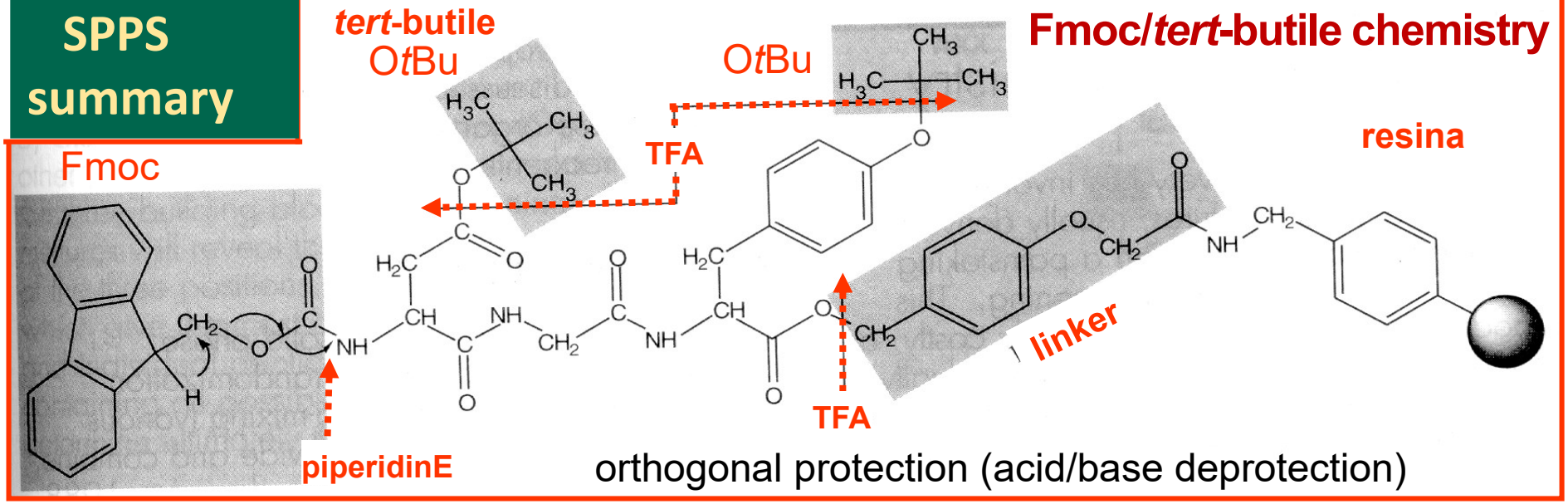
Boc  Lys, Trp

Trt  Cys, His,
Asn, Gln



# SPPS summary

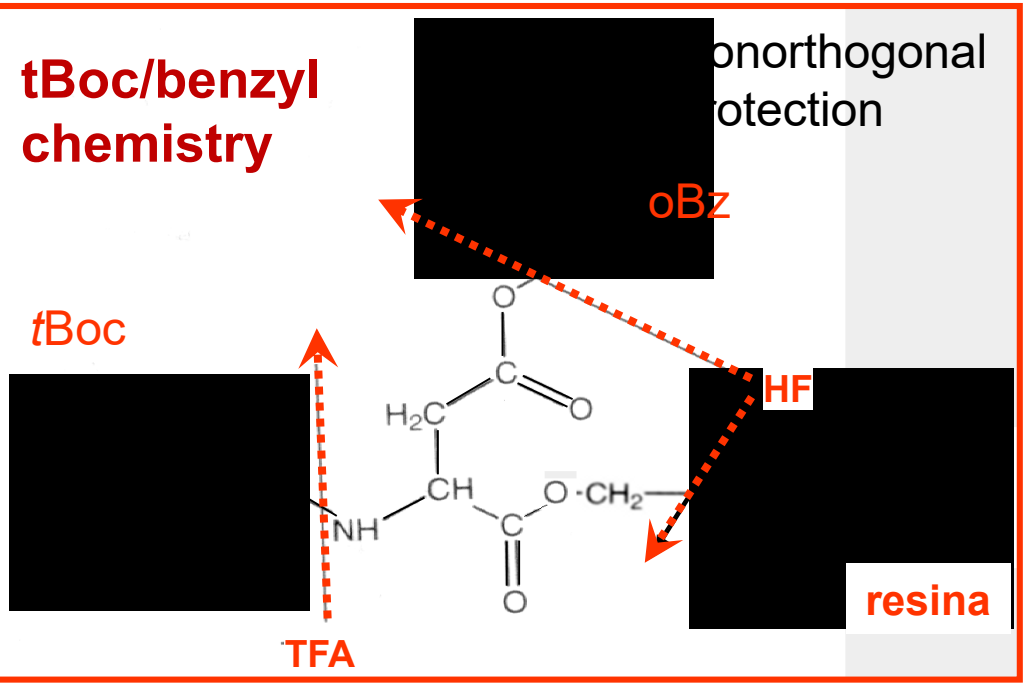
## Fmoc/*tert*-butile chemistry




orthogonal protection (acid/base deprotection)

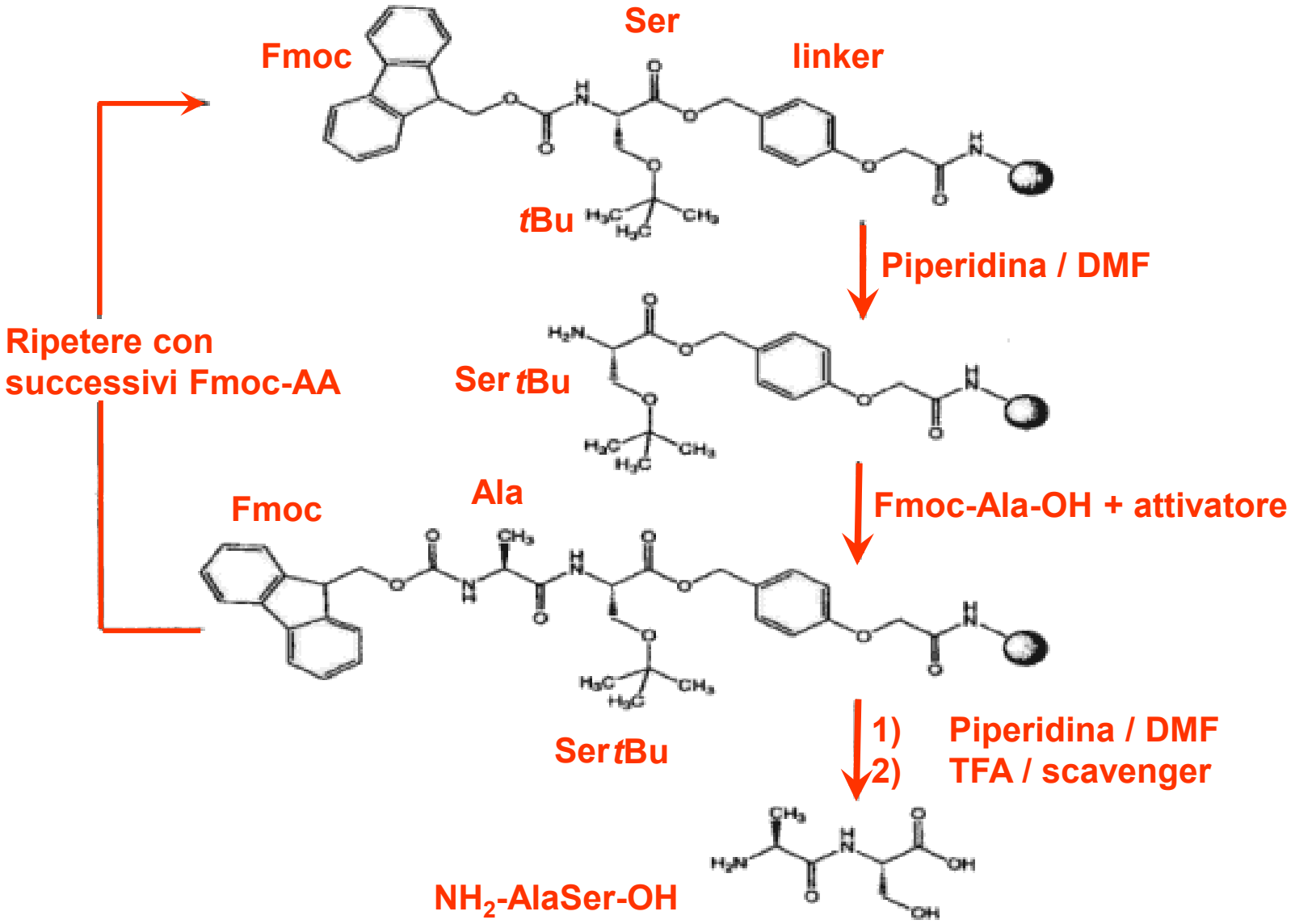
## tBoc/benzyl chemistry

onorthogonal
otection




- **Fmoc / *tert*-butile**:
  - Fmoc base-labile (20% piperidine)
  - Side-chains/resin link acid-labile (TFA)
- **tBoc / benzyl**:
  - tBoc acid-labile (TFA)
  - side-chains/anchor strong acid labile (hydrofluoric acid, HF)

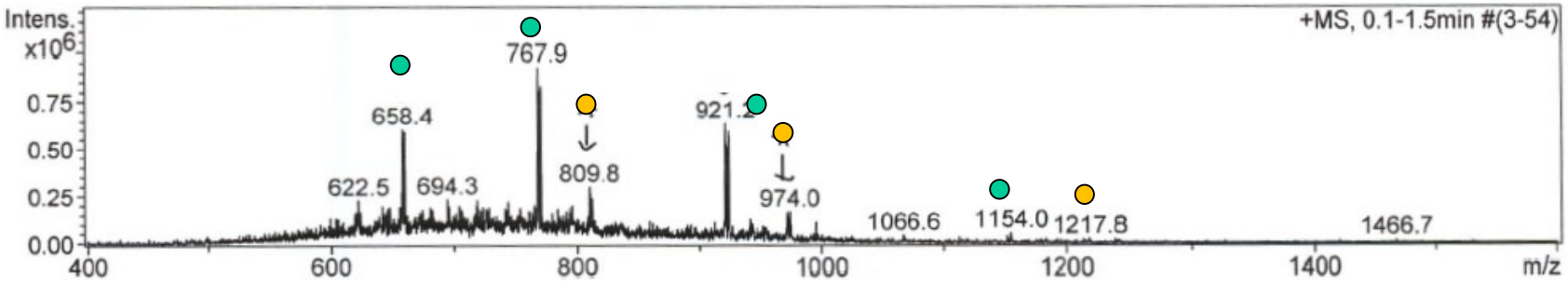
# SPPS Fmoc – cicli di sintesi

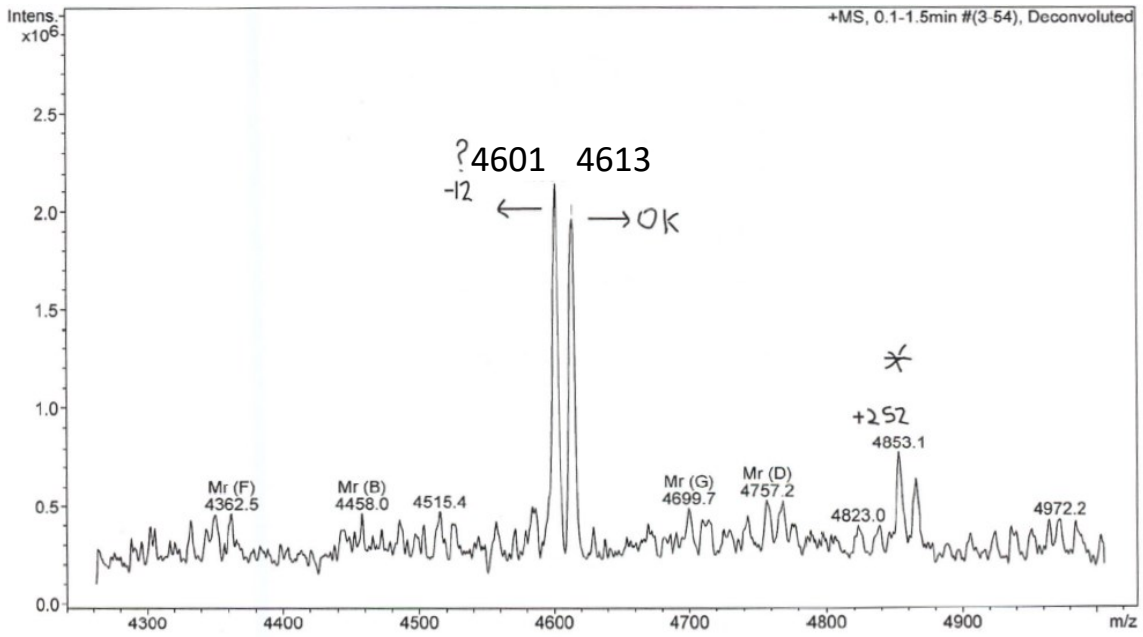


# SPPS – esempio di sintesi

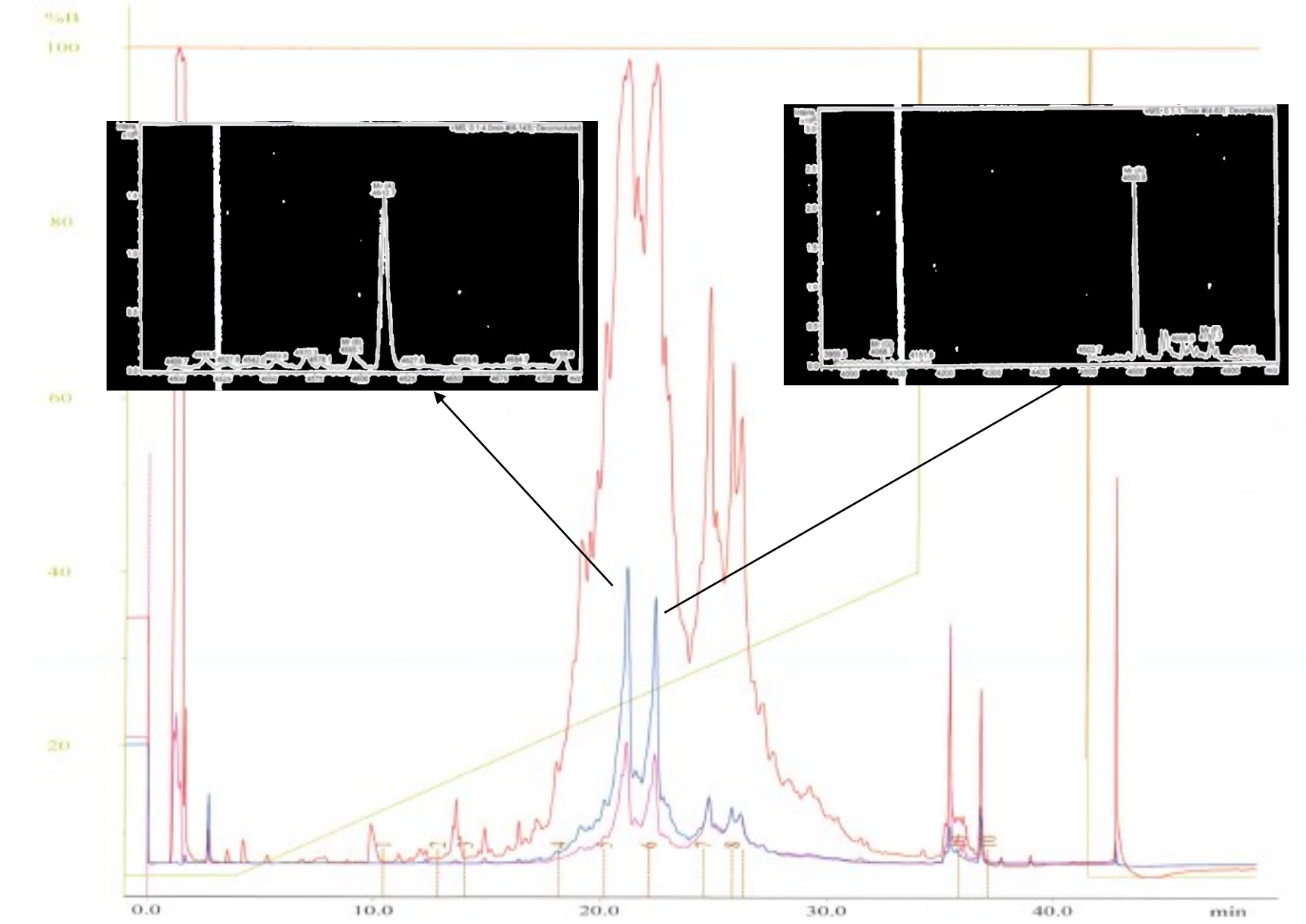
Sintesi di un peptide antimicrobico di mitile

YSWPRMPRIPRLPRYPRYPRYPG MW = 4613 Da

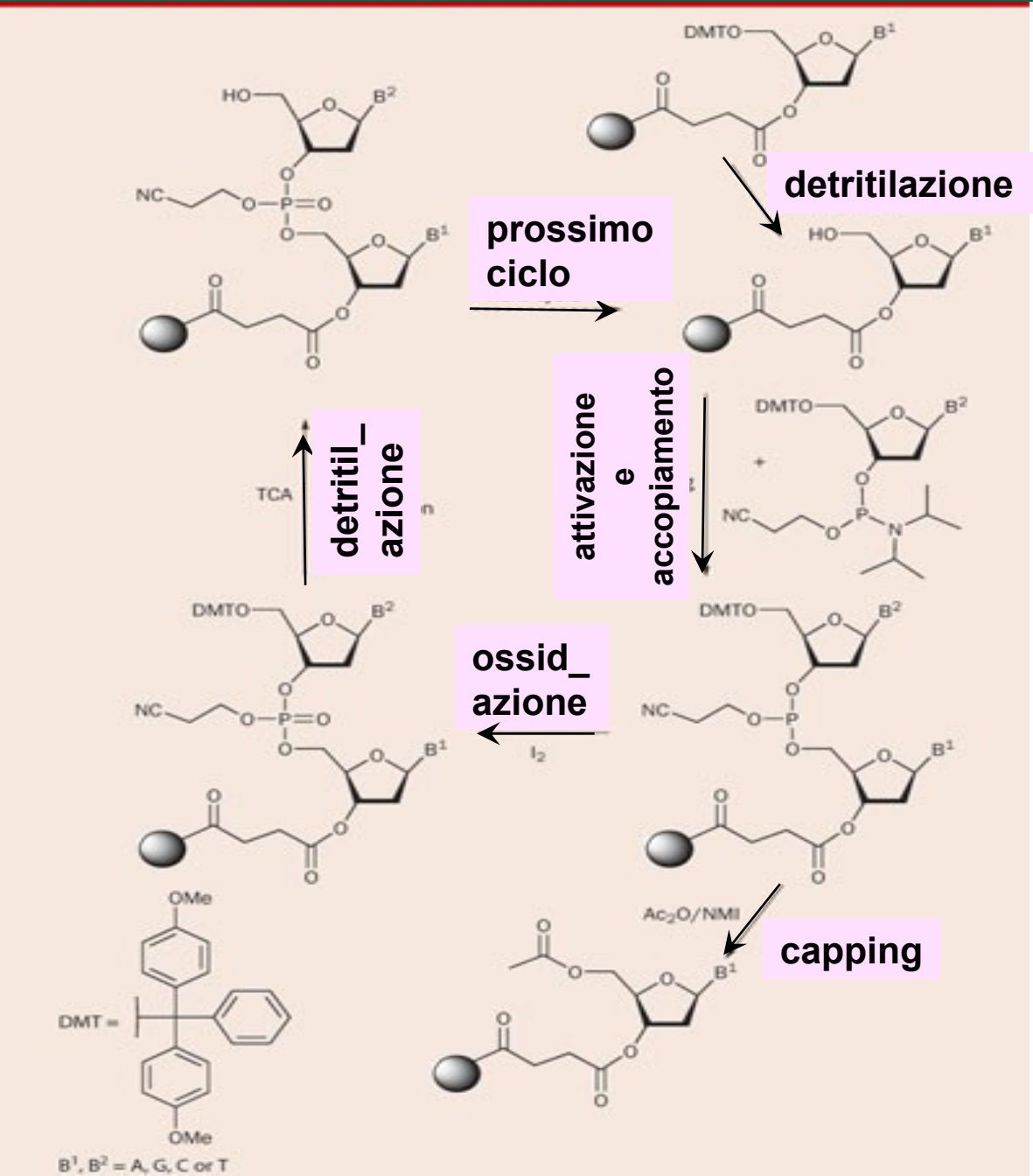


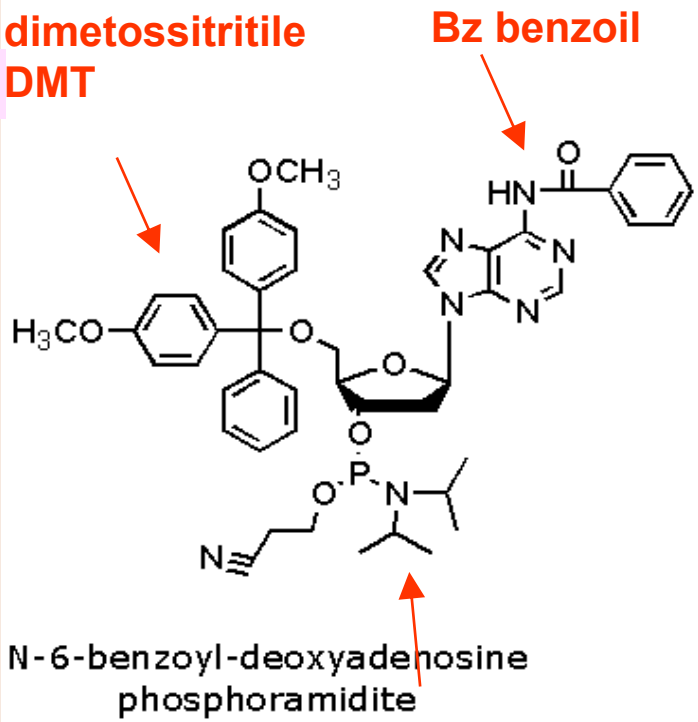
# SPPS – esempio di sintesi (cont.)



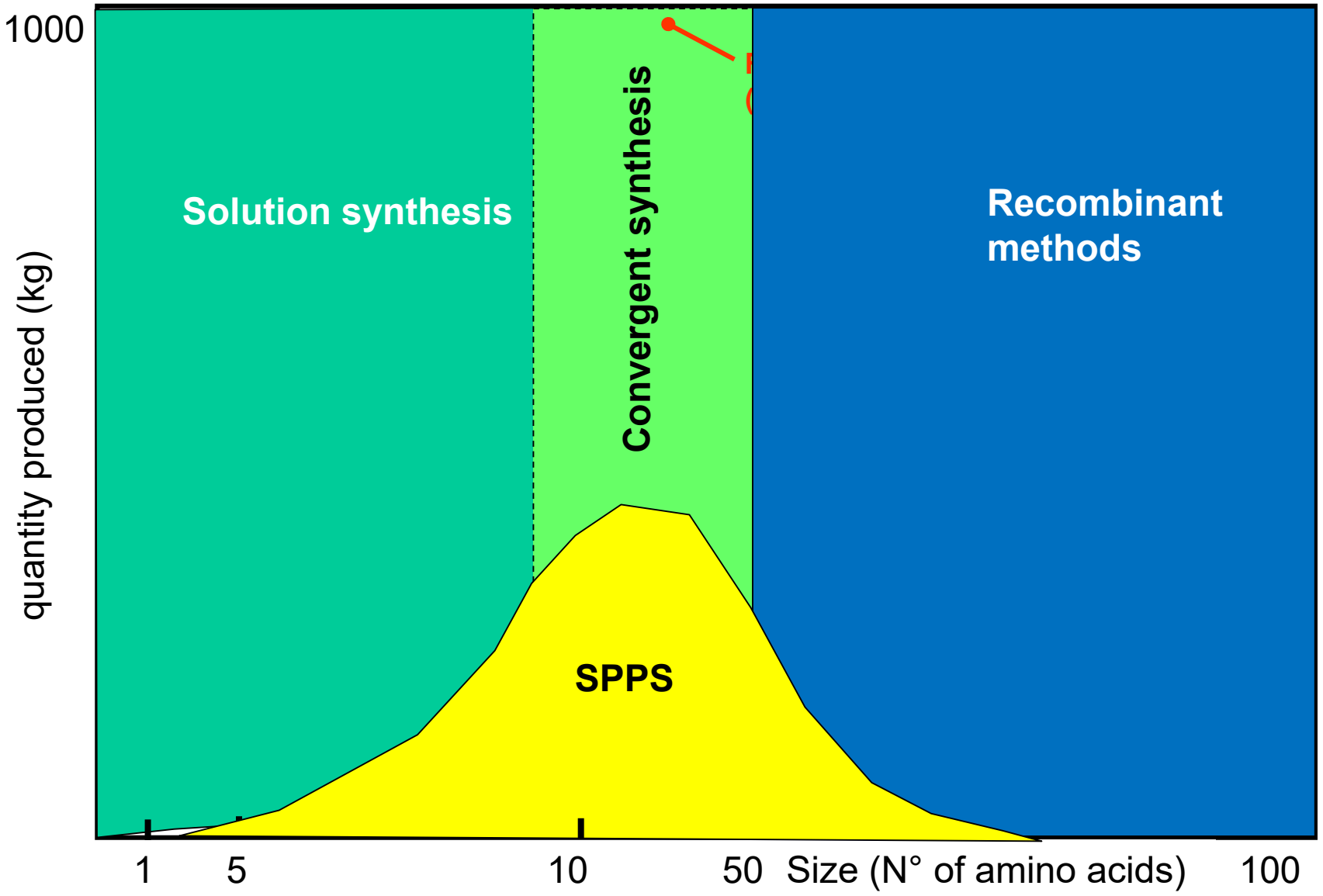
# Sintesi in fase solida di DNA




**Residuo nucleotidico protetto**



# Polyeptide synthesis – Choice of method



# Synthetic peptide applications

- **USO TERAPEUTICO -** **AIDS, controllo nascite, antitumorali, controllo della crescita, ipertensione, immunostimolazione e soppressione, infertilità, osteoporosi, diabete**
  **(fuzeon, insulina, interferone/interleuchine, calcitonina)**
- **USO VETERINARIO -** **fattori di crescita, ormoni, vaccini**
- **PRODOTTI ALIMENTARI -** **dolcificanti, esaltatori antiossidanti**
  **(aspartame)**
- **AGRICOLTURA -** **erbicidi, insetticidi, metabolismo vegetale, antibiotici**
- **PRODOTTI INDUSTRIALI -** **fibre, sostanze adesive**

**Miliardi di $ per anno**