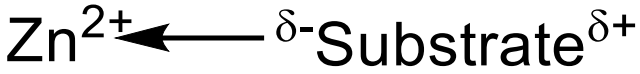
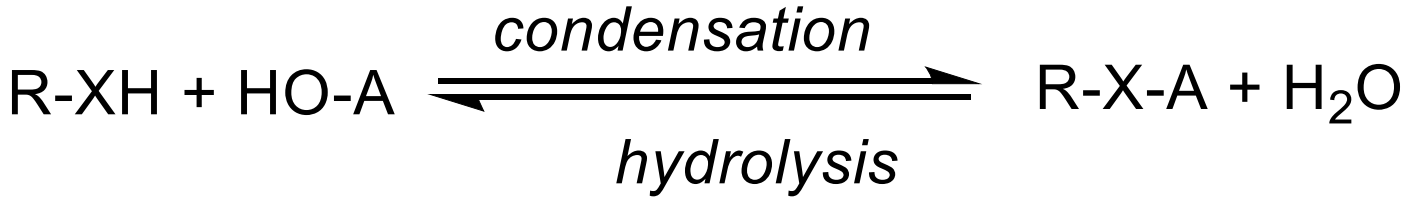
Zn^{2+} as a Lewis acid



The hydroxide ion bound to zinc, $[Zn\text{-}OH]^+$, is a weaker nucleophile compared to free OH^-, but definitely stronger than H_2O and much more abundant than OH^- at physiological pH.

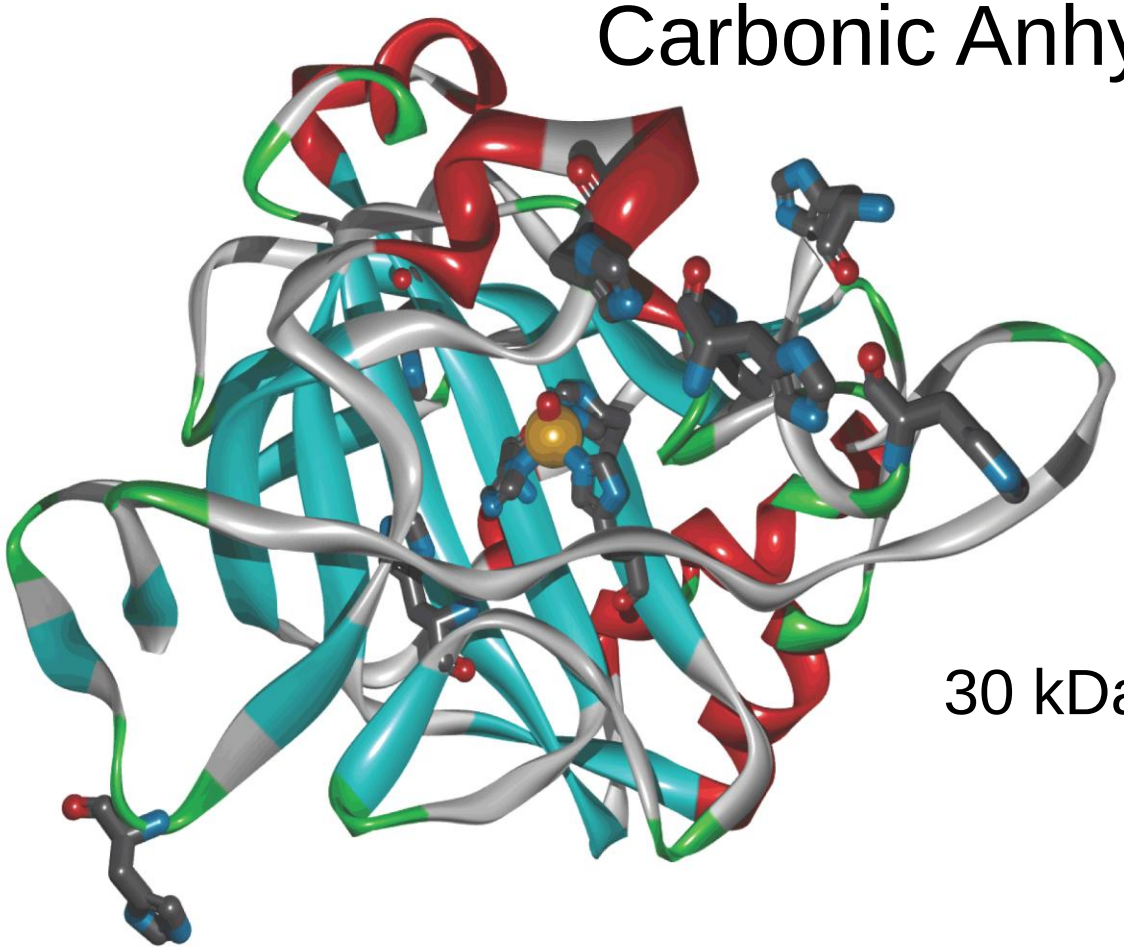


X = NH, A = -CO-R	*peptidase, lactamase, collagenase*
X = O, A = -CO-R	*esterase*
X = O, A = PO_3^{2-}	*phosphatase, nuclease*

Main features of biological zinc

- Exclusively as Zn^{2+}
- d^{10} (no LFSE)
- Flexible coordination number and geometry
- Catalytic (as Lewis acid) or structural role
- More than 200 Zn-proteins known (*zincosome*)

Carbonic Anhydrase

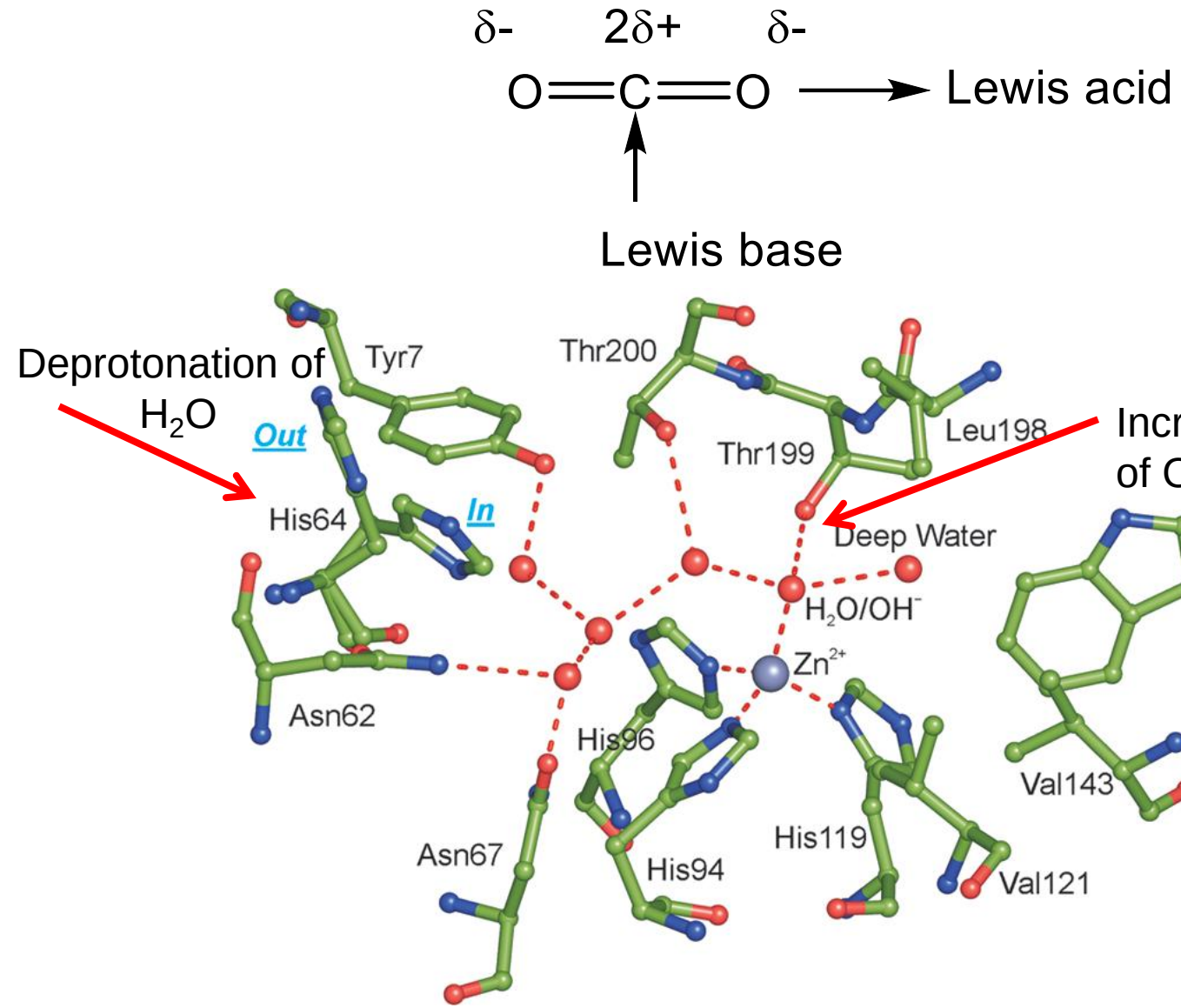


30 kDa, 259 a.a.

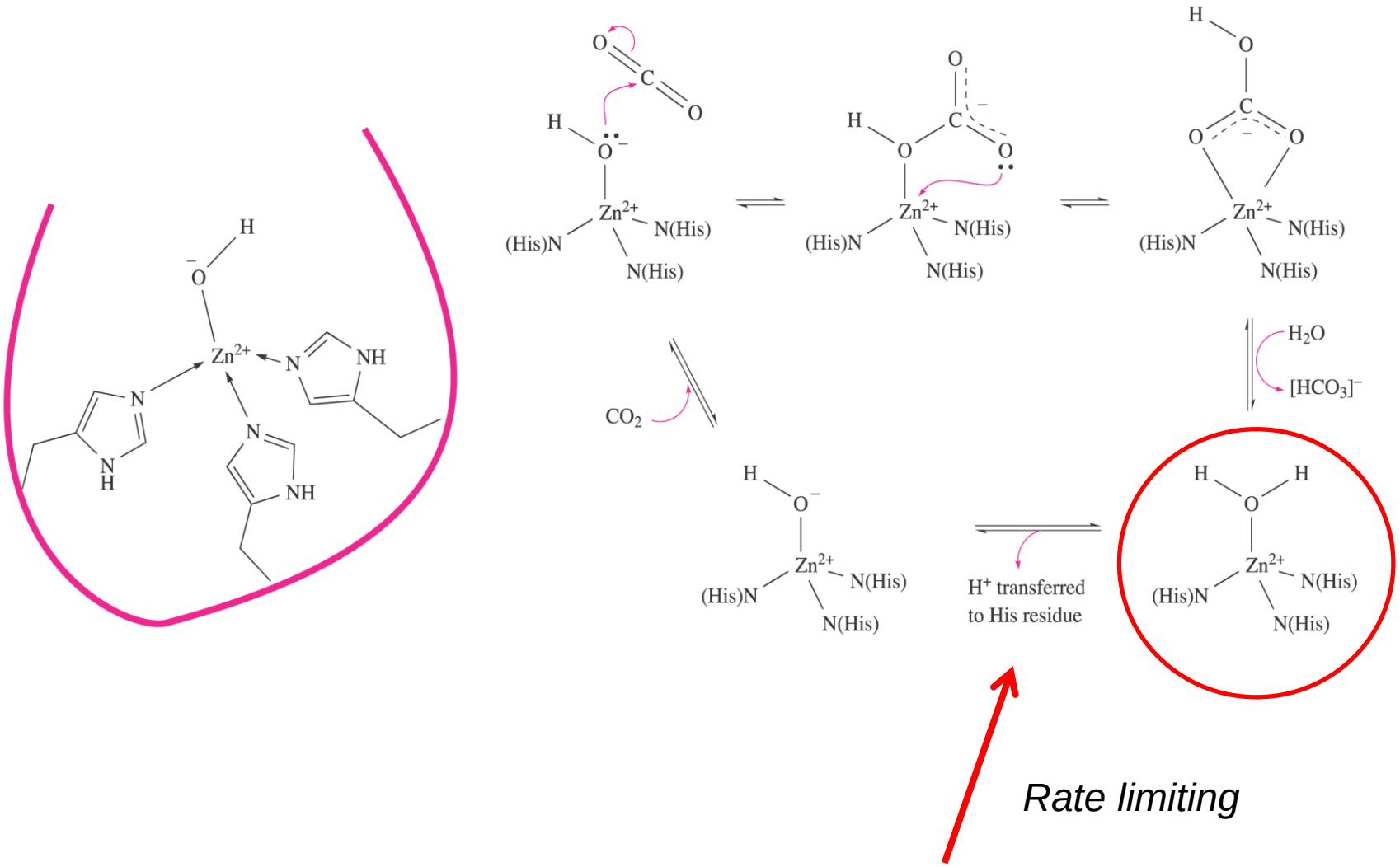
$$H_2O + CO_2 \rightleftharpoons HCO_3^- + H^+$$

$k \approx 10^{-1}\ s^{-1} \rightarrow 10^{6}\ s^{-1}$

Catalytic site of carbonic anhydrase

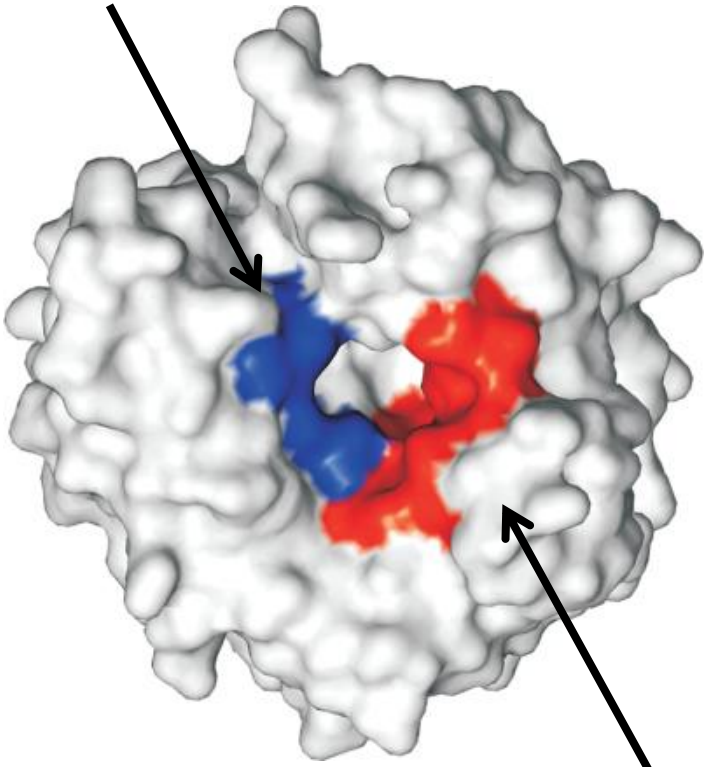


Catalytic cycle of carbonic anhydrase

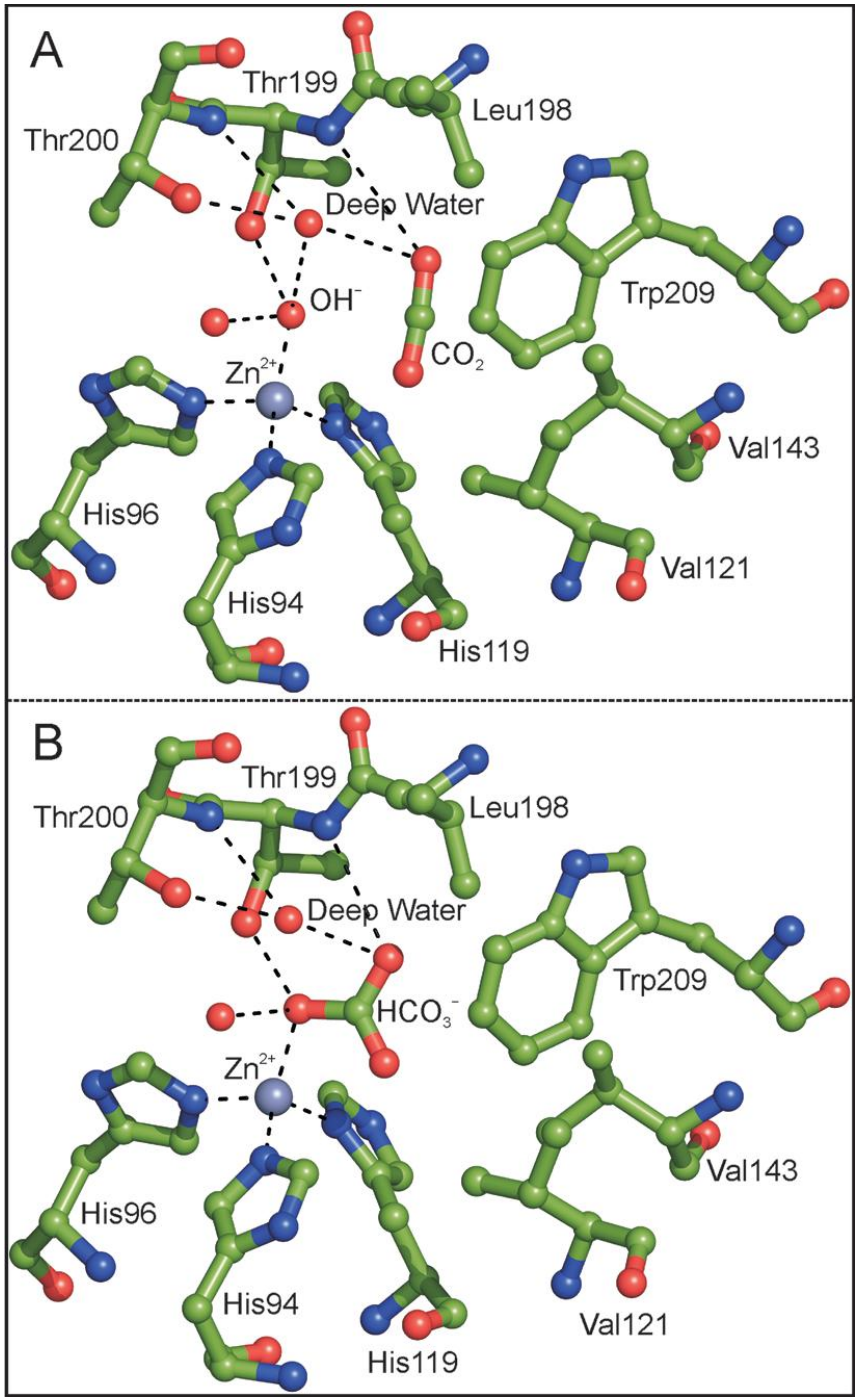


Catalytic cleft in CA

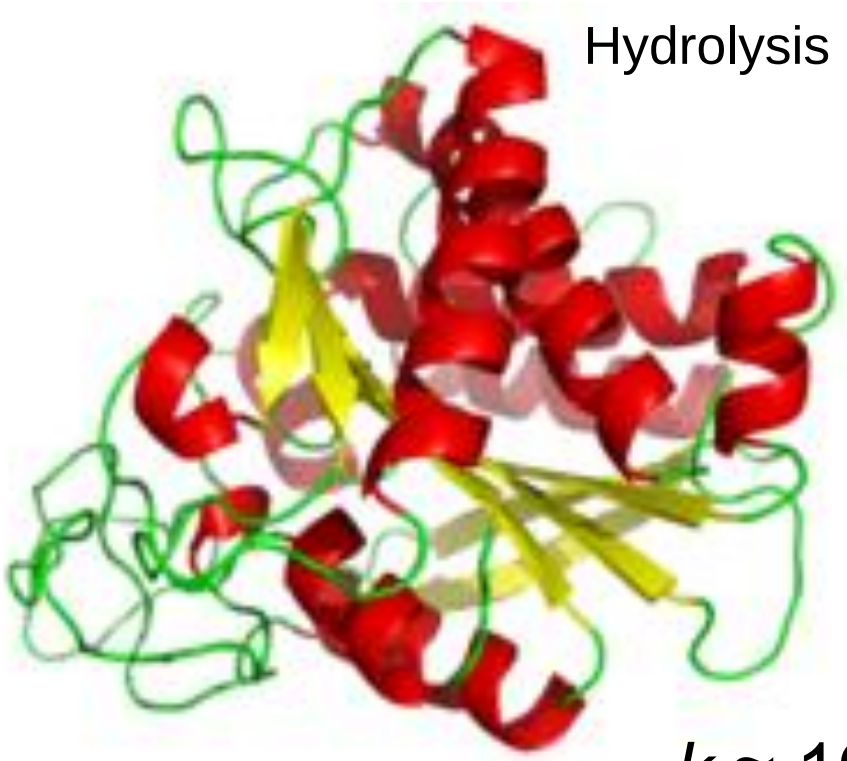
Hydrophilic region



Hydrophobic region



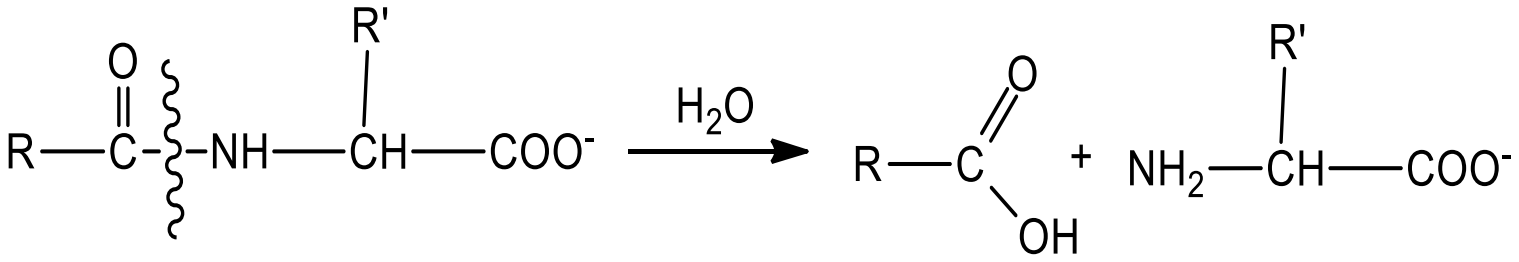
Carboxypeptidase A (CPD A)



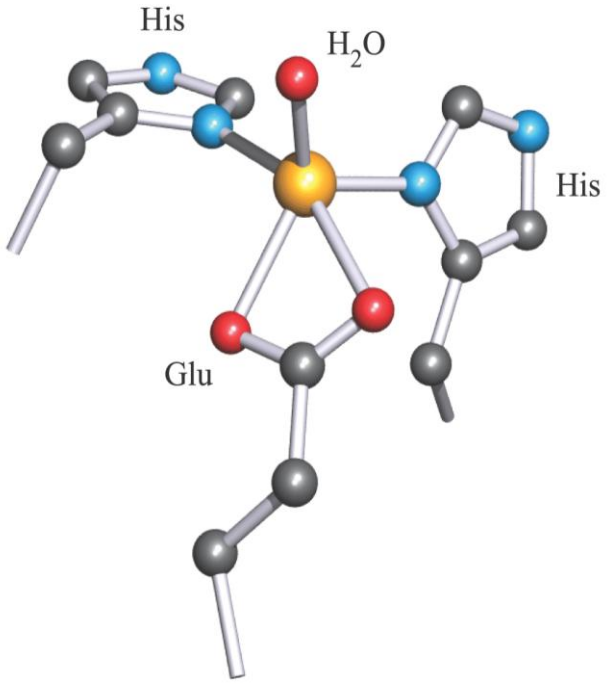
Hydrolysis of C-terminal aminoacids

34 kDa, 300 a.a.

$k \approx 10^{-11}\ s^{-1} \rightarrow 10^{4}\ s^{-1}$

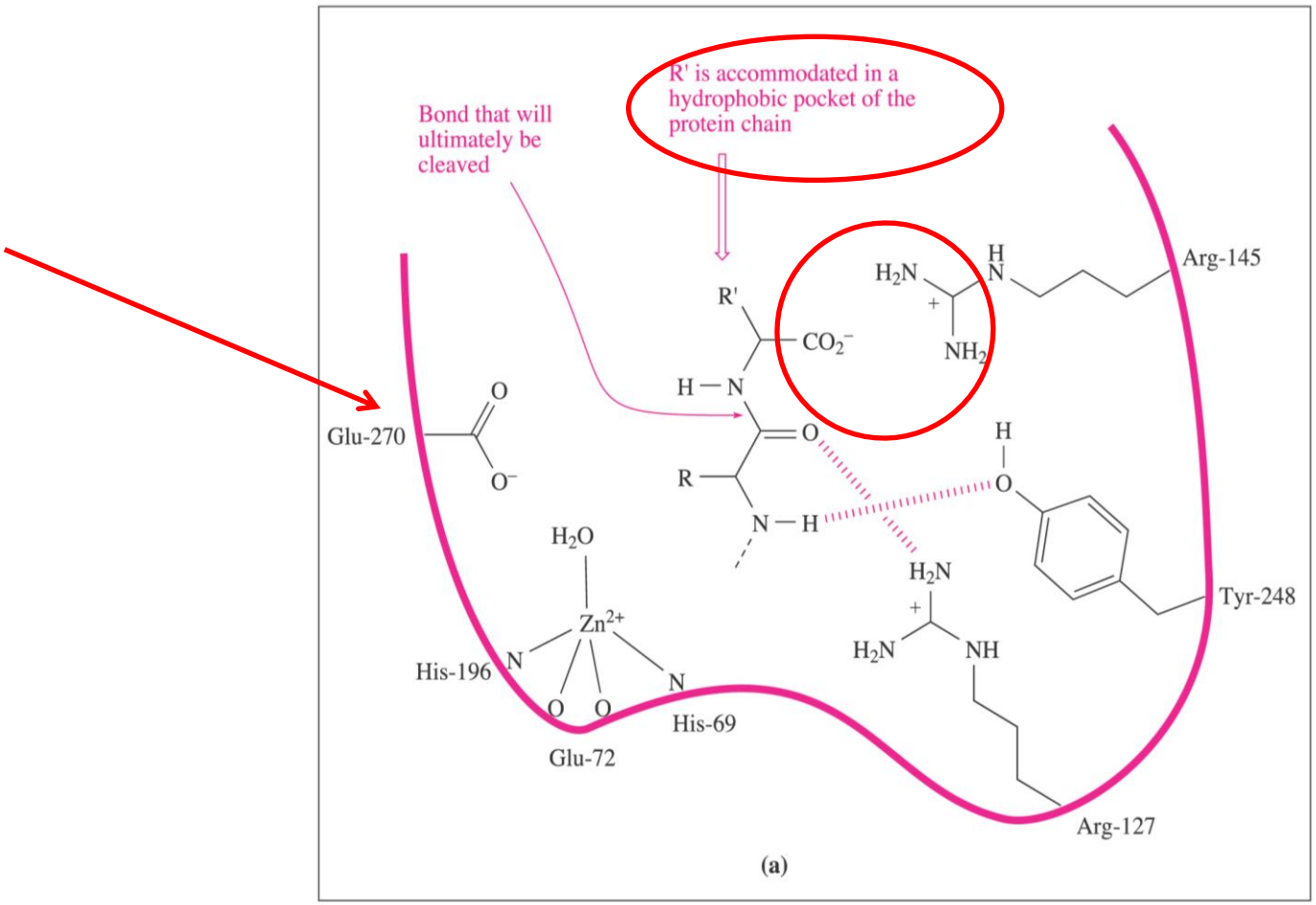


Active site in CPD A

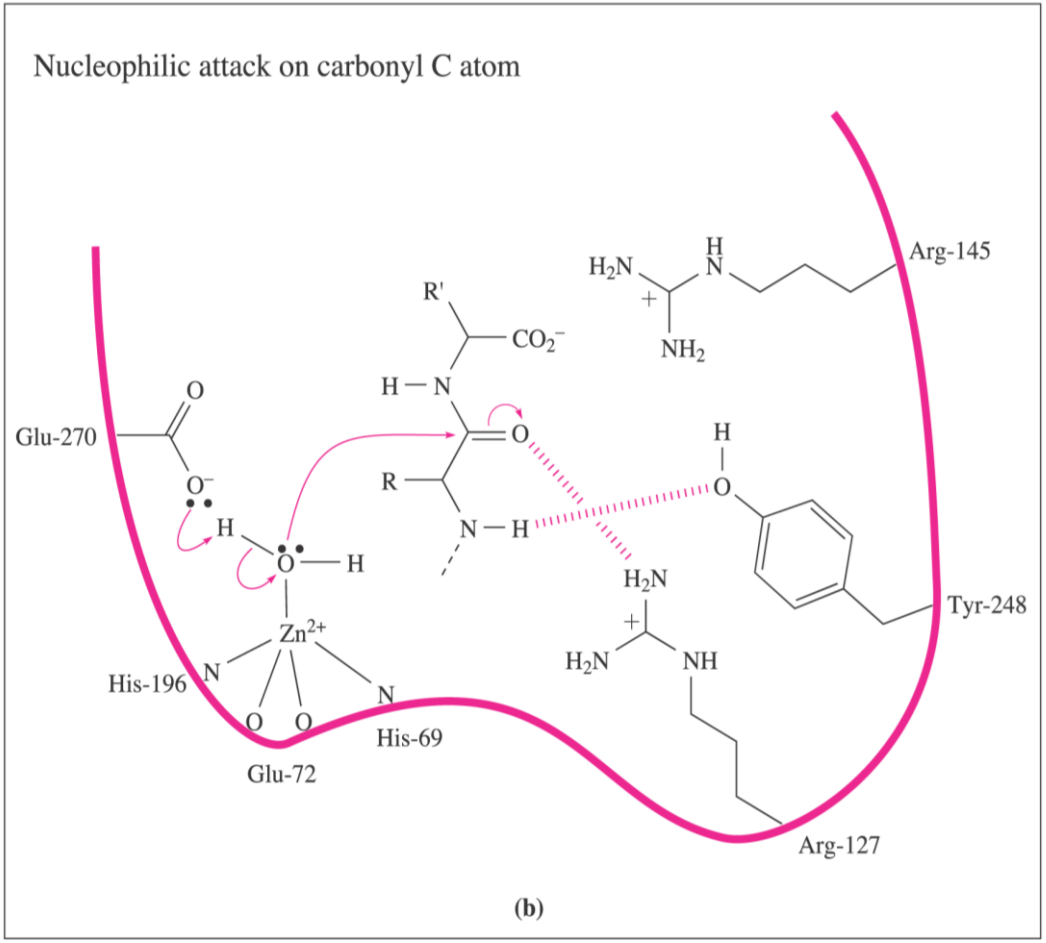


Carboxypeptidase A (CPD A, bovine)

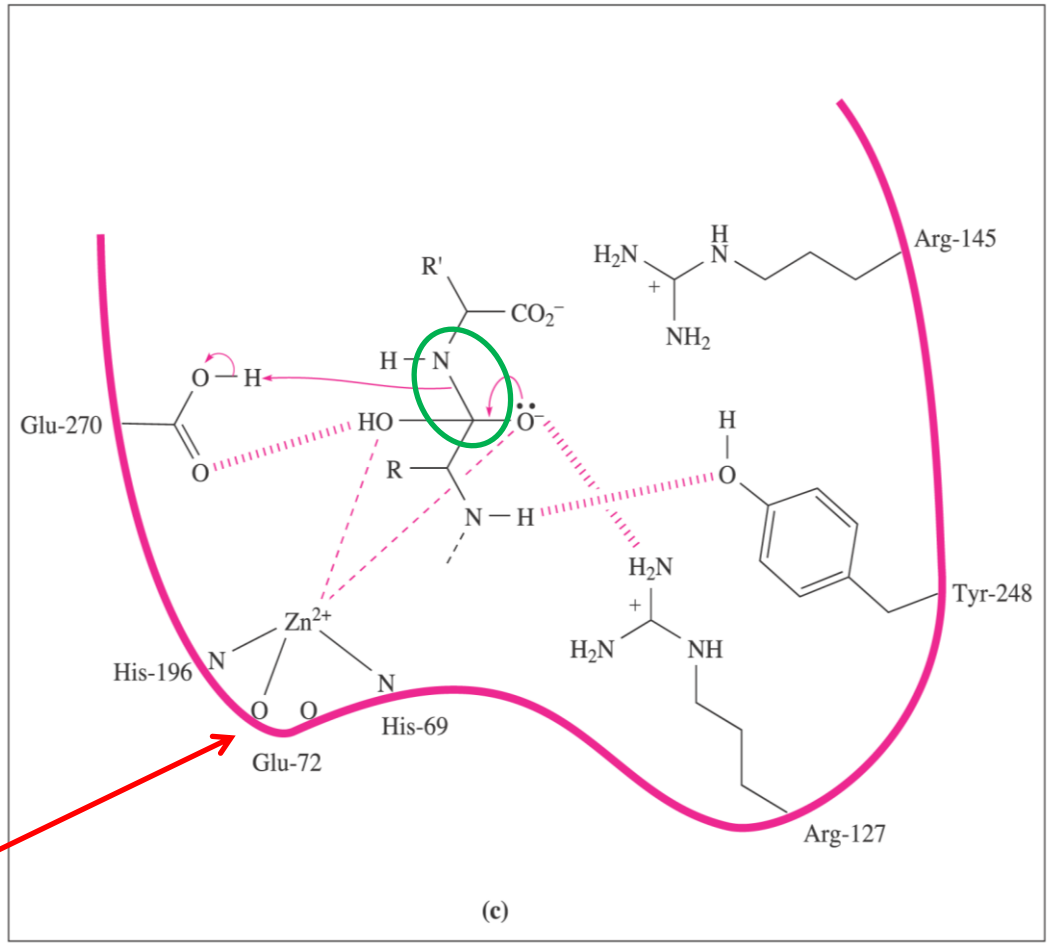
Positioning of the substrate close to the active site of CPA



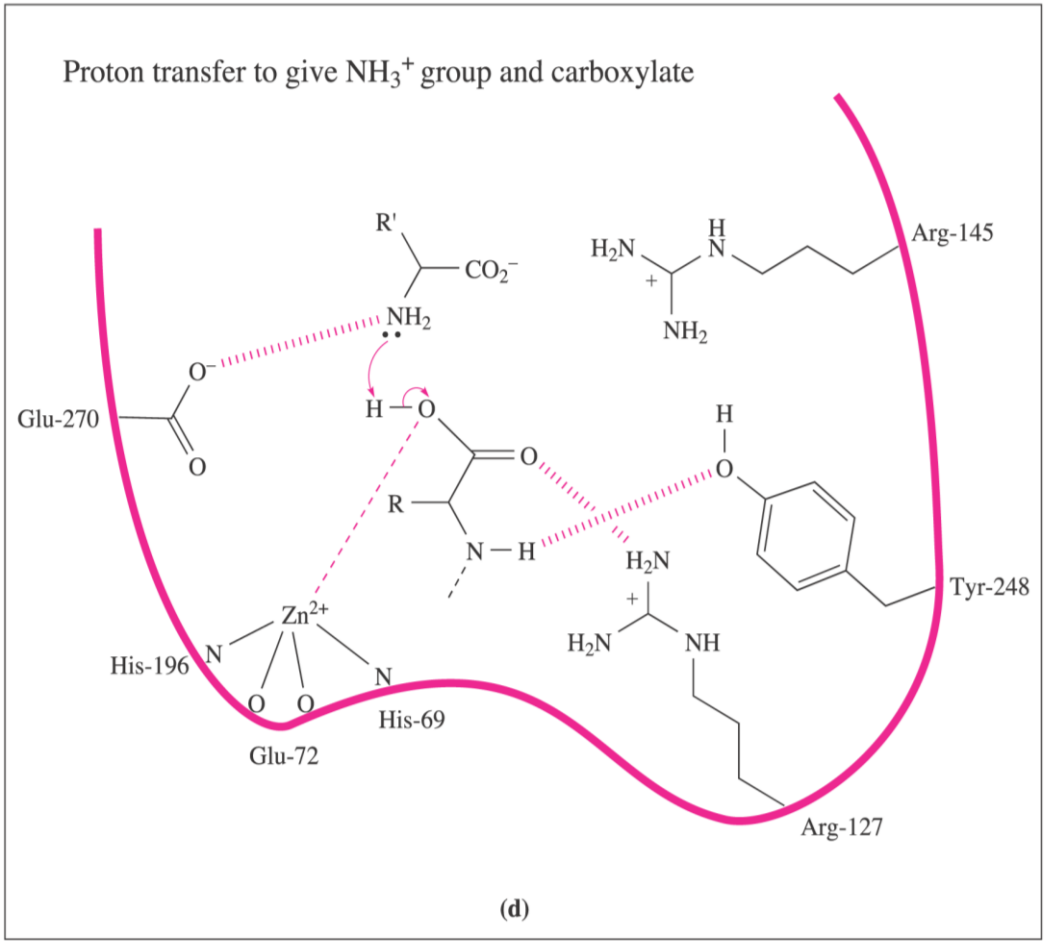
Deprotonation of water molecule and nucleophilic attack



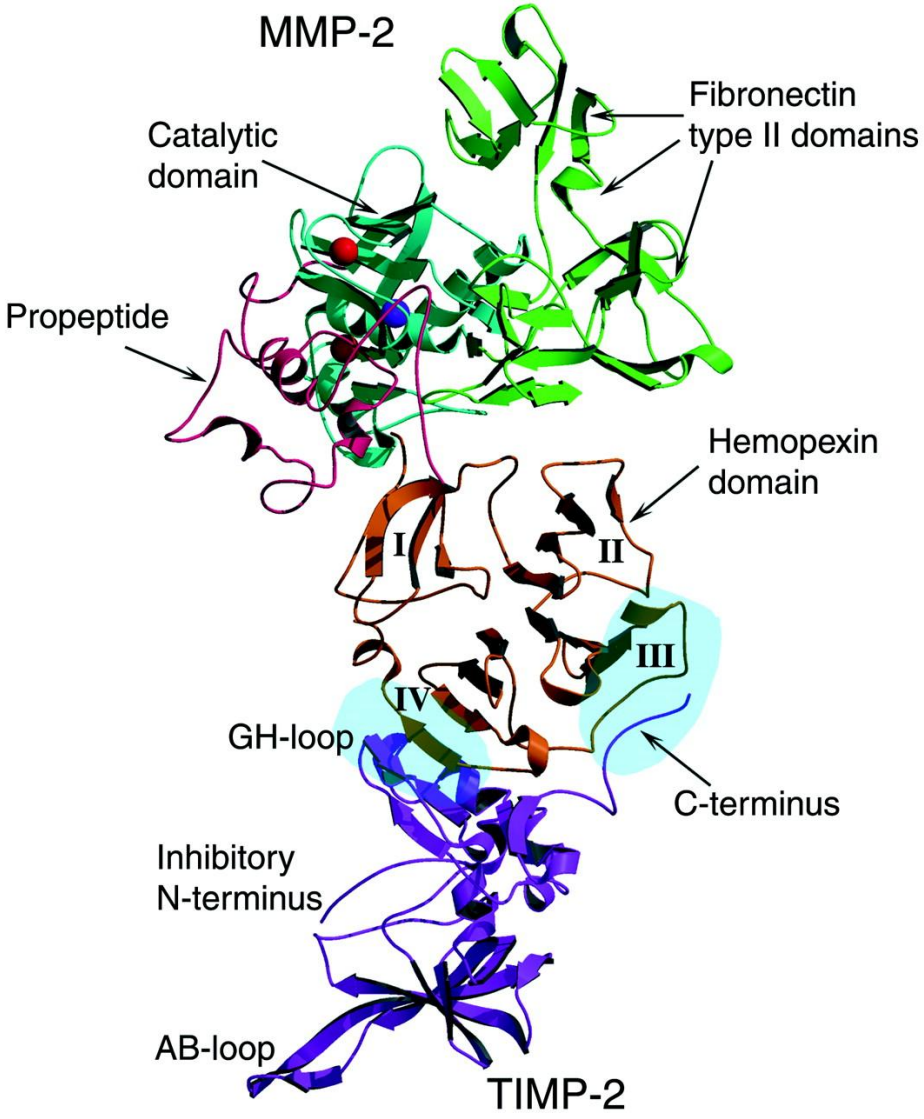
Cleavage of the C–N peptidic bond



Proton transfer with formation of the NH_3^+ and COO^- groups



Matrix MetalloProteinases (MMPs) + Tissue Inhibitors of MetalloProteinases (TIMPs)

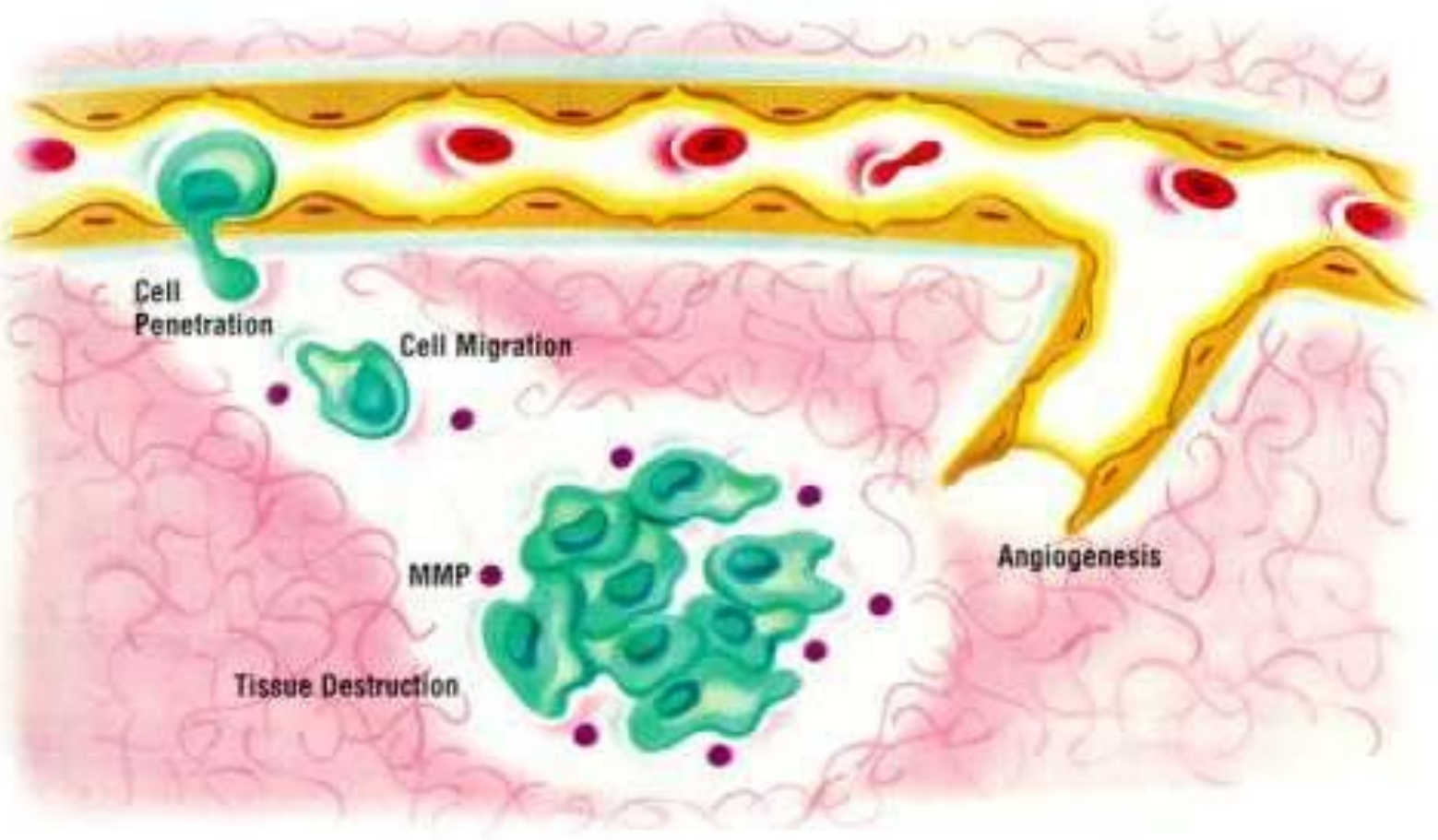


= Zn

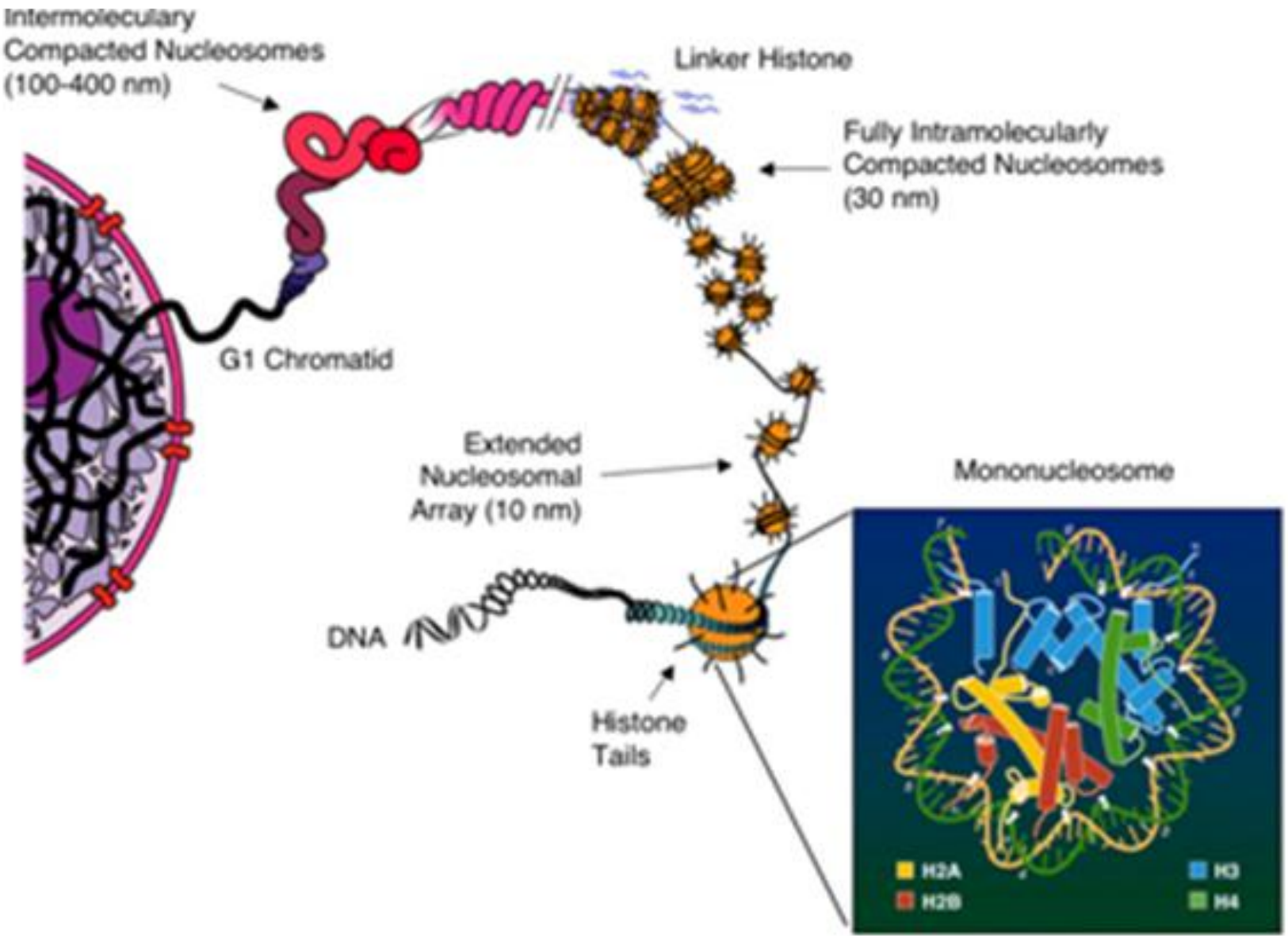
= Ca

Zinc-endopeptidases that degrade the proteins constituting the extracellular matrices (e.g. collagen)

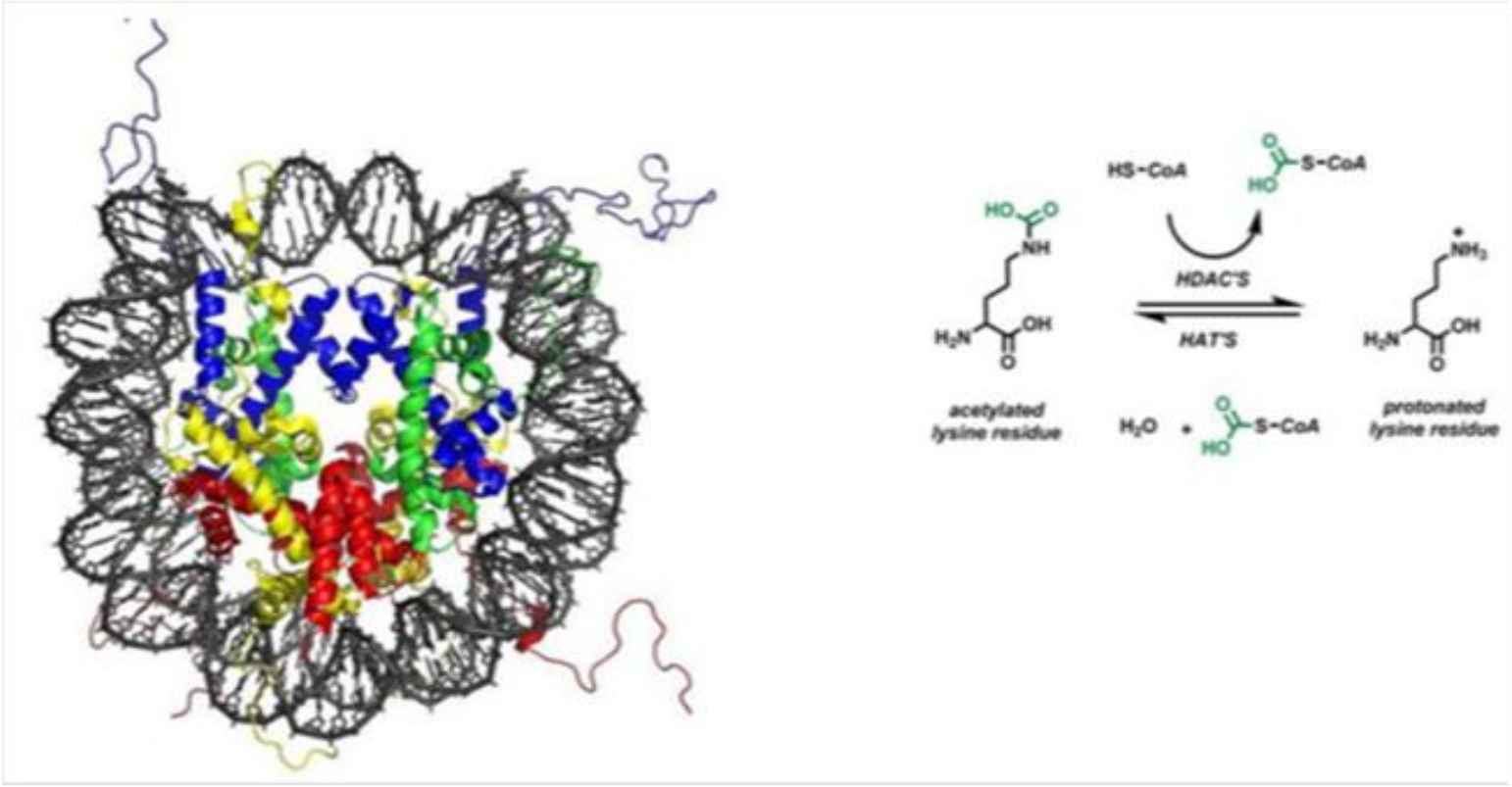
Metastatic process facilitated by MMP



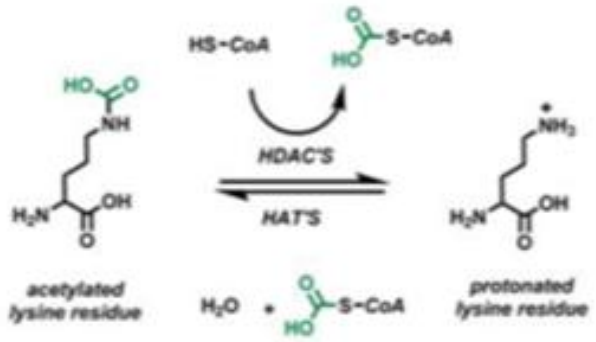
Chromatin, Nucleosomes and Histones



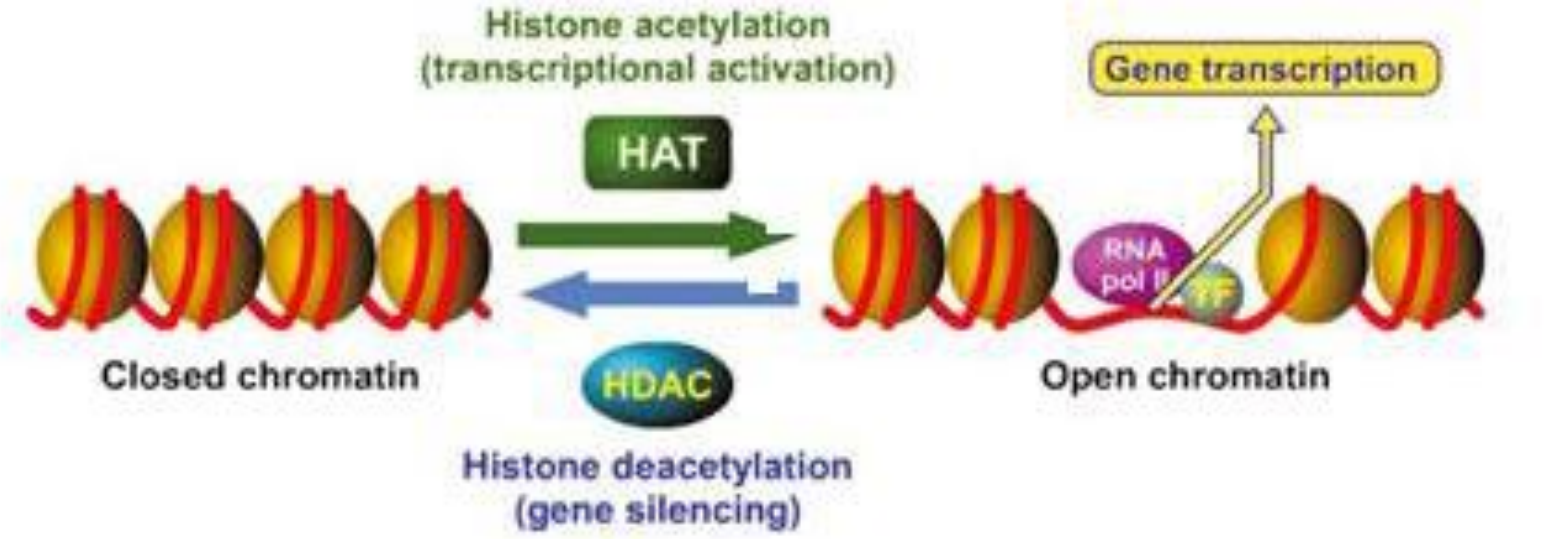
Histone deacetylase (HDAC)
and
Histone acetyltransferase (HAT)



Nucleosome and Histones

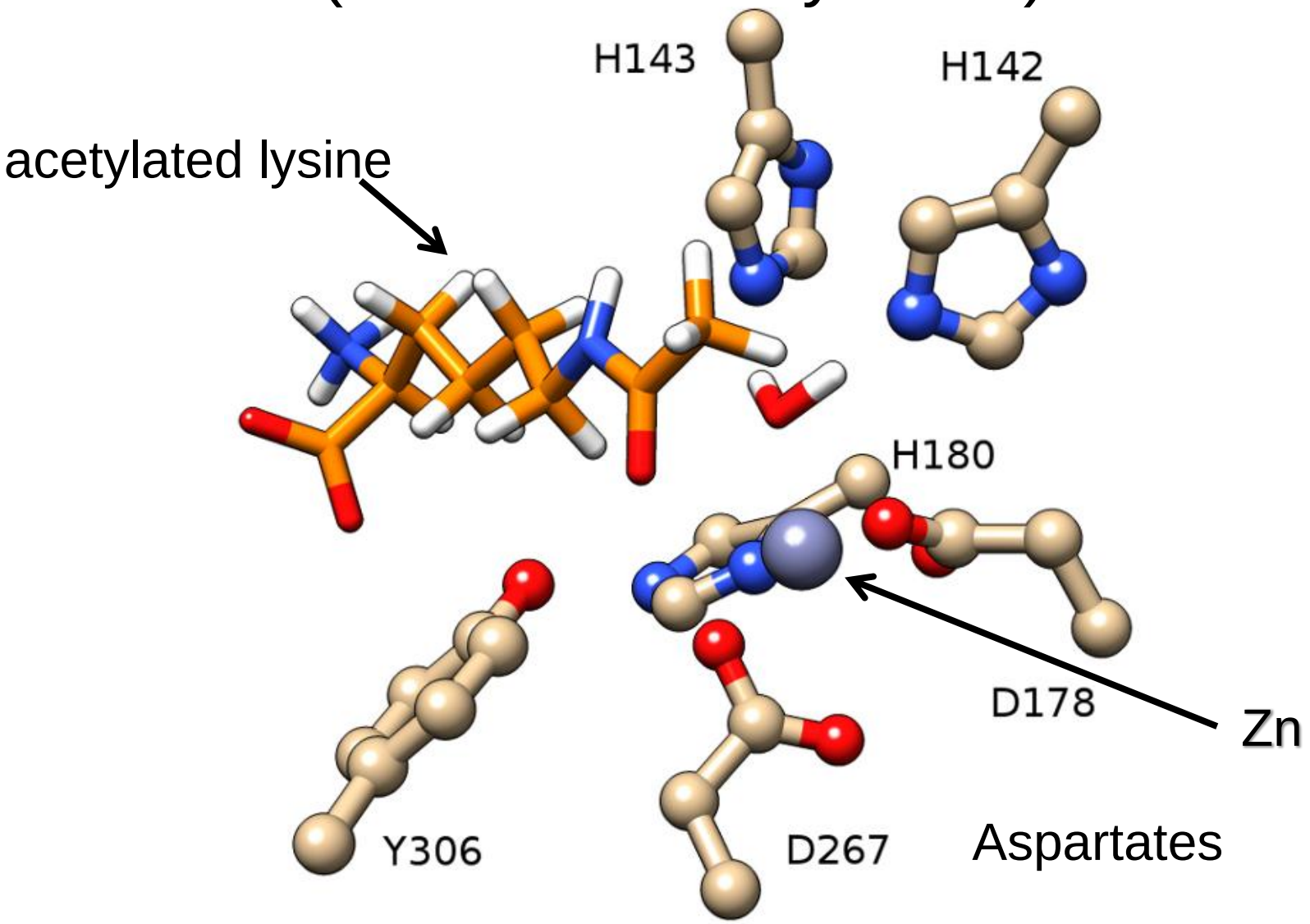


acetylation and deacetylation of histone lysins

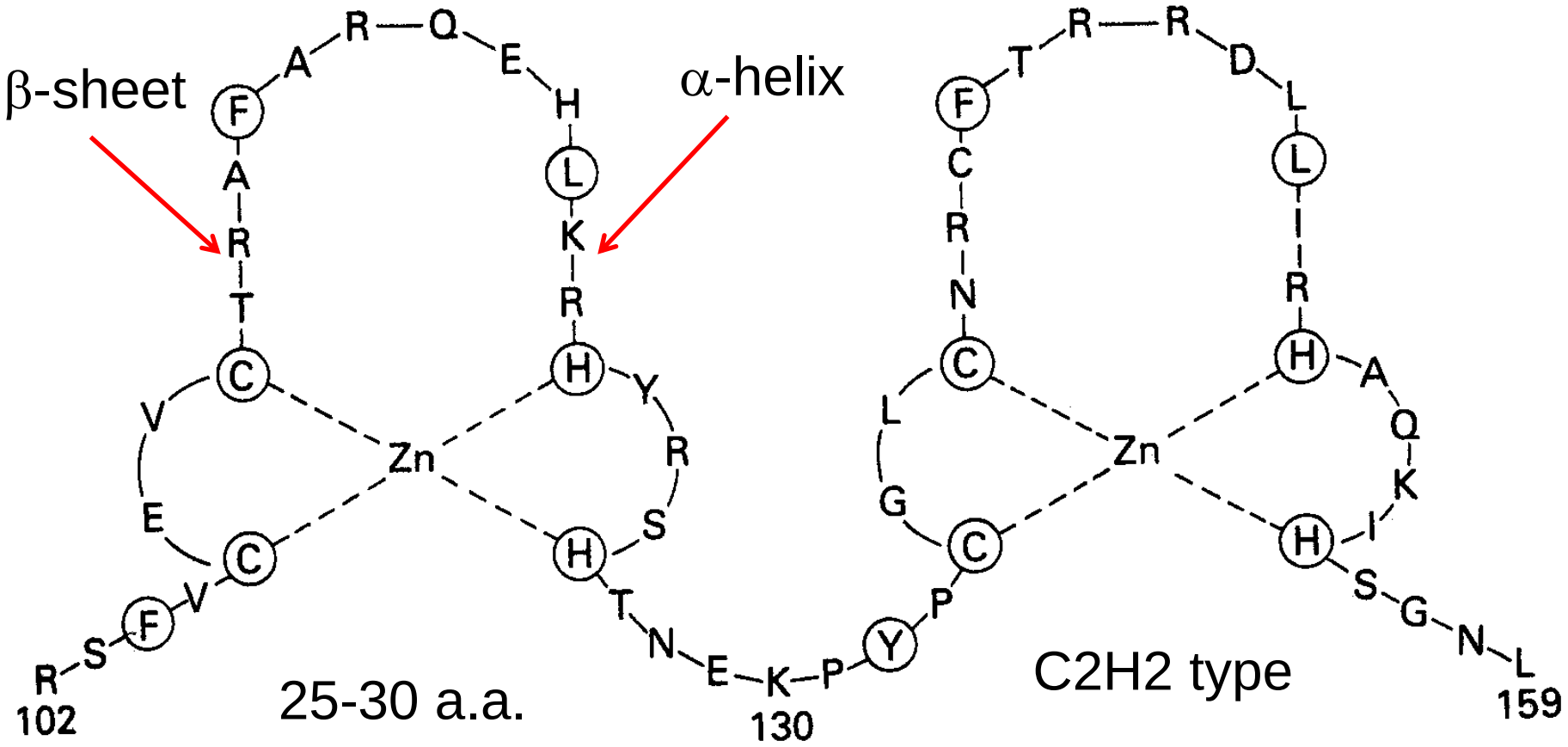


epigenetic modulation

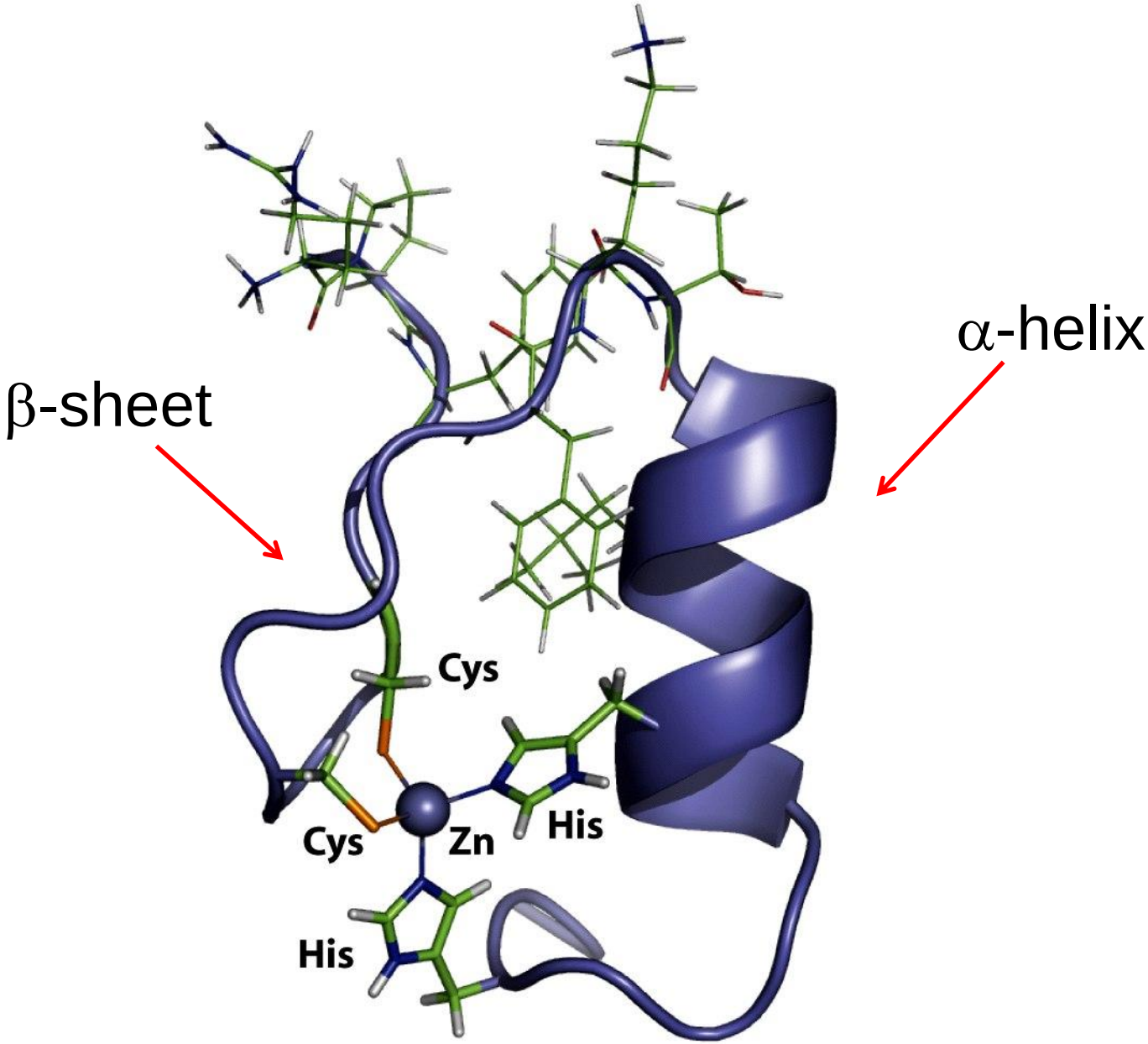
Active site of HDAC8 (histone-deacetylase 8)

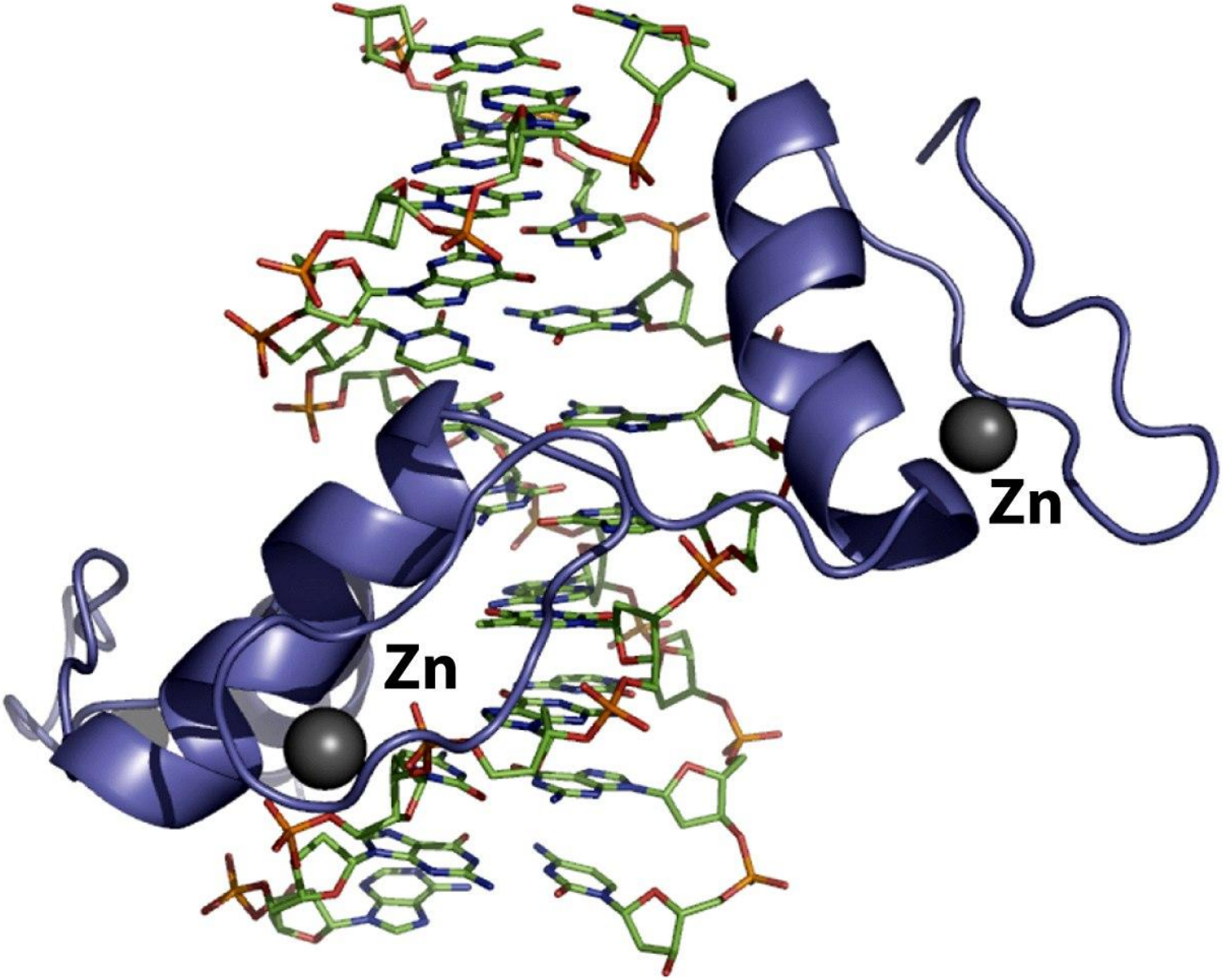


Zinc fingers



gene regulatory proteins e *transcription factors*


β-sheet
α-helix
Cys
Cys
Zn
His
His



Interaction between zinc-fingers and DNA