Structure and Function of Antibodies

Folder Title: Antibody

Filename: antibodyNoTP.ppt

Updated: Sept. 17, 2012
This presentation was revised Monday September 17th, 7 PM.
Revised version wasadded to Class Schedule and Graphics 9/18/12.

Targets and Weapons in the Specific Adaptive Immune Response

Responds to Antigenic Determinants (Epitopes)

Responds With:

Lymphocyte	Receptor	Primary "Weapon"
B-Cell	Membrane-bound Antibody	Extra-cellular Antibody
T-Cell	T-Cell Receptor	Extra-cellular Cytokines

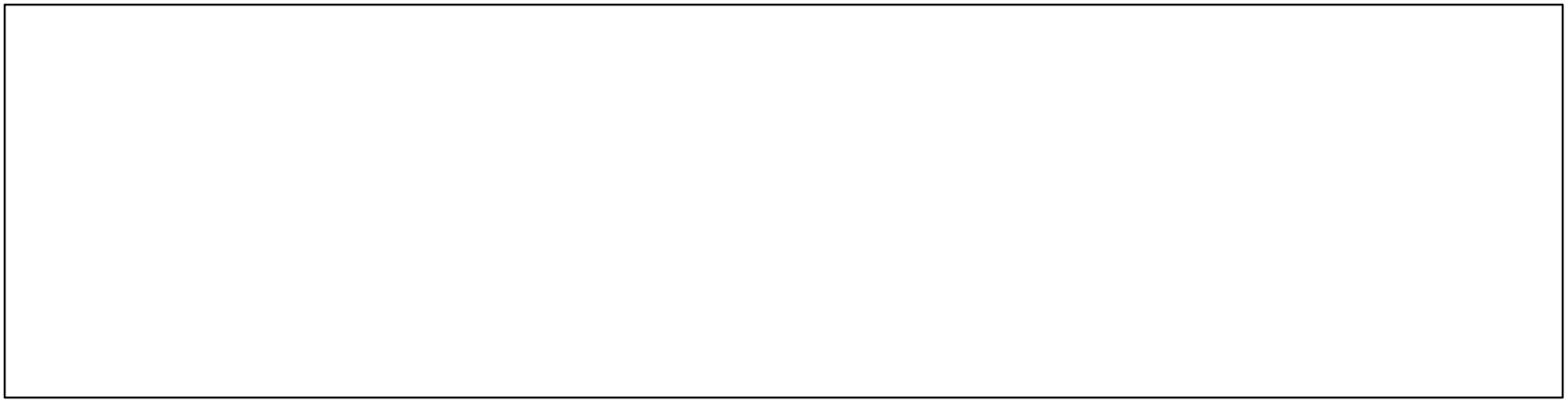
Rec&Resp

Questions About B-Cell Responses

Biochemical: How can Ig's Recognize so many different epitopes?

What does an antibody protein look like?

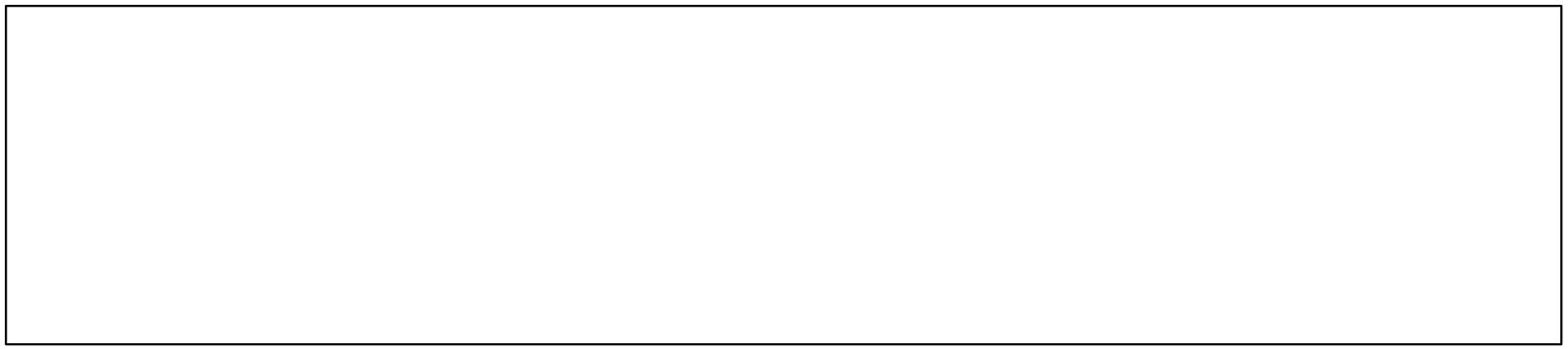
How do antibodies work?



Antibody Function

Binding to Target Antigens

V–Region Function

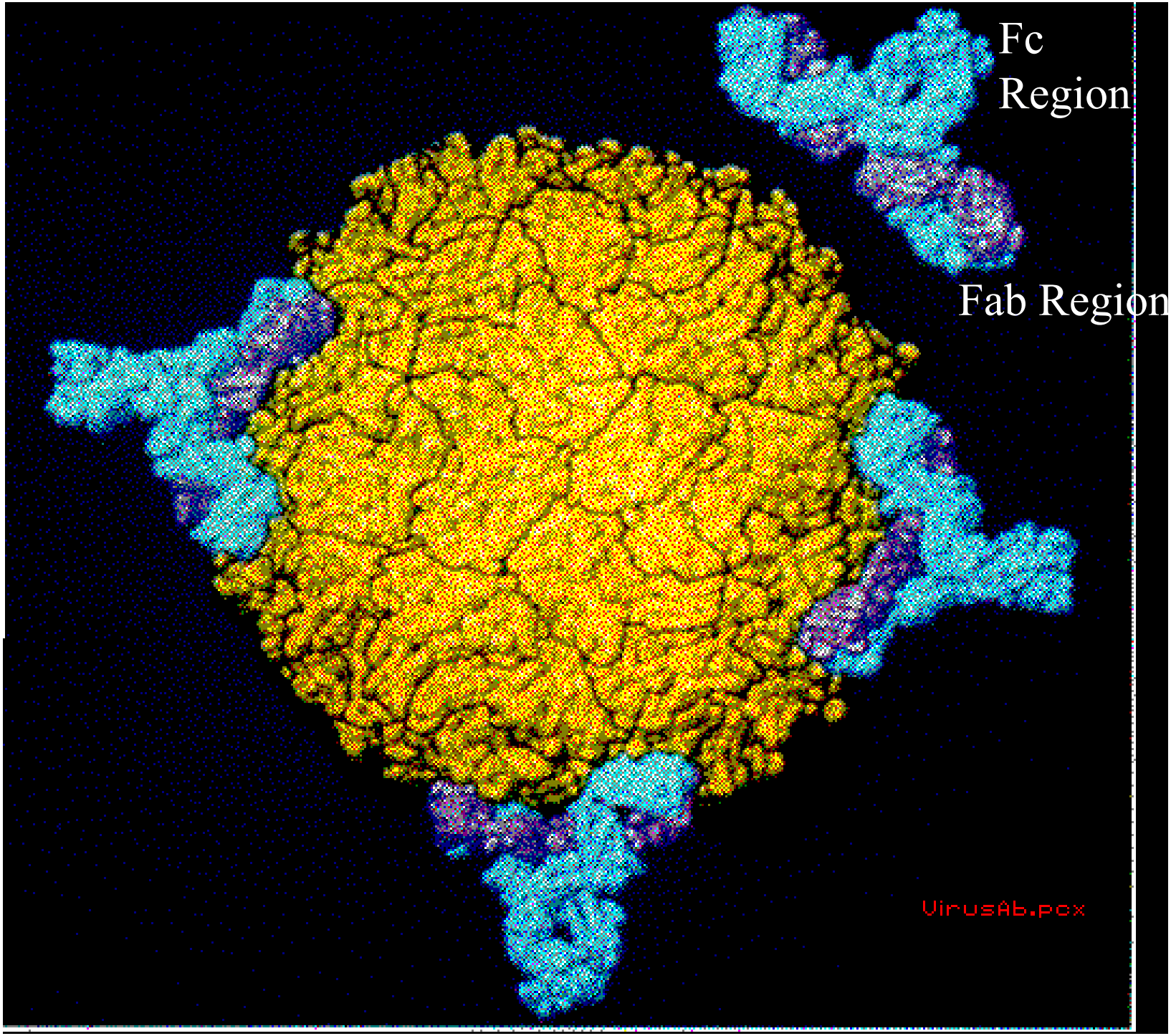


V&CRoles.pcx

From:

Golub &
Green

Plate 7-1

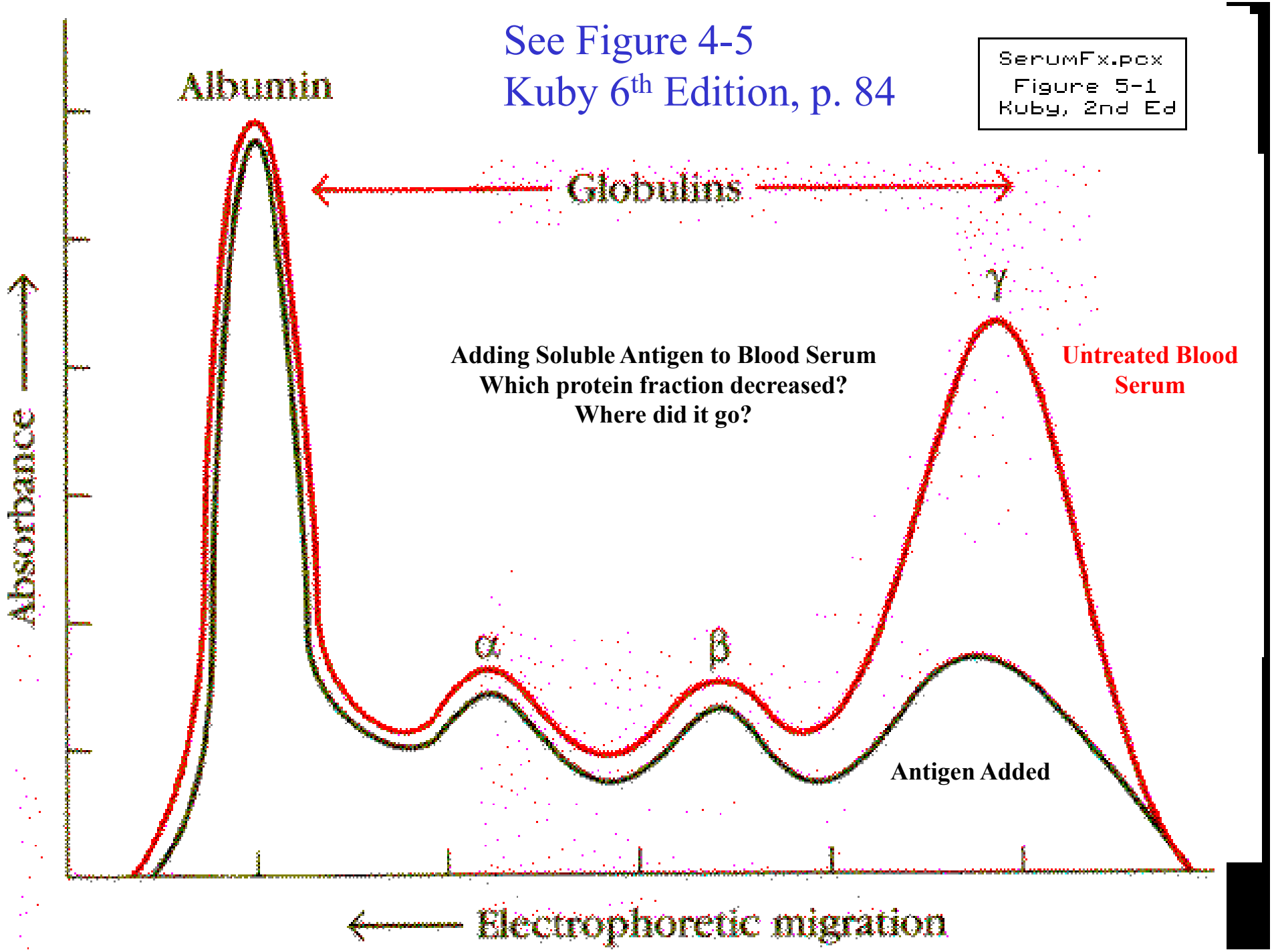


Protein Structure of Antibodies

A dimeric protein

Heavy and Light Chains
Multiple times depending on the antibody isotype

See Figure 4-5
Kuby 6th Edition, p. 84



Tetrameric Structure of IgG

See Figure 4-7
Kuby, 6th Edition
p. 86

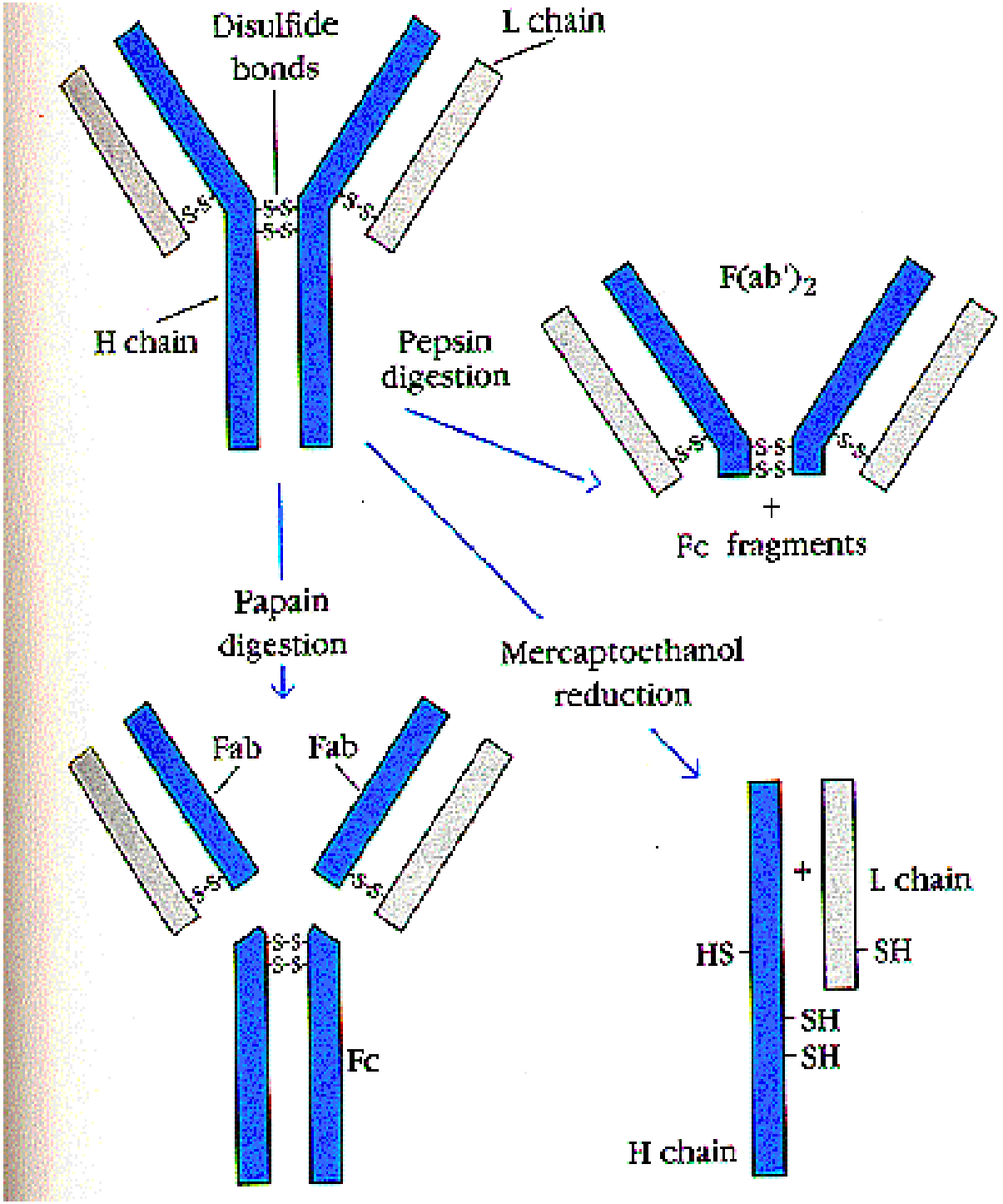


Figure 5-2, Kuby 3rd Ed.

IgG4mer

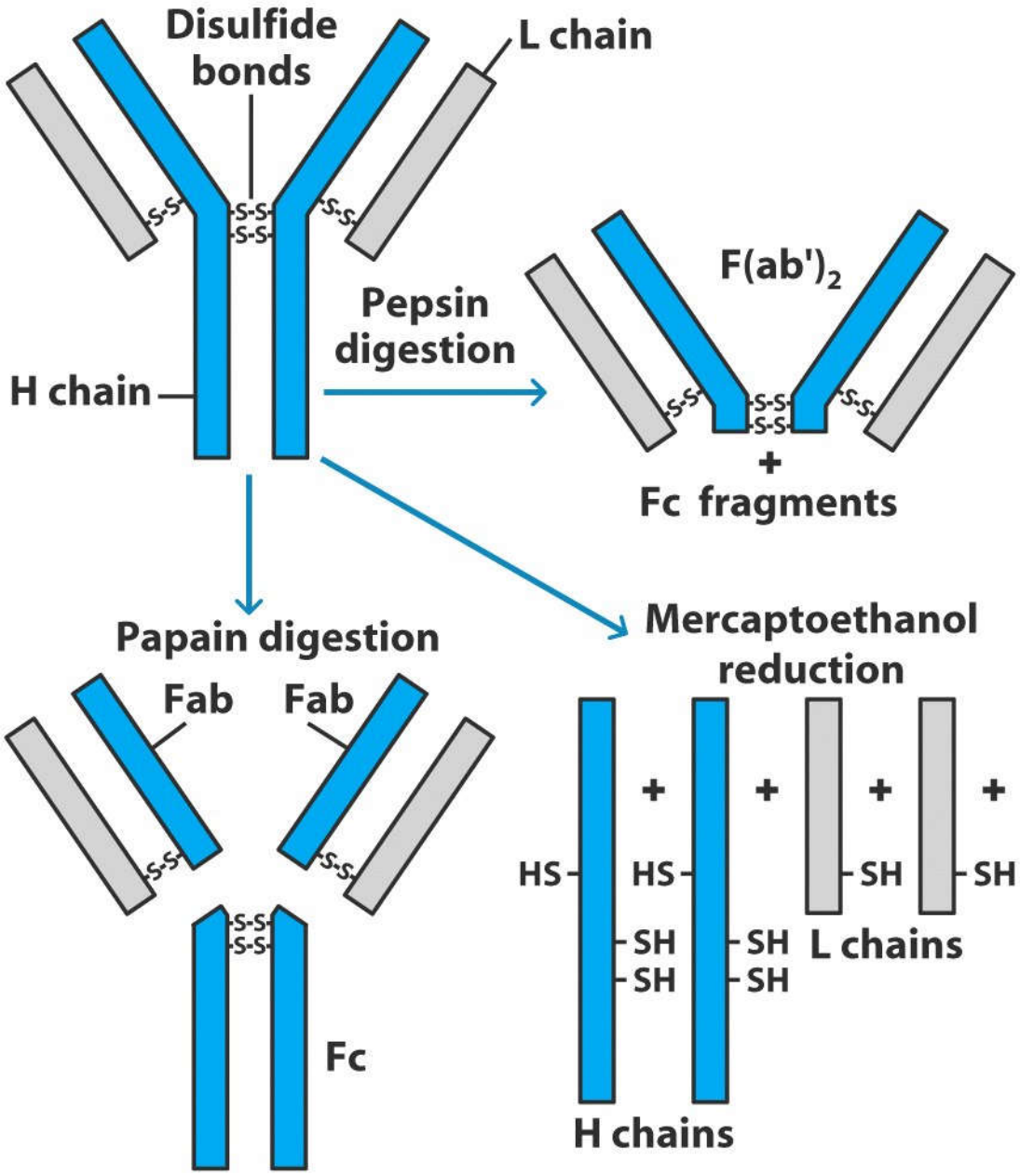
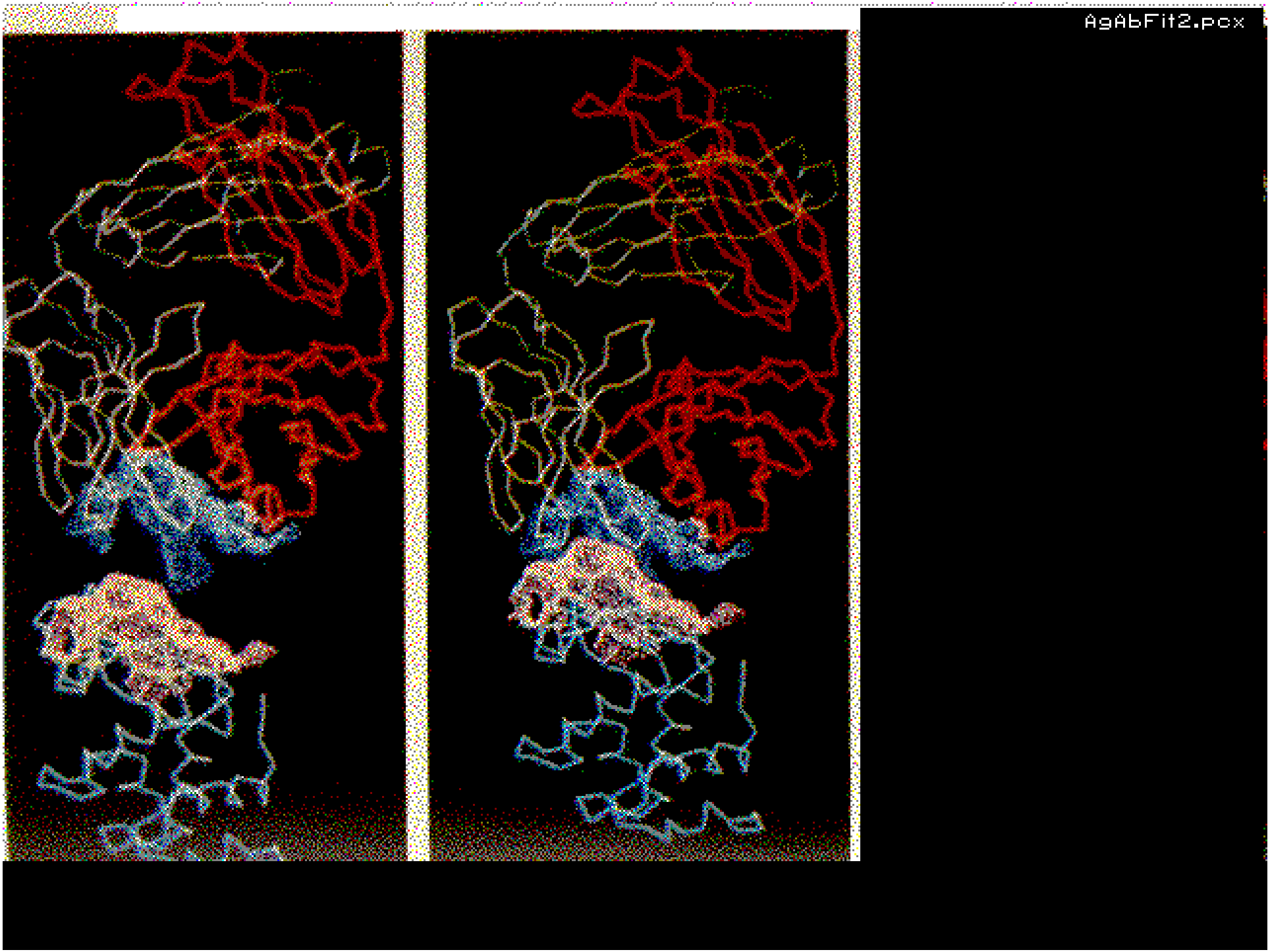


Figure 4-7
Kuby IMMUNOLOGY, Sixth Edition

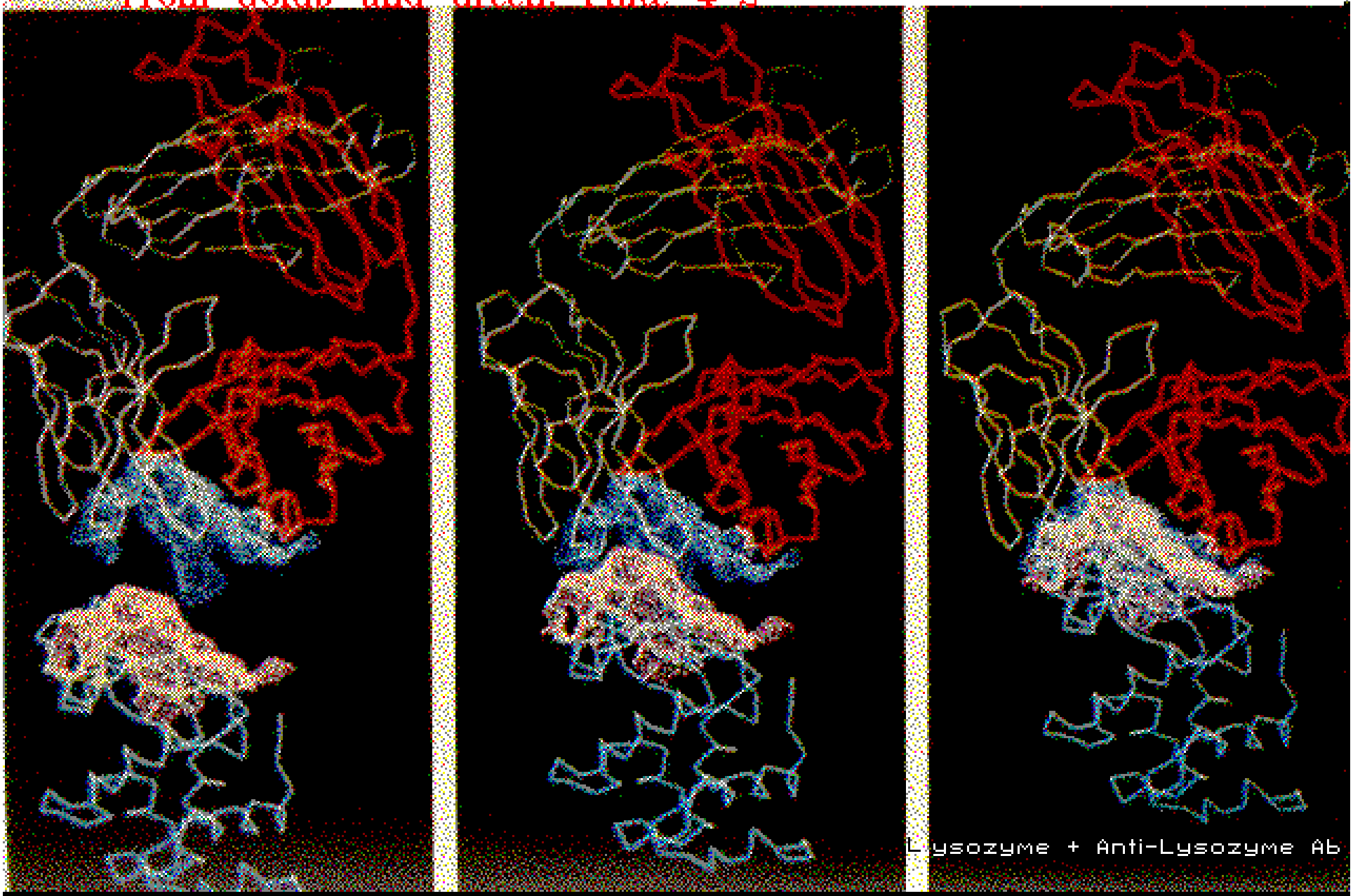
Complementarity of Antibody – Antigen Binding

AgAbFit1.pcx

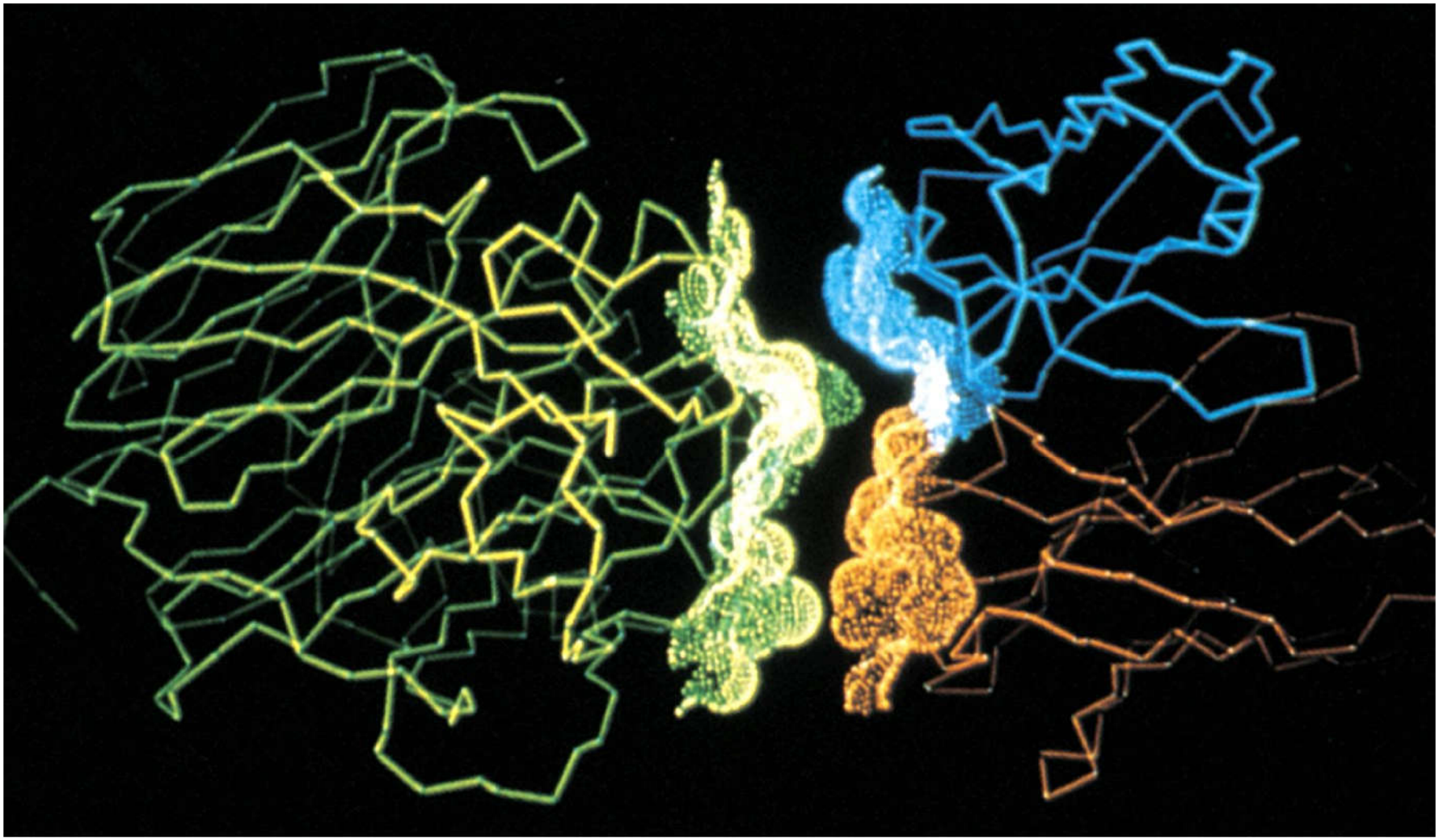

AgAbFit2.pcx

From Golub and Green: Plate 4-2

AgAbFit.pcx



See Also: Color Plate 8, 2nd Edition, Kuby



Chapter 4 Opener
Kuby IMMUNOLOGY, Sixth Edition

As Proteins:

How Do Antibodies Bind to Virtually an Infinite Number of Different Possible Antigens?

Representation of Sequence Comparisons Among Light Chains from Antibodies with Three Different Antigen Specificities

H3N-Ser-Val-Ile-Thr-Gly-Gly-Tyr-Ala... Thr-Glu-Ala-Val-Tyr-Ser-Met-COO-

H3N-Ser-Ile-Met-Thr-Arg-Leu-Tyr-Gly..Thr-Glu-Ala-Val-Tyr-Ser-Met-COO-

H3N-Thr-Gly-Gly-Thr-Lys-Leu-Tyr-Ile..Thr-Glu-Ala-Val-Tyr-Ser-Met-COO-

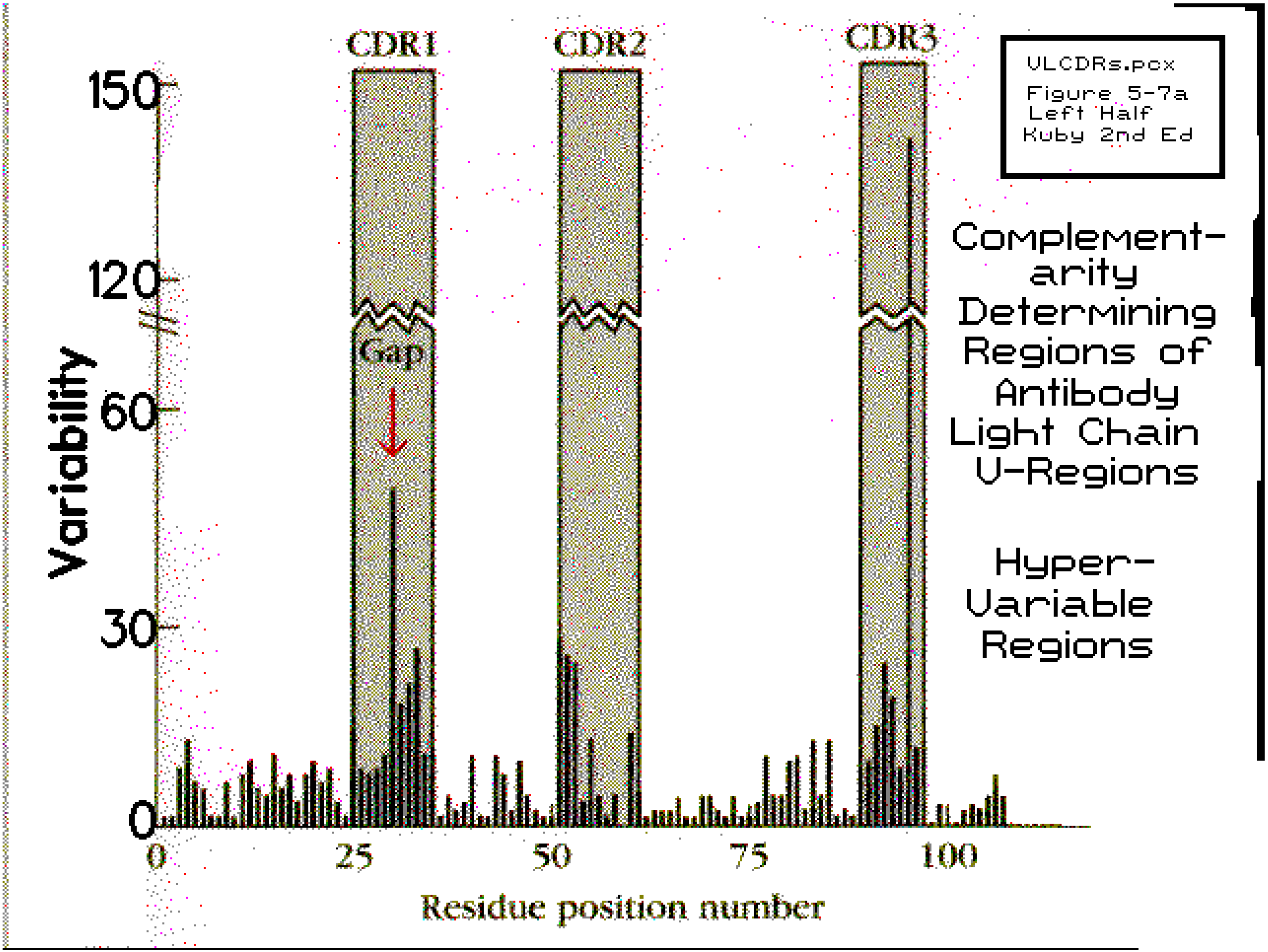
Variable Amino Terminal Half

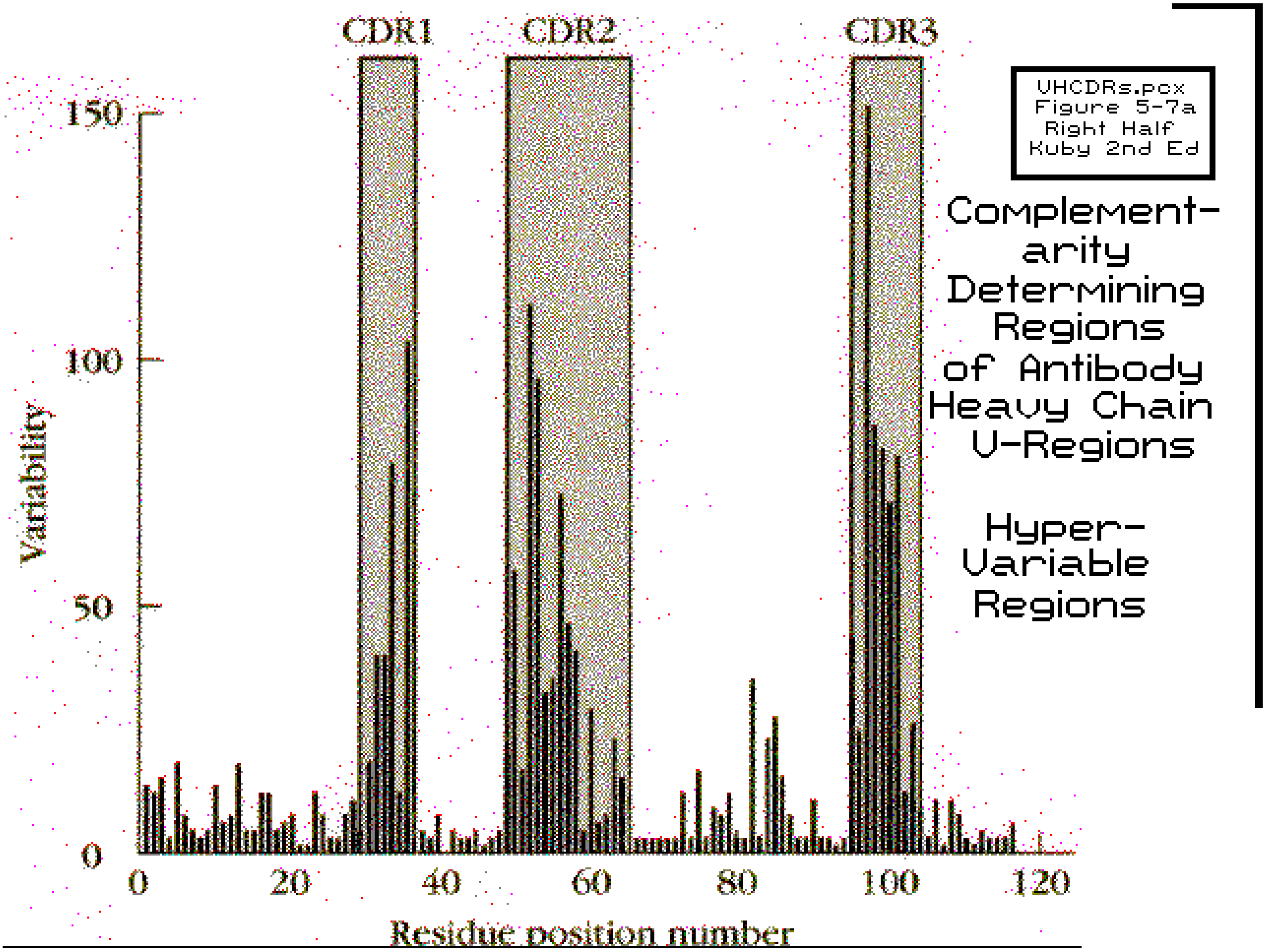
(Positions 1 to 107)

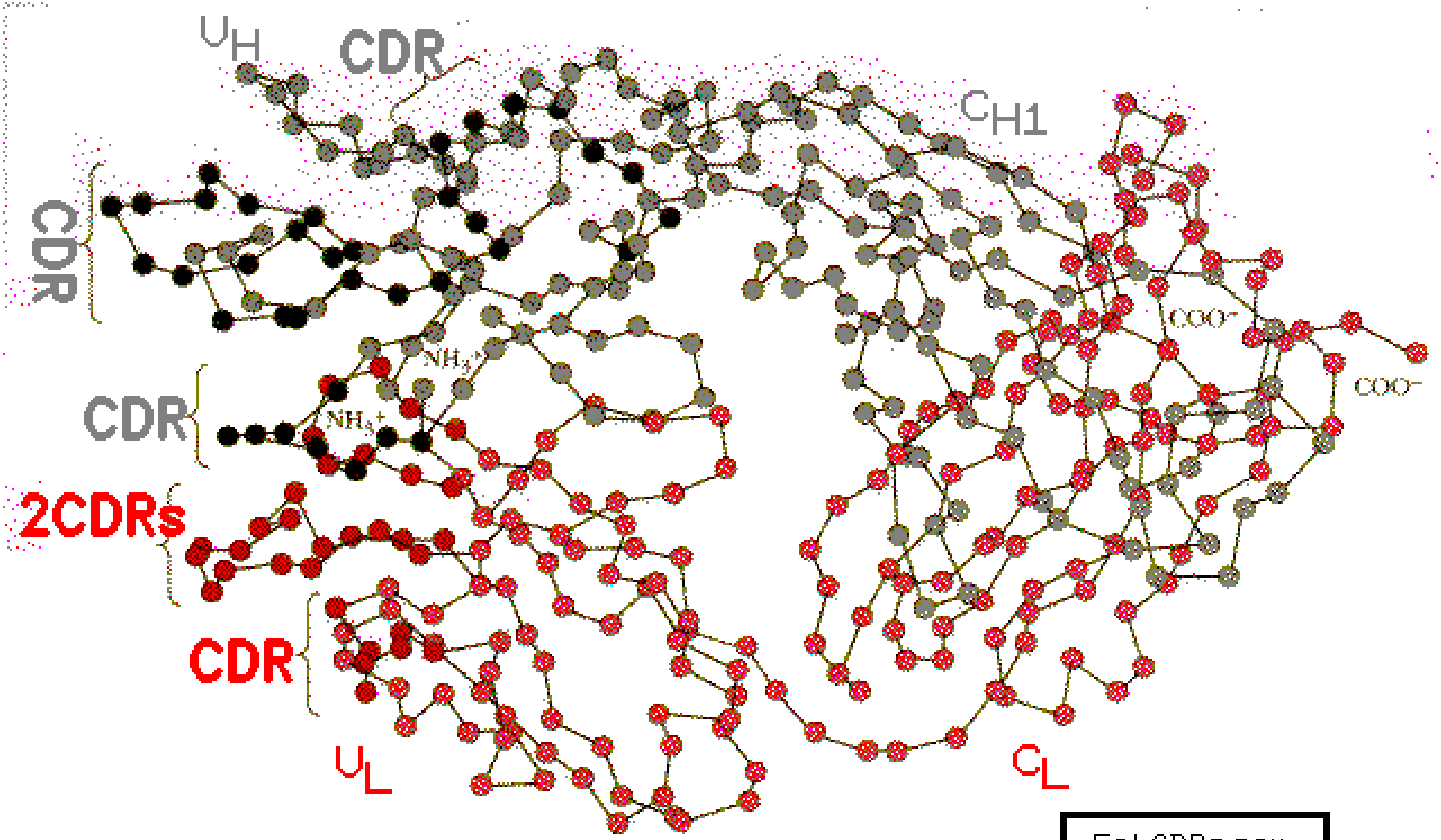
Conserved Carboxyl Terminal Half

(Positions 108 - 214)

LiteComp


CDR1
CDR2
CDR3
VLCDRs.pcx
Figure 5-7a
Left Half
Kuby 2nd Ed
Complement-
arity
Determining
Regions of
Antibody
Light Chain
V-Regions
Hyper-
Variable
Regions
Gap
Variability
150
120
60
30
0
0
25
50
75
100
Residue position number


CDR1
CDR2
CDR3
150
100
50
0
Variability
0
20
40
60
80
100
120
Residue position number
VHCDRs.pcx
Figure 5-7a
Right Half
Kuby 2nd Ed
Complement-
arity
Determining
Regions
of Antibody
Heavy Chain
V-Regions
Hyper-
Variable
Regions



FabCDRs.pcx

Figure 5-7b
Kuby, 2nd Ed

Complementarity-determining Regions (CDR's) from **Light** and **Heavy** Chains Come together in 3 dimensions to give the antigen-recognizing site.

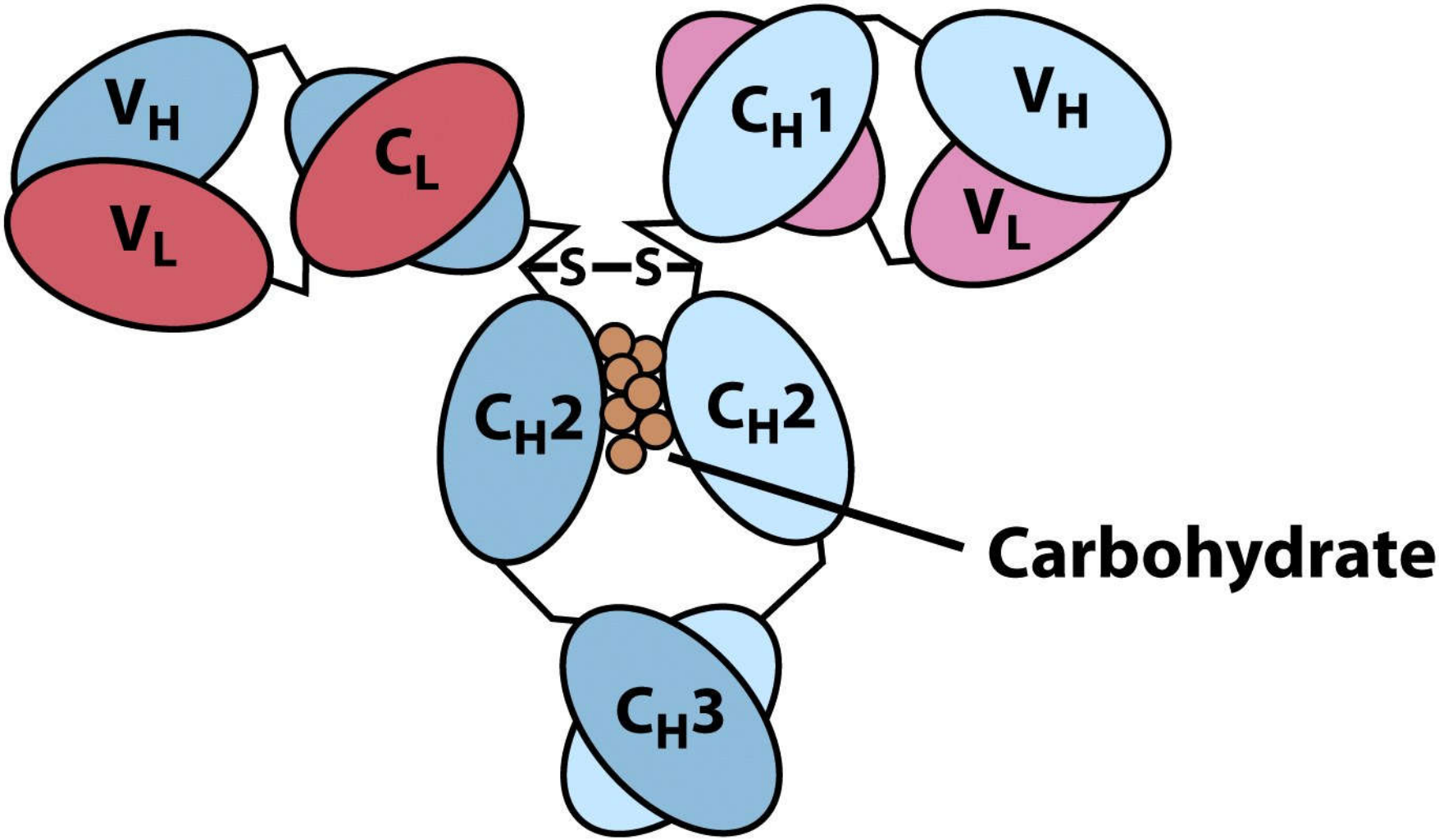
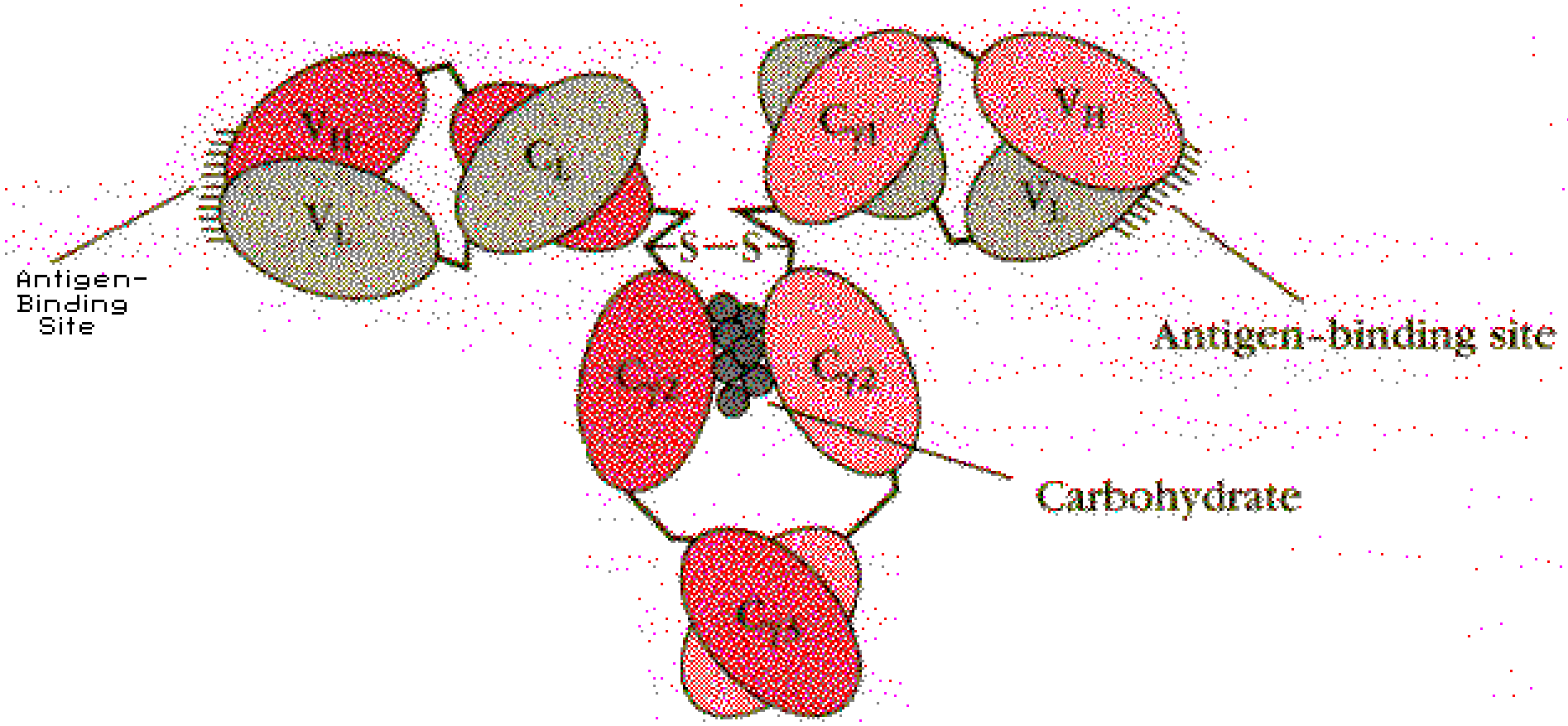
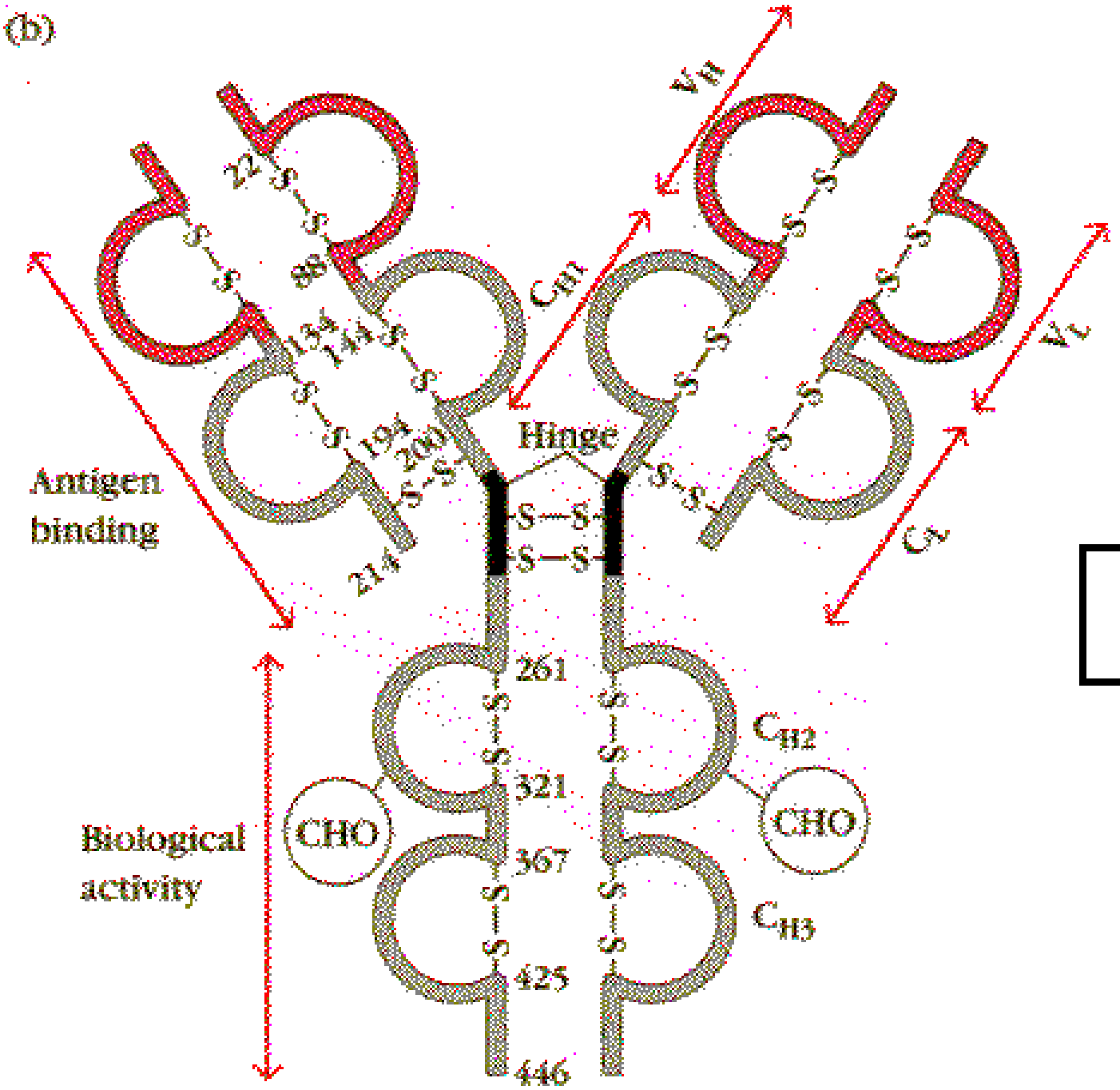


Figure 4-9b
Kuby IMMUNOLOGY, Sixth Edition

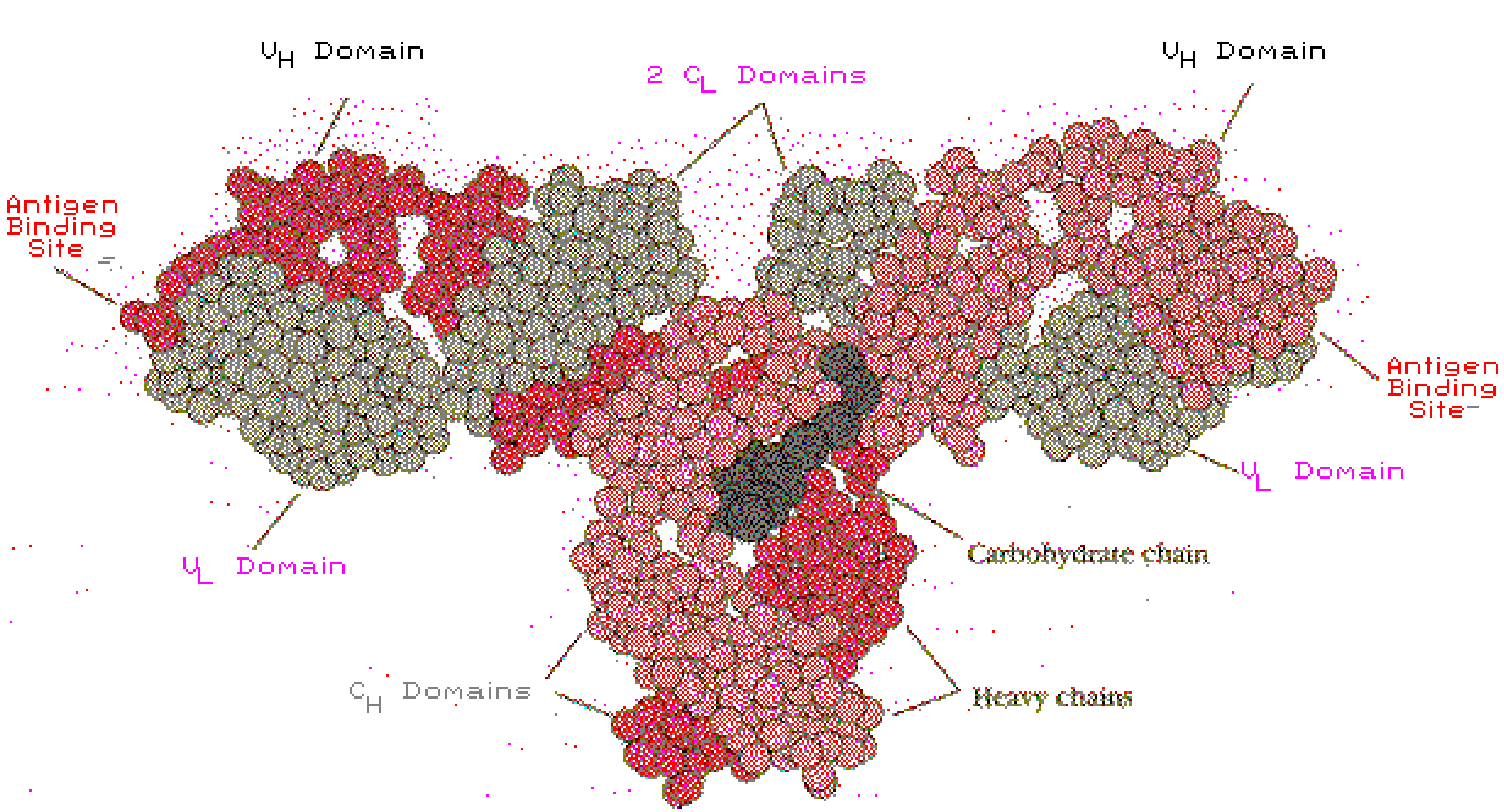


GDomains.pcx

Figure 5-6b
Kuby, 2nd Ed



HLDomain.pcx
Figure 5-4b
Kuby 2nd Ed

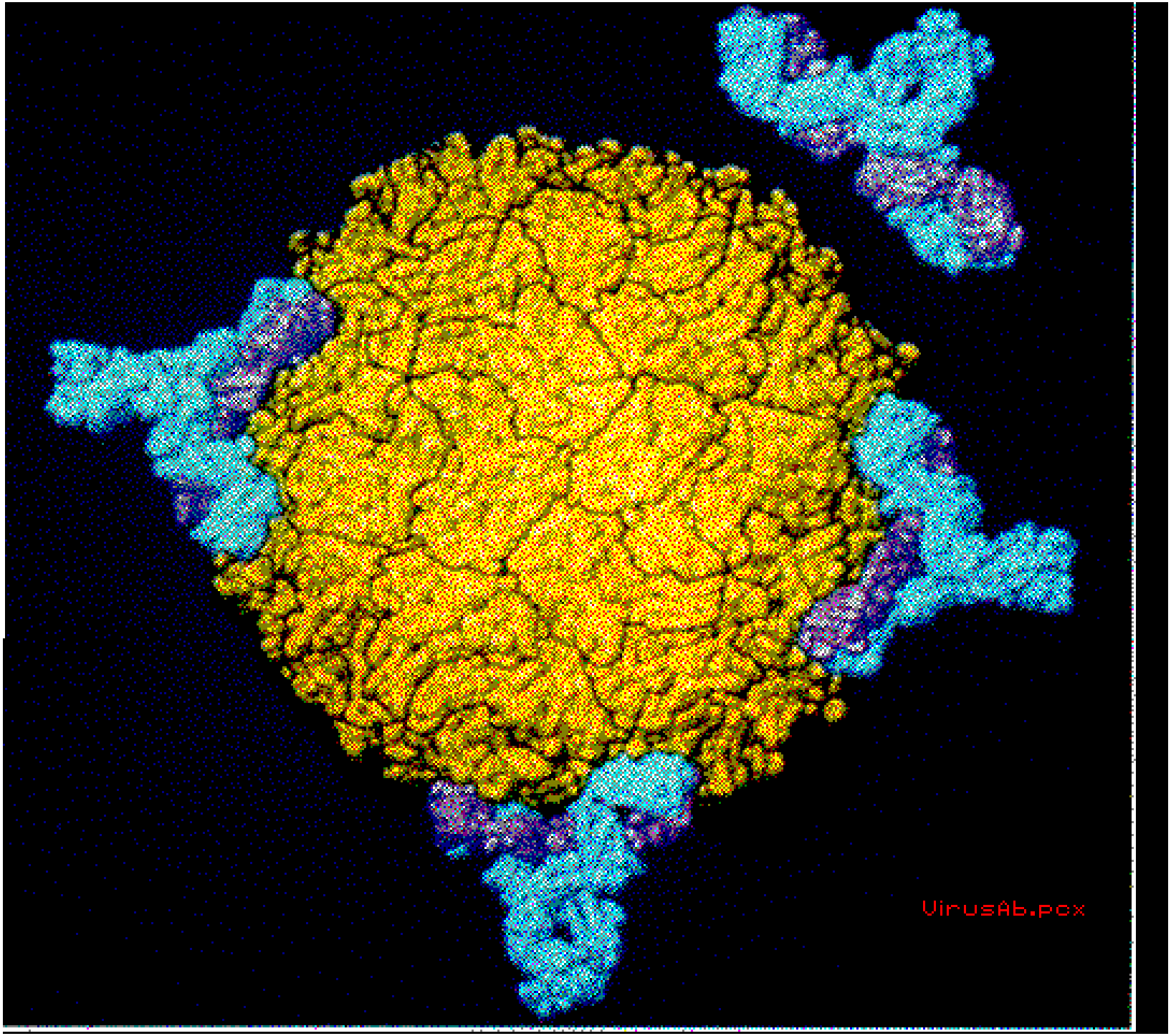


IgGSpace.pcx
Figure 5-6a
Kuby, 2nd Ed

From:

Golub &
Green

Plate 7-1

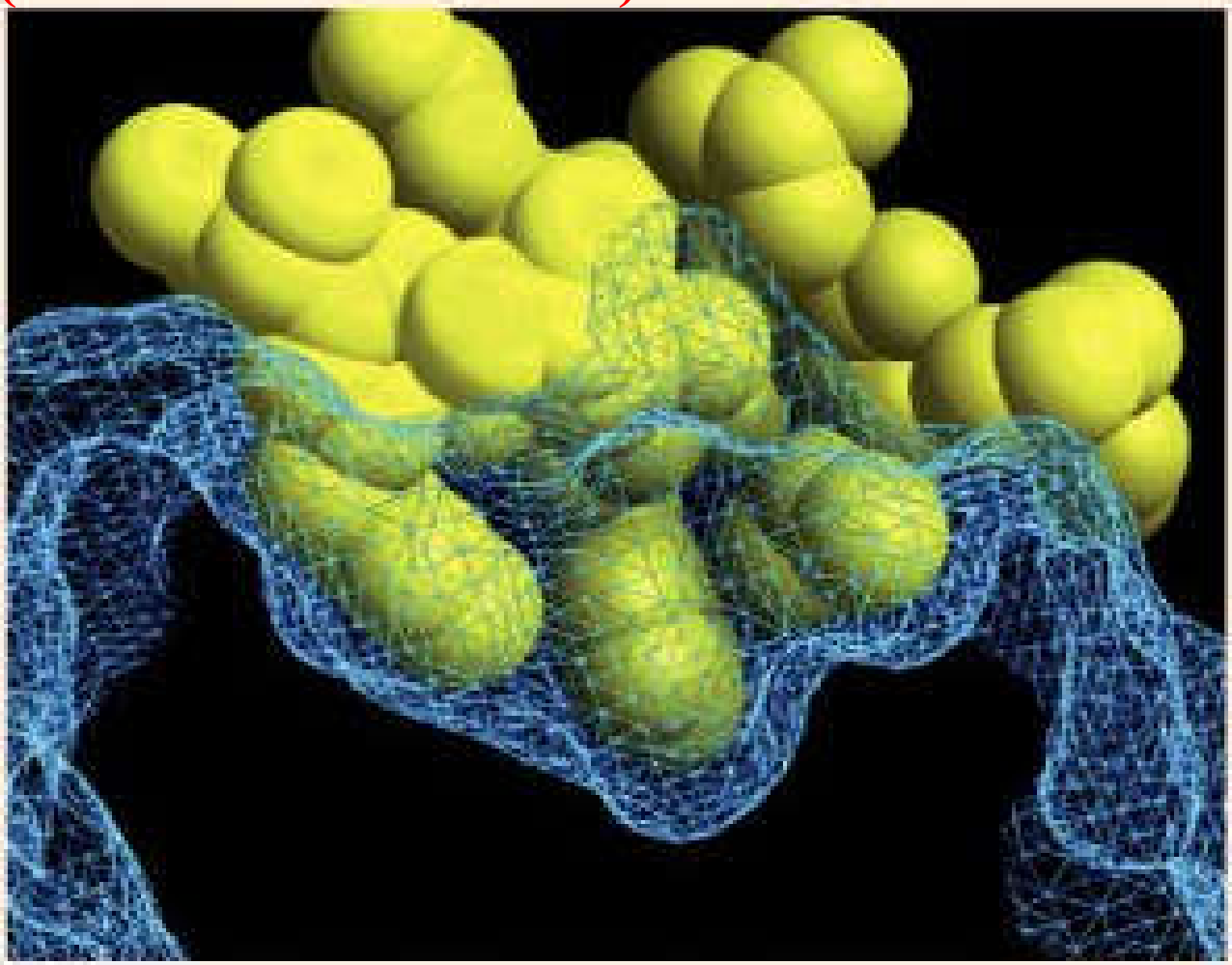


How does the antibody protein recognize its complementary antigen so precisely?

Blue shows topology of pocket in MDM2 protein that binds to p53

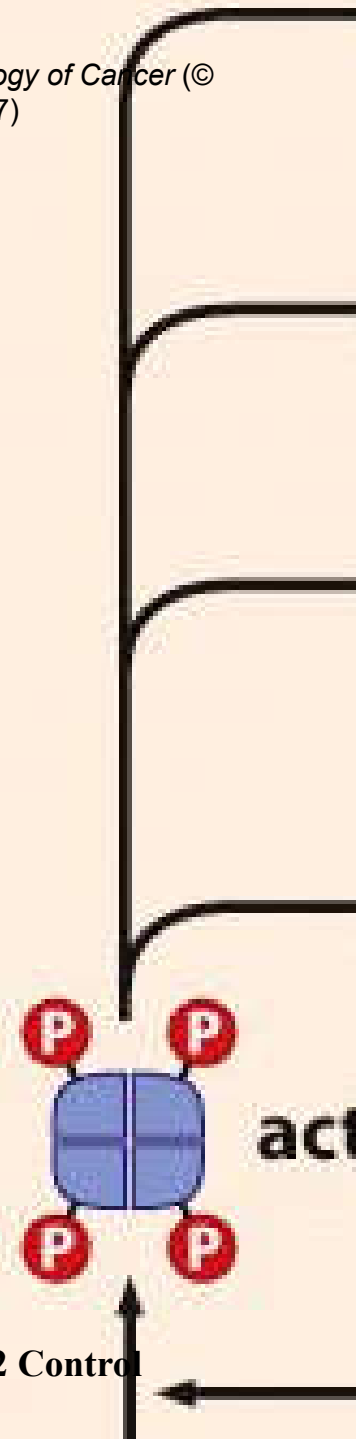
Figure 9.13 *The Biology of Cancer* (© Garland Science 2007)

How proteins recognize each other topologically (3-dimensional surfaces)

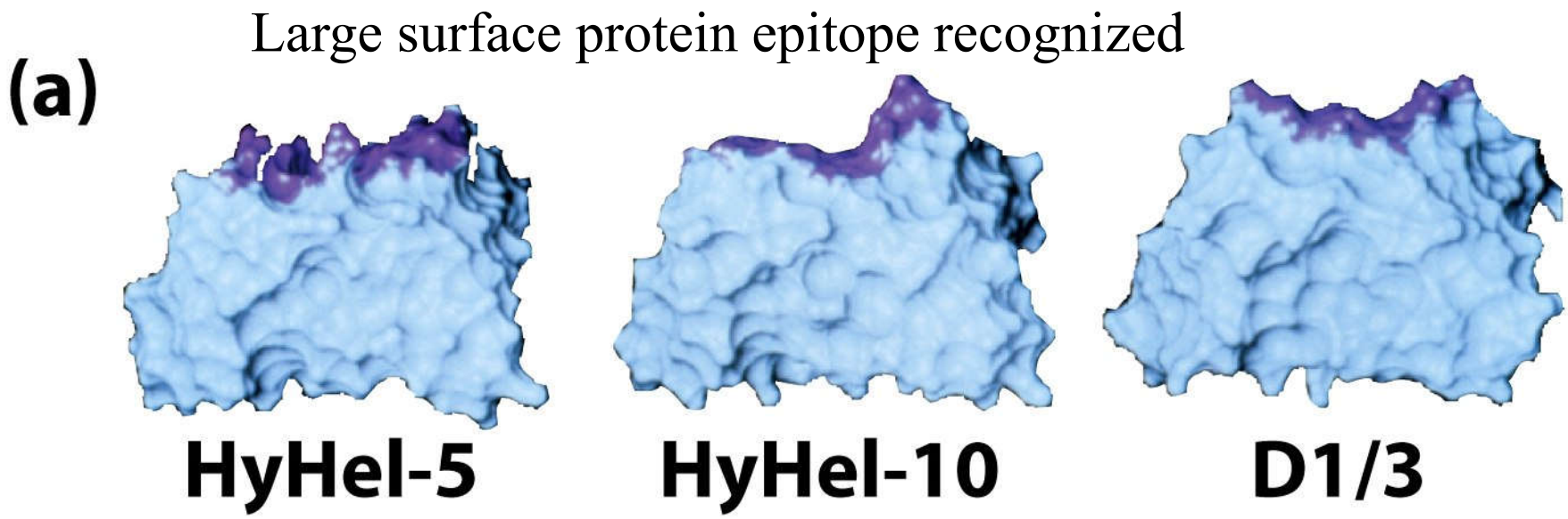


(B)

Yellow is p53 protein showing peptide domain sequence that binds to MDM2 Control Protein



Large surface protein epitope recognized



Smaller low molecular size epitopes recognized

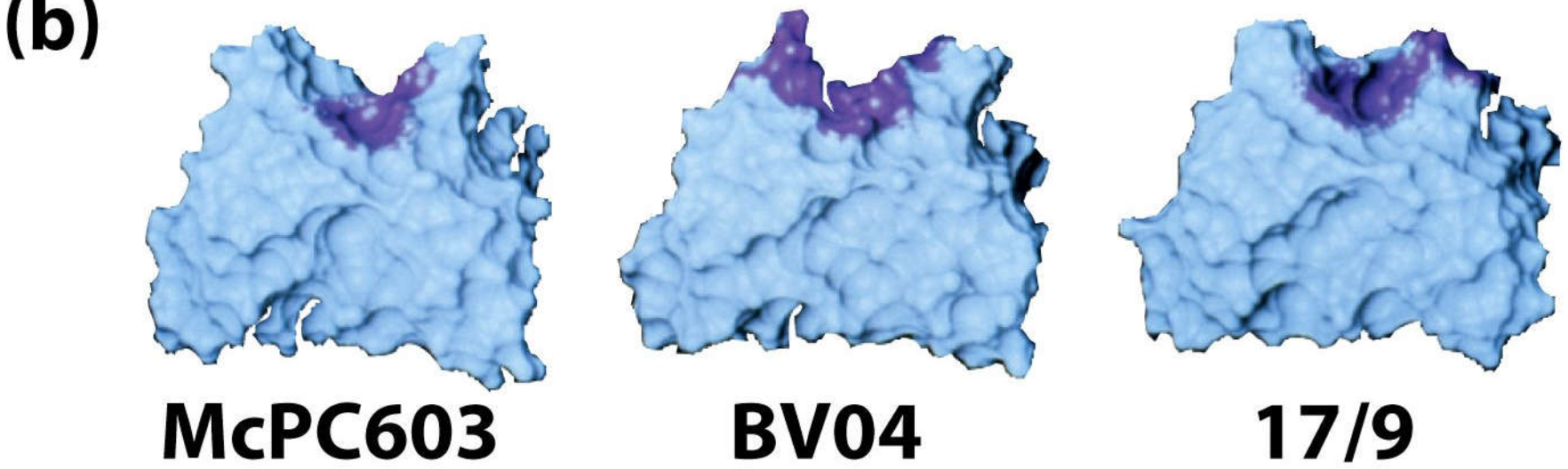


Figure 4-14ab
Kuby IMMUNOLOGY, Sixth Edition

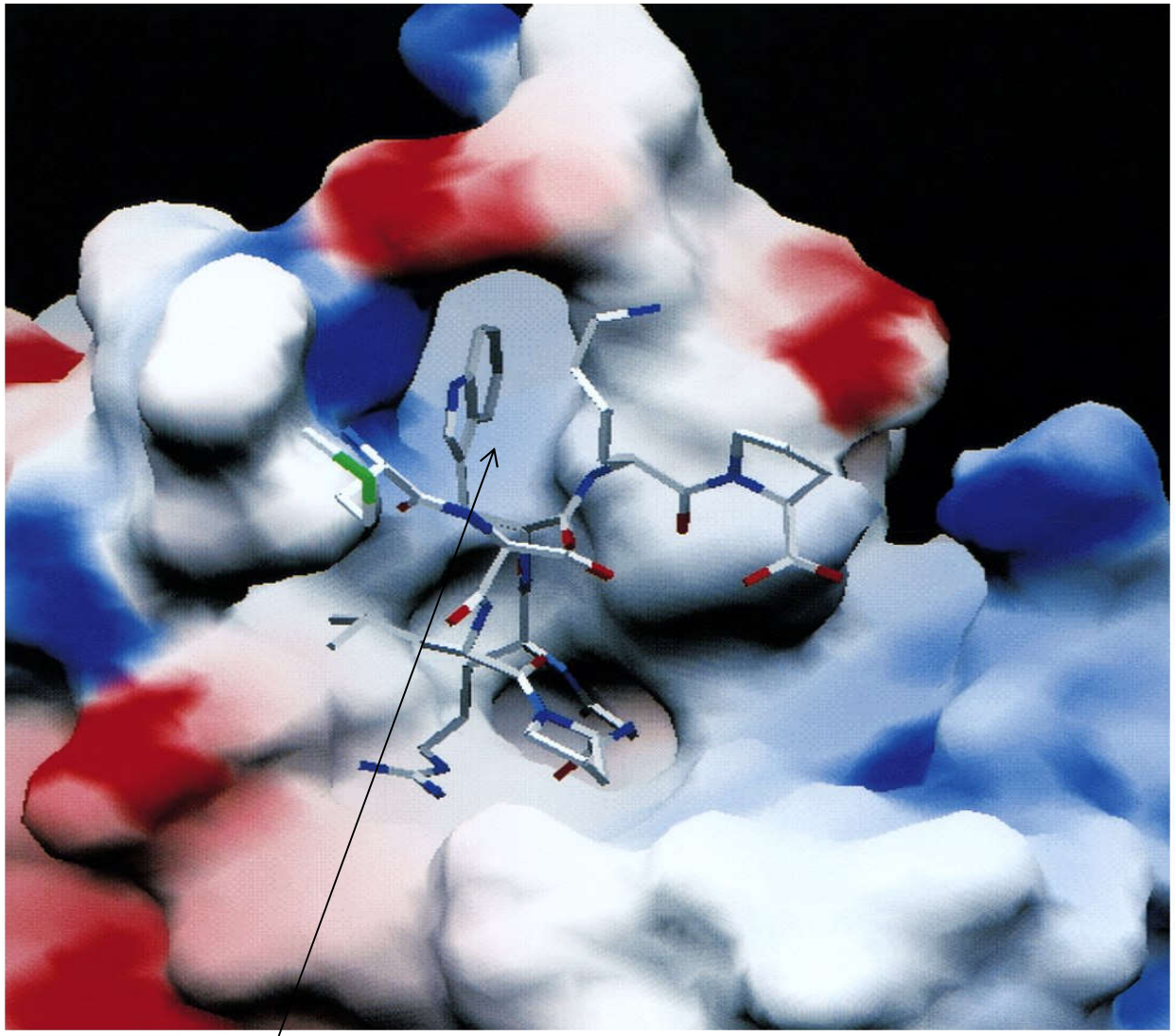


Figure 4-14c
Kuby IMMUNOLOGY, Sixth Edition

Small peptide antigen binding to an Fab (Fragment-antibody-binding) fragment of a complementary antibody

Light and heavy chain CDR regions move to better complement the antigen

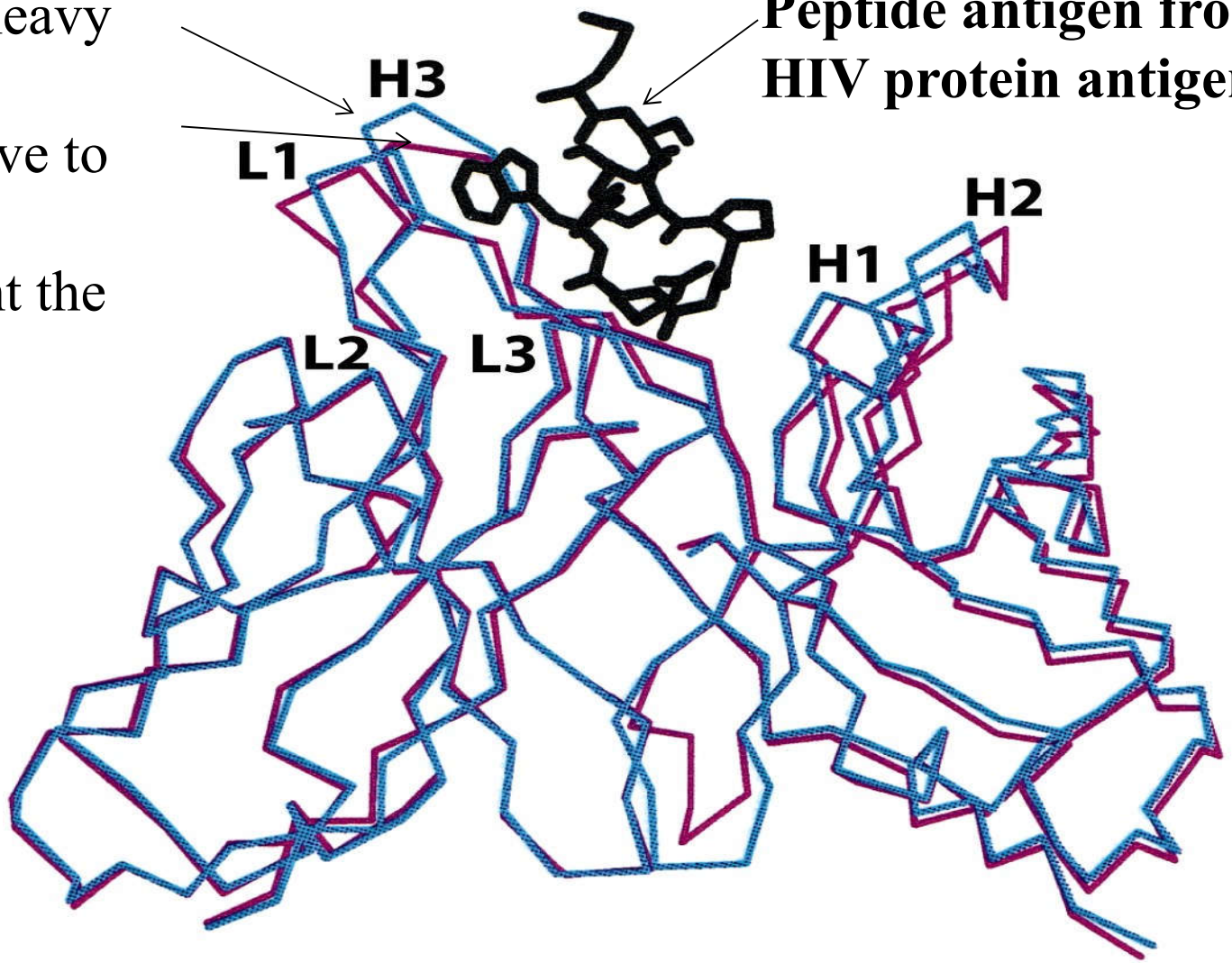
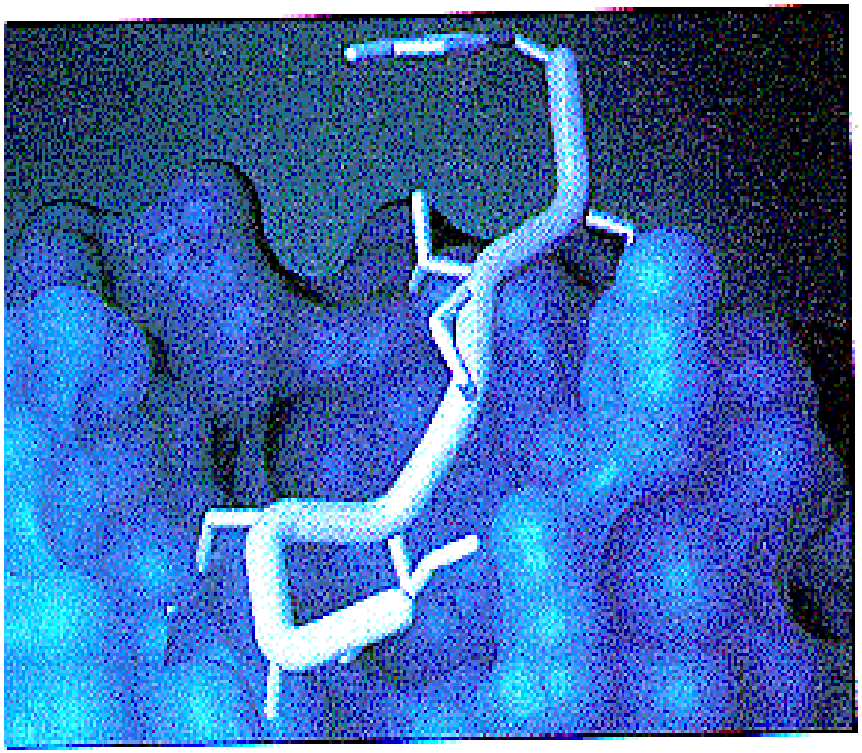


Figure 4-15
Kuby IMMUNOLOGY, Sixth Edition

Conformational change in antibody upon binding antigen ("induced fit")

Movement of Peptide-binding Pocket Accompanying Antigen Binding: Fab Fragment of Antibody to Hemagglutinin Peptide



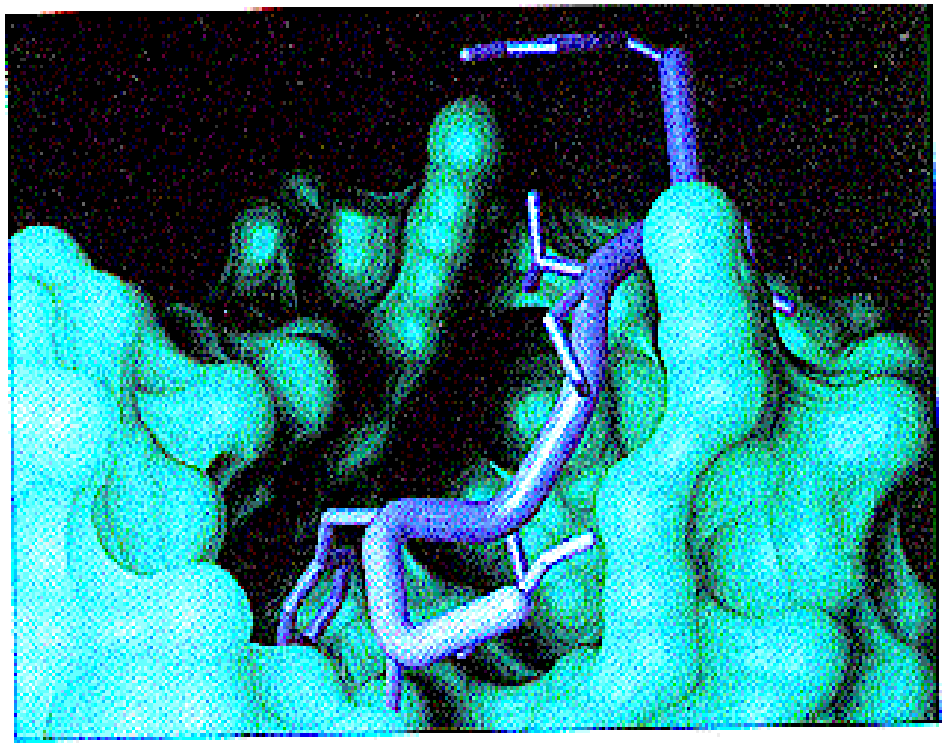
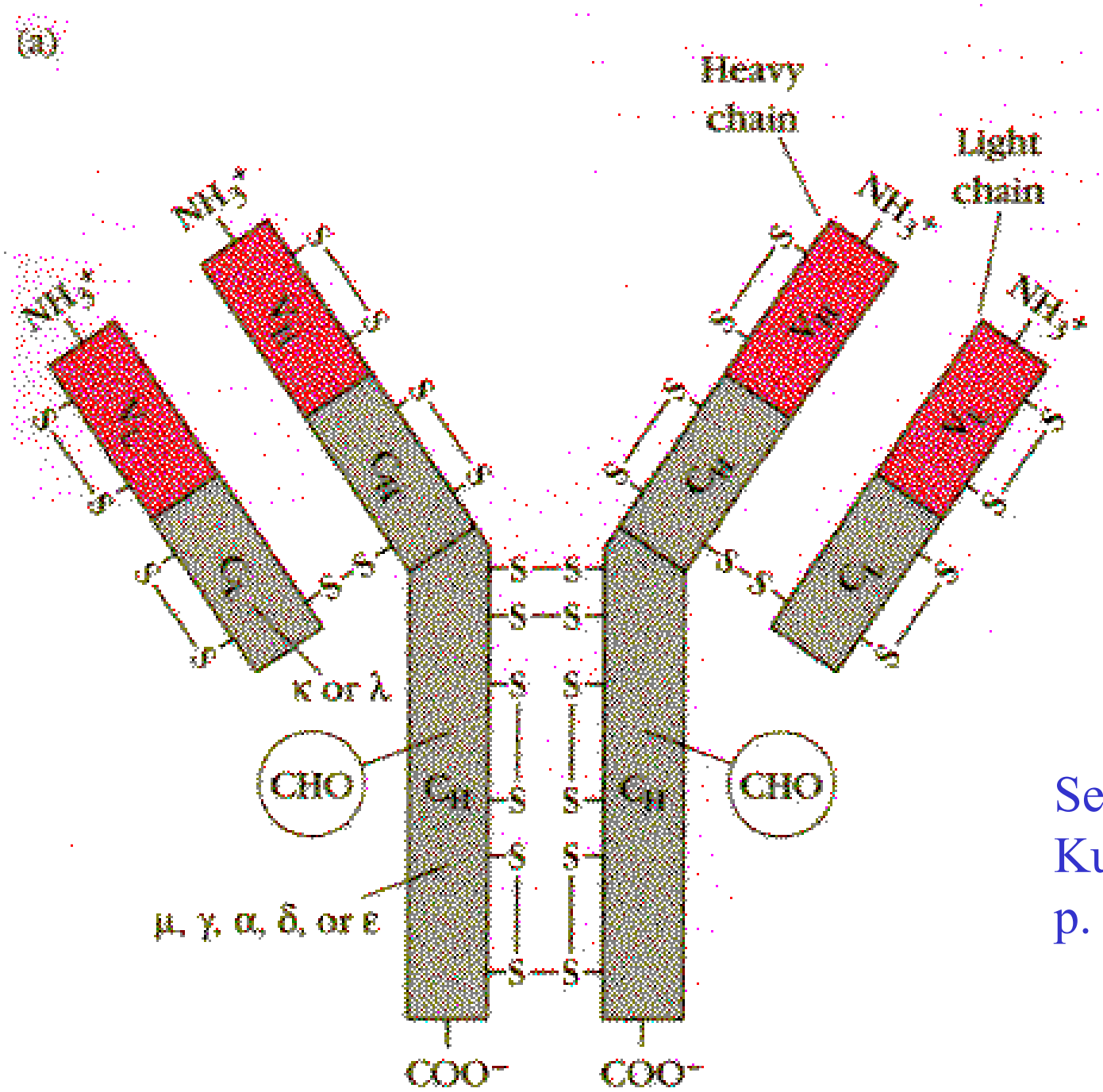


Figure 5-11
Kuby, 3rd Ed

AgAbMove

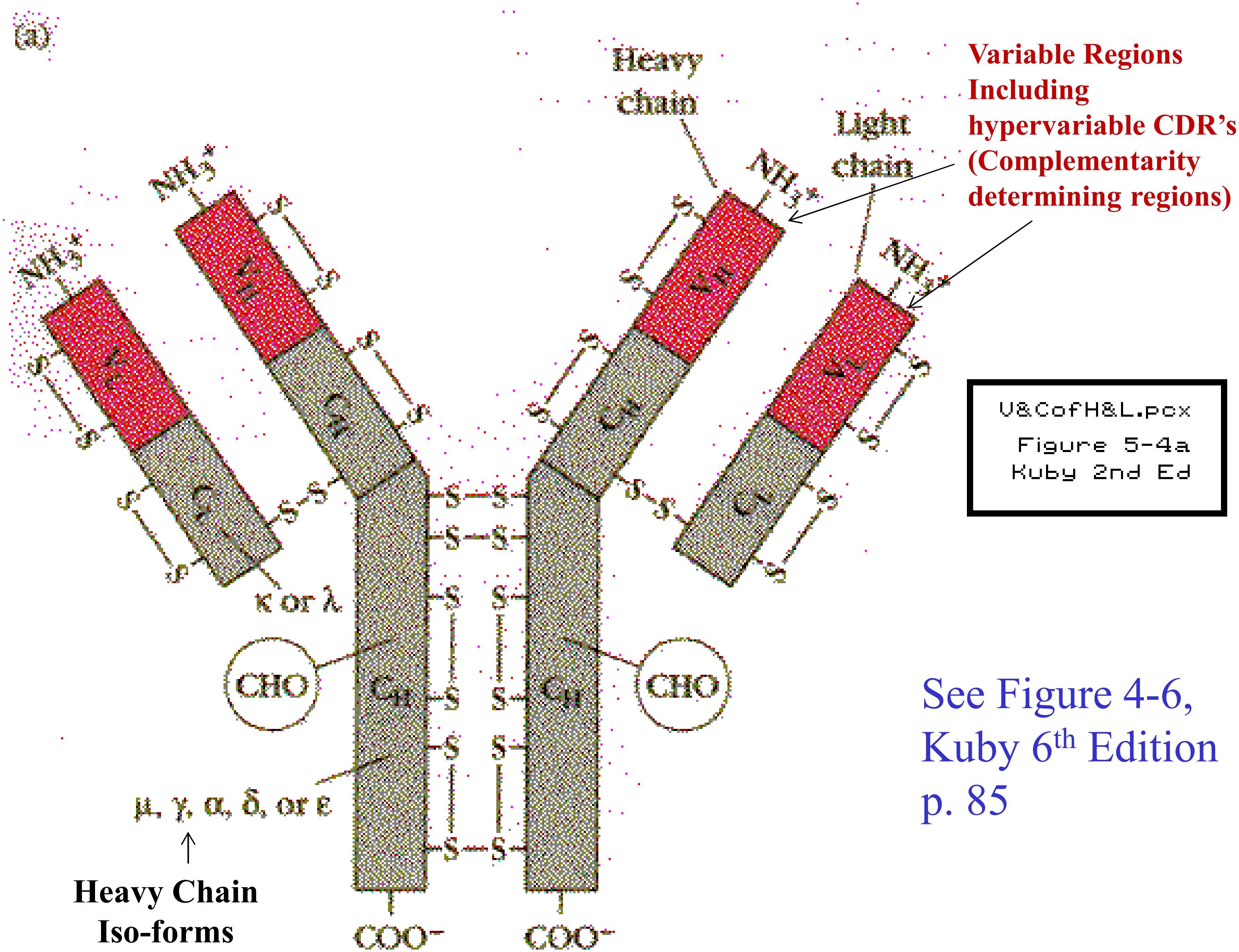
Immunoglobulin Isotypes

Structures and Functions



V&CofH&L.pcx
Figure 5-4a
Kuby 2nd Ed

See Figure 4-6, Kuby 6th Edition p. 85



V&CofH&L.pcx
Figure 5-4a
Kuby 2nd Ed

See Figure 4-6, Kuby 6th Edition p. 85

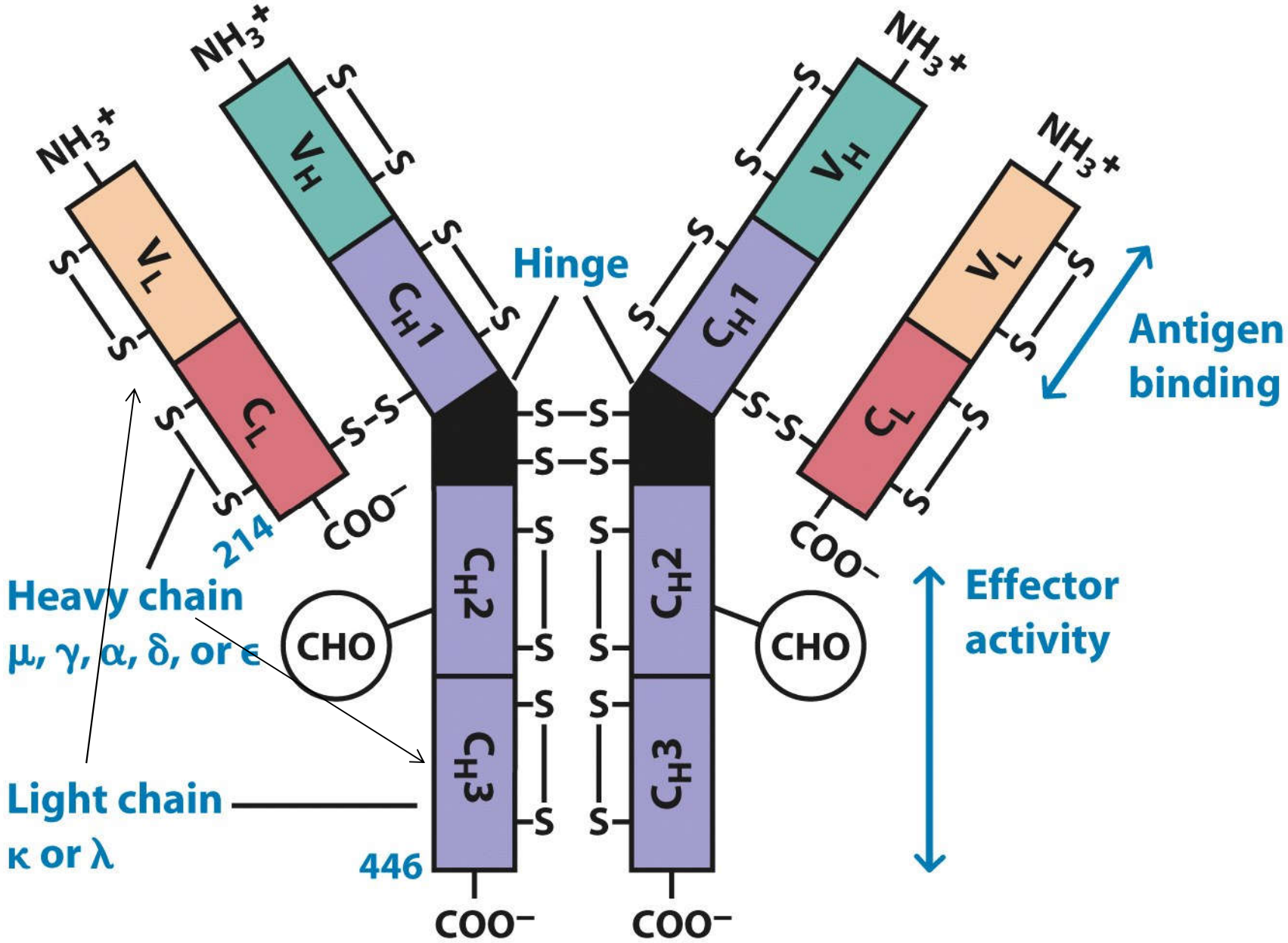


Figure 4-6
Kuby IMMUNOLOGY, Sixth Edition

The Heavy and light chains are labeled incorrectly in the Kuby Immunology Powerpoint slides. The figure is labeled correctly in the book.

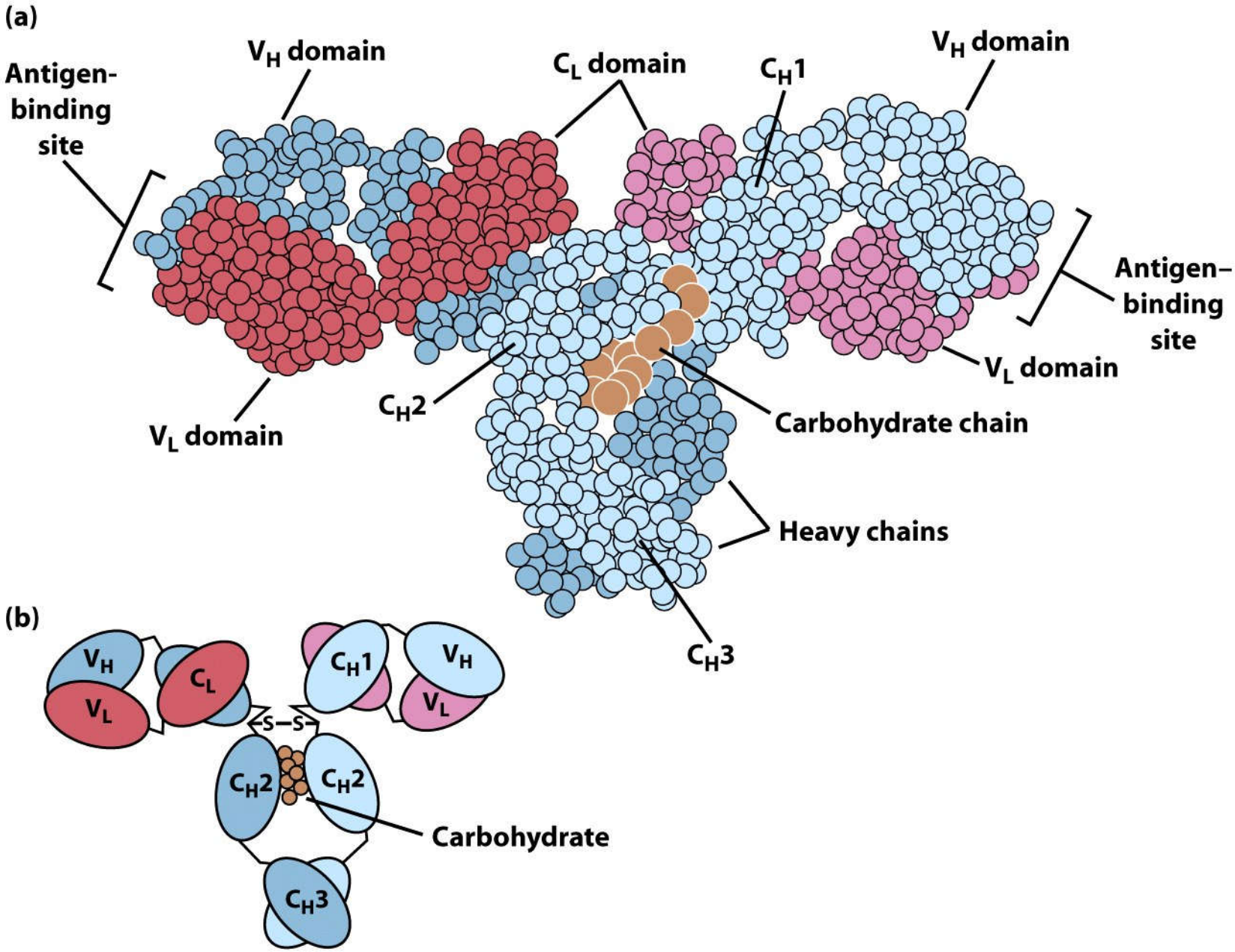


Figure 4-9
Kuby IMMUNOLOGY, Sixth Edition

Chain Structures of the five immunoglobulin classes in humans

(adapted from Kuby, 2nd edition)

Class	Heavy Chain	Light Chain	Sub-Classes	Subunit Formula
IgG	**γ**	κ or λ	γ1, γ2, γ3, γ4	γ2κ2 γ2λ2
IgA	**α**	κ or λ	α1, α2	(α2κ2)n (α2λ2)n n =1,2,3,4
IgM	**μ** ~ ~	κ or λ	None	(μ2κ2)n (μ2λ2)n n = 1 or 5
IgD	**δ**	κ or λ	None	δ2κ2 δ2λ2
IgE	**ε**	κ or λ	None	ε2κ2 ε2λ2

IgClass

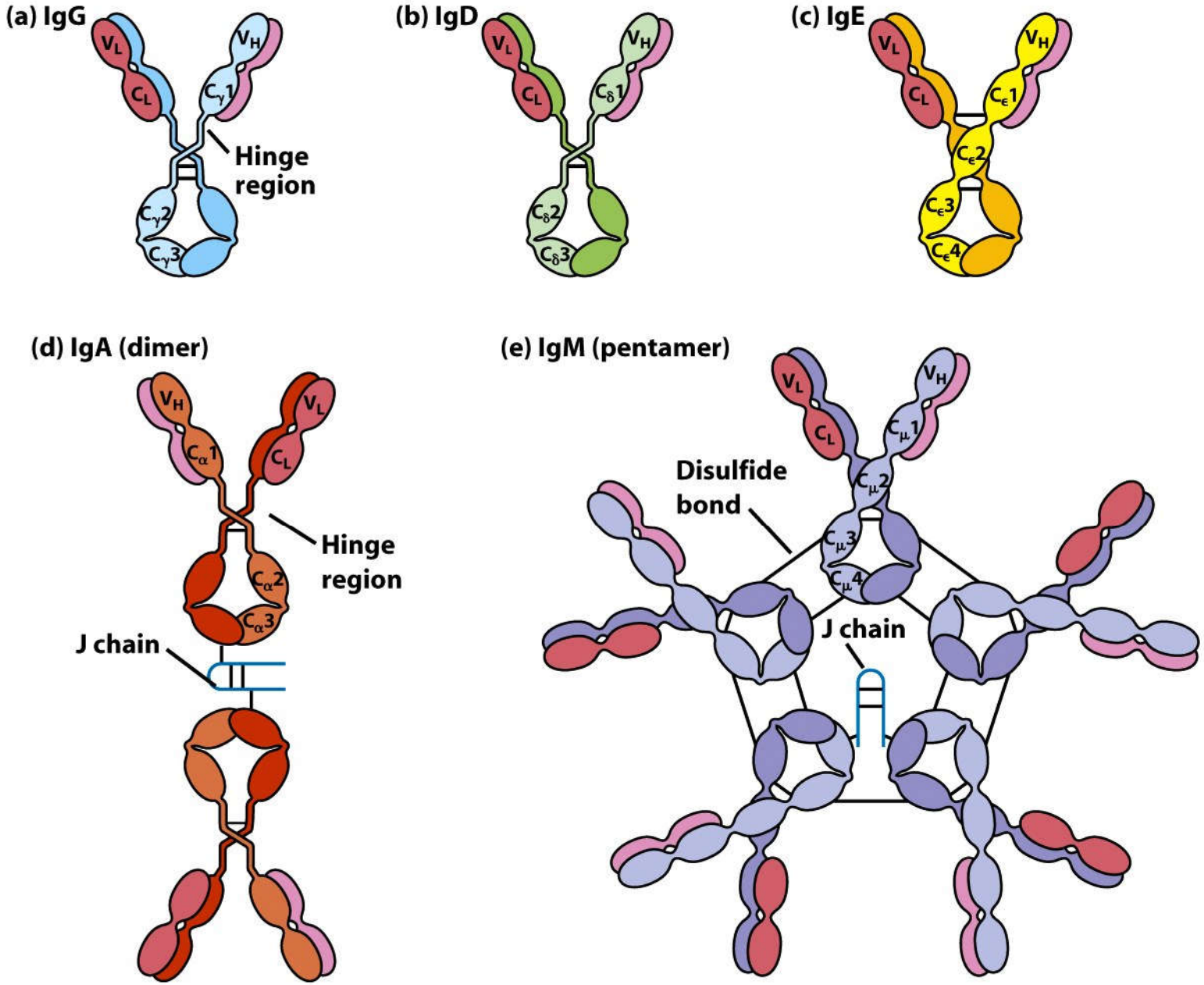


Figure 4-17
Kuby IMMUNOLOGY, Sixth Edition

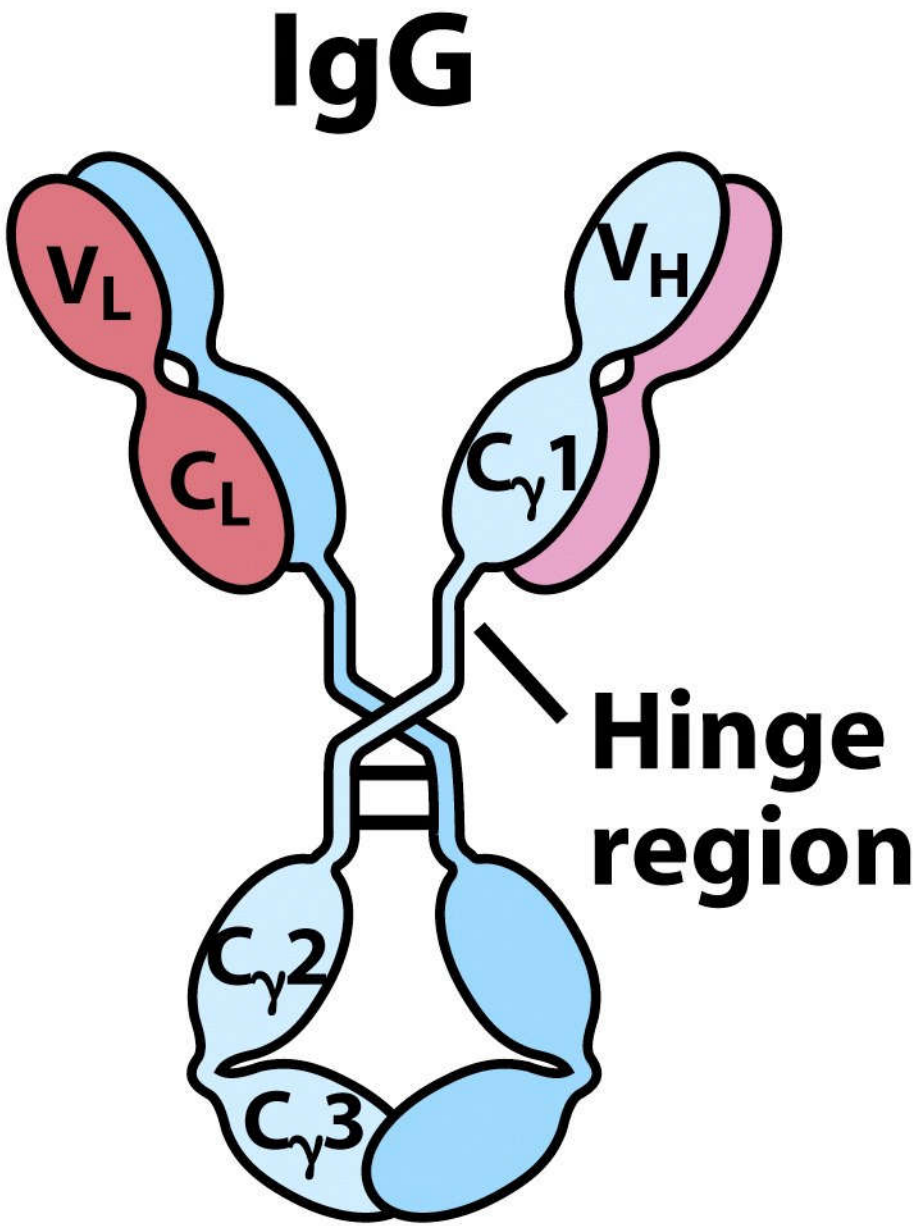


Figure 4-17a
Kuby IMMUNOLOGY, Sixth Edition

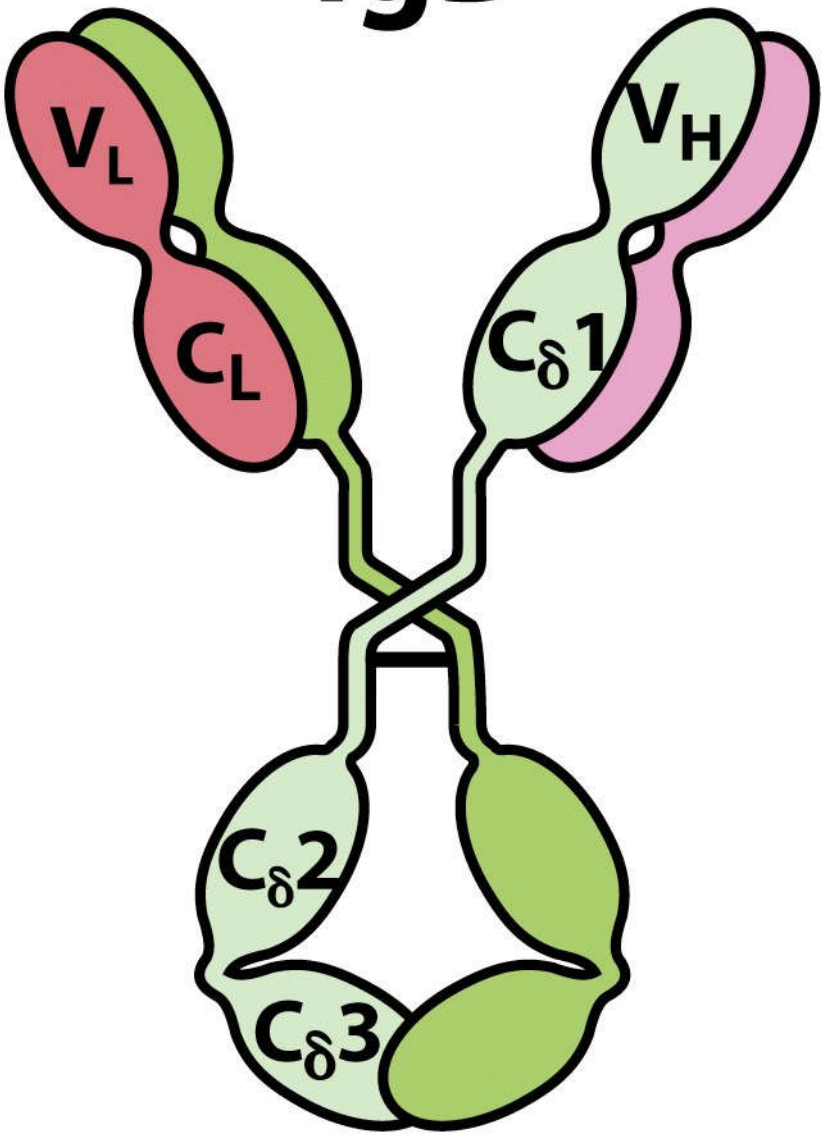


Figure 4-17b
Kuby IMMUNOLOGY, Sixth Edition

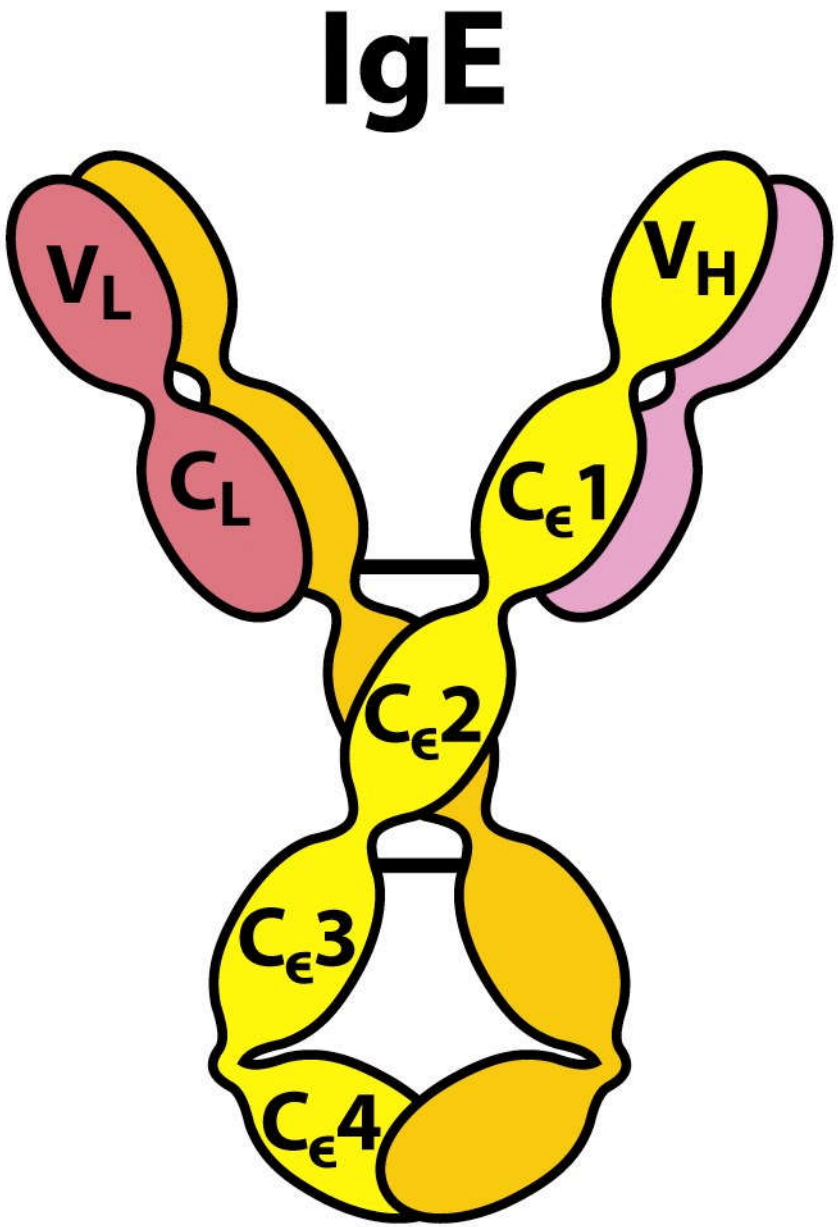


Figure 4-17c
Kuby IMMUNOLOGY, Sixth Edition

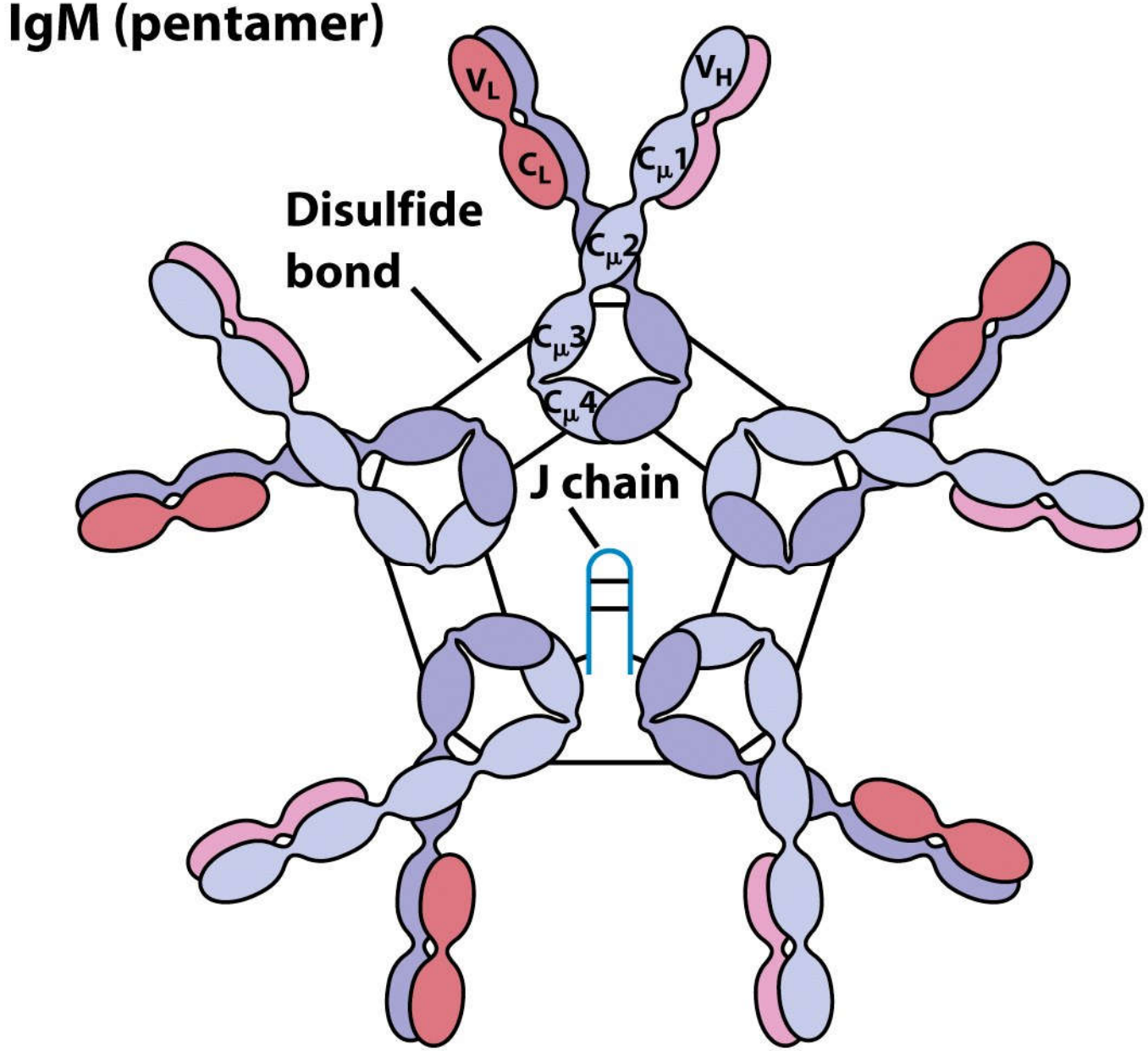


Figure 4-17e
Kuby IMMUNOLOGY, Sixth Edition

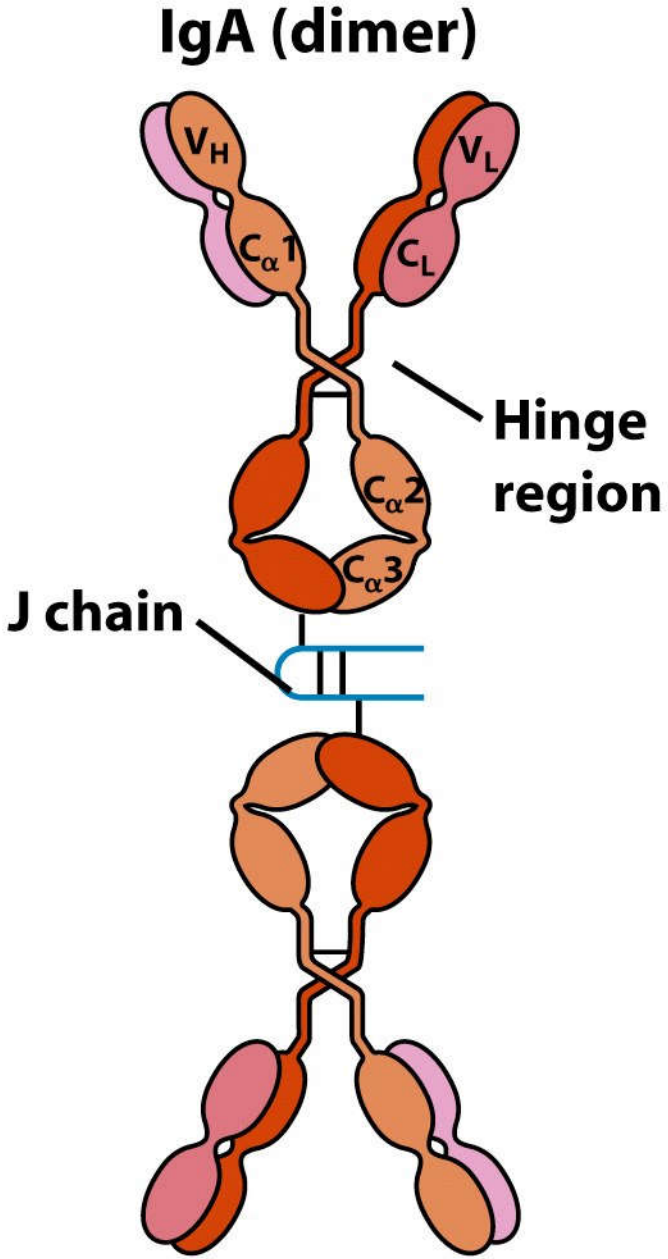


Figure 4-17d
Kuby IMMUNOLOGY, Sixth Edition

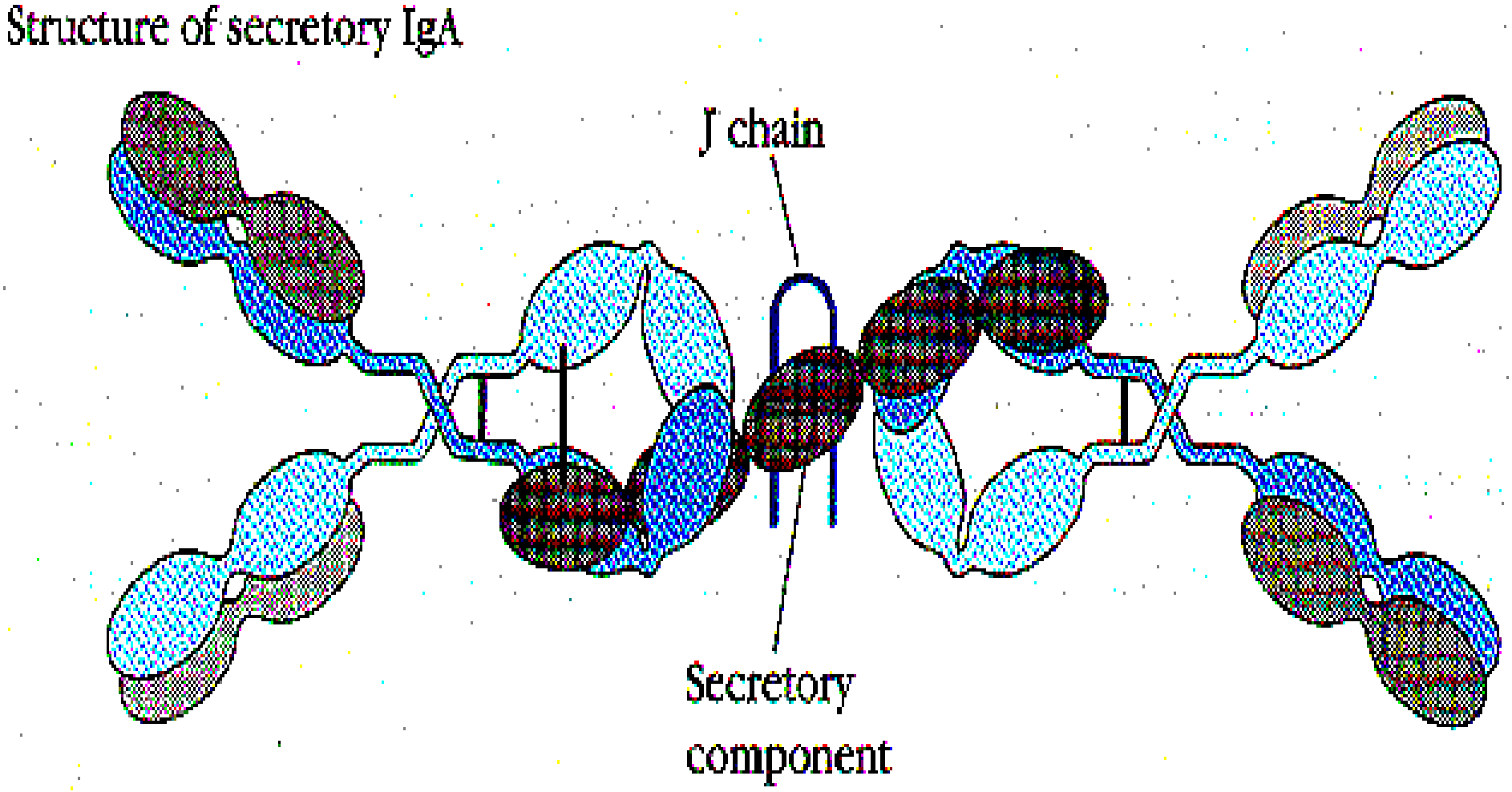
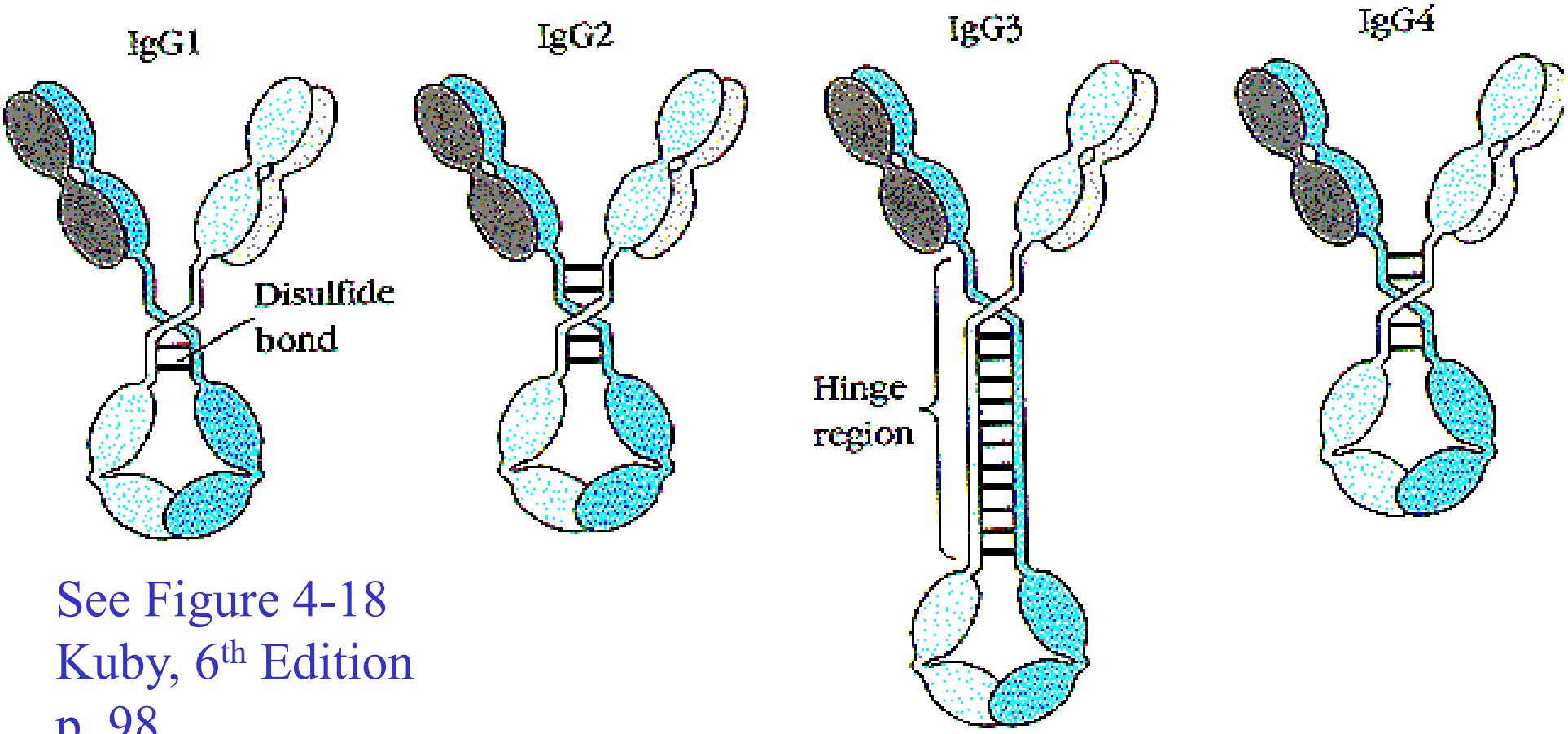


Figure 5-17(a)

Kuby, 3rd Ed.

IgAModl

Structures of Four Sub-types of IgG



See Figure 4-18
Kuby, 6th Edition
p. 98

IgGSubs

Figure 5-16, Kuby, 3rd Ed.

Properties & Activities of Human Serum Immunoglobulins

(from Table 4-2, Kuby Immunology, 4th Ed. p. 96)

Property or Activity	IgG*	IgA**	IgM	IgE	IgD
Mol Wt (KD)	150	150 – 600	900	190	150
H Chain	gamma	alpha	mu	epsilon	delta
Serum Conc (mg/ml)	0.5 – 9	0.5 - 3	1.5	0.0003	0.03
Serum Half-life (dys)	8 - 23	6	5	2.5	3
Activate Complement	Yes	No	Strong	No	No
Cross Placenta	Yes	No	No	No	No
Membrane (mIg) Form	No	No	Yes***	No	Yes
Fc Binds Macrophages	Yes	No	?	No	No
Mucosal Presence	No	Strong	Yes	No	No
Induces Mast Cell	No	No	No	Yes	No

*** 4 Sub-classes IgG1, IgG2, IgG3, IgG4**

****2 Sub-classes IgA1, IgA2 (exists as mono-, di-, tri, tetramer)**

***** mIgM is monomer. Serum igM is pentamer**

Effector Functions of Antibodies

Functions of Fab Binding

Neutralization or Blocking of Target Molecule or Particle

Cross-linking and Agglutination of Target

(Bivalent Fab Binding)

Functions of Fc Region

Complement Fixation and Lysis of Target

Opsonization (Coating by Ab) and Phagocytosis of Target

Targeting by Antibody for Cell-mediated Destruction (Antibody-dependent Cell-mediated Cytotoxicity: ADCC)

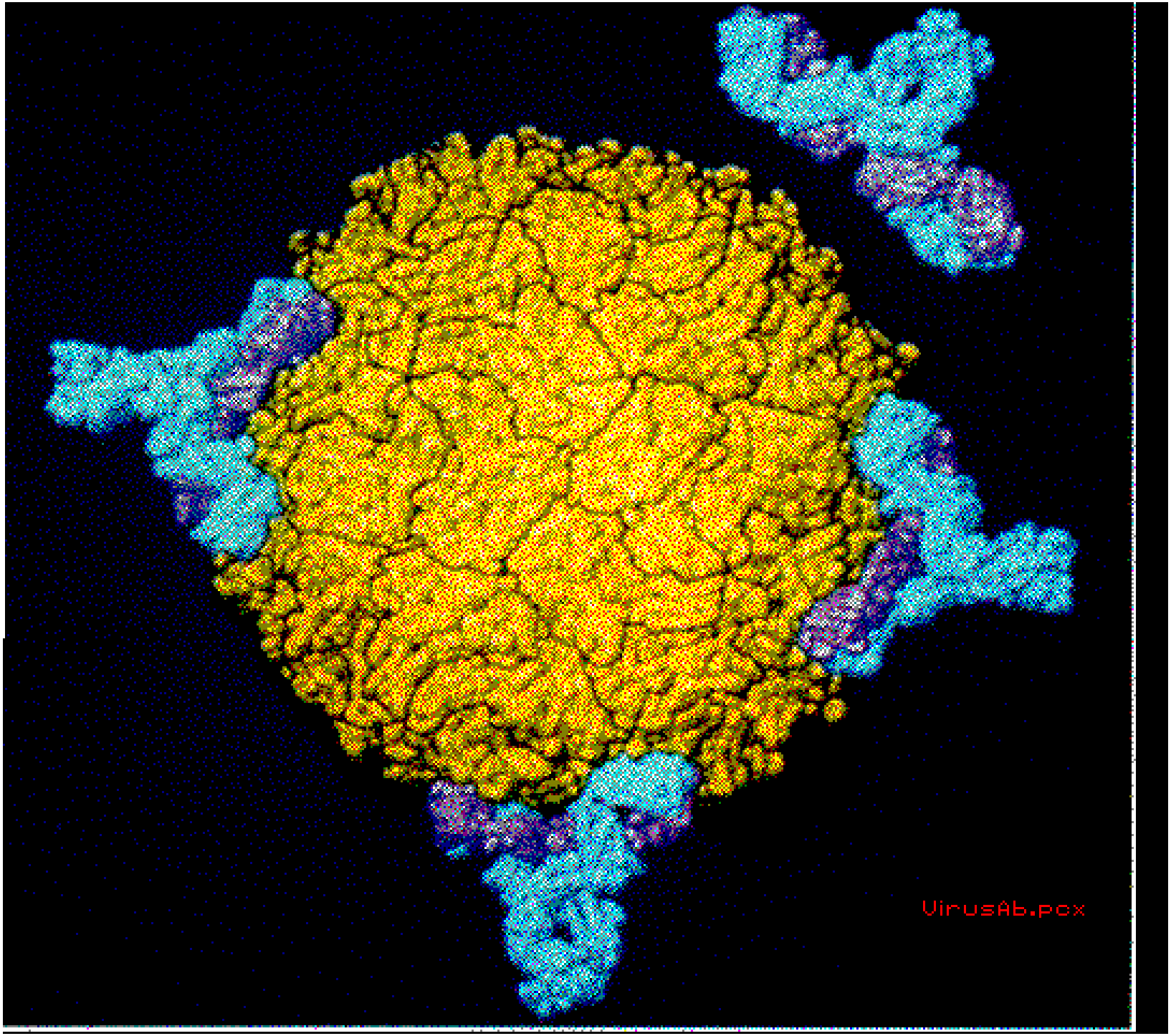
Mast Cell Attraction and Activation by Bound IgE

Immediate Type I Hypersensitivity, Type I Allergic Response, Localized and Systemic Anaphylaxsis

From:

Golub &
Green

Plate 7-1



Antibodies as Antigens

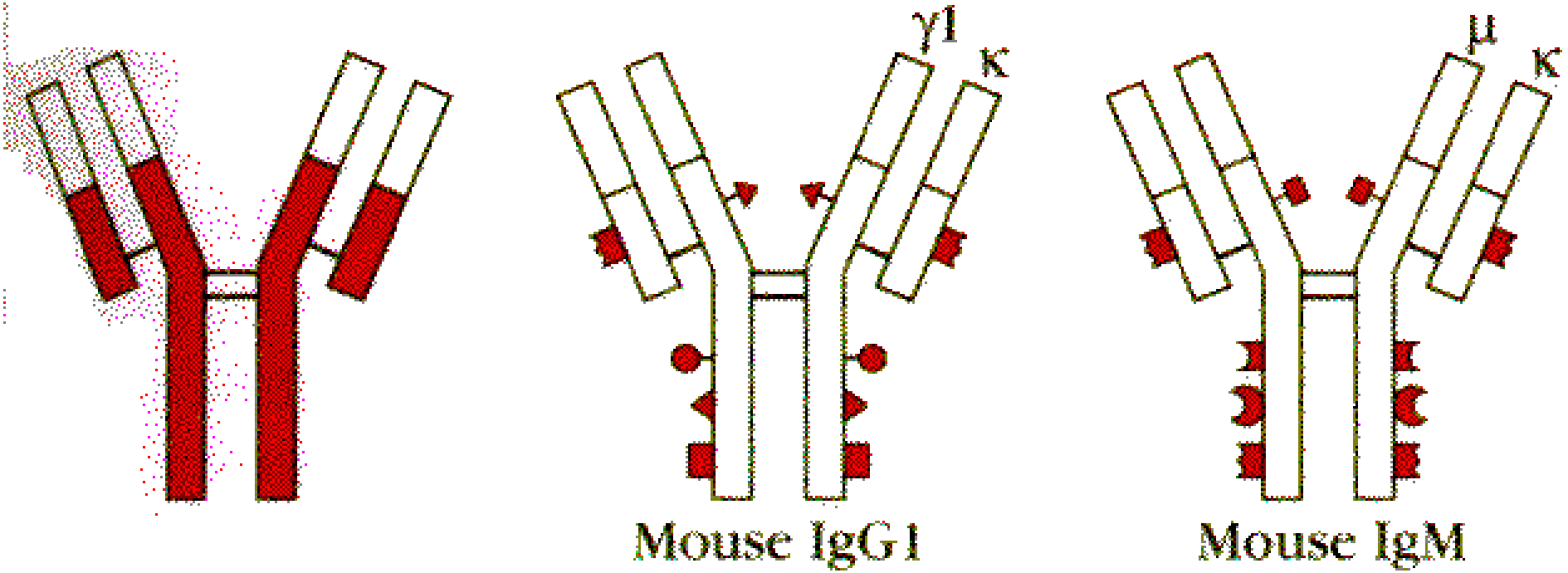
1. Different Heavy Chain Isotypes (gamma, alpha, mu, epsilon, delta):
Anti-isotype Antibodies
(Also differences in constant regions of kappa and lambda light chains)
2. Different individual mouse strains (or different people):
Anti-allotype Antibodies

(1 and 2: Like any other proteins with multiple molecular forms)

3. Different antigen-recognition abilities:
Anti-idiotype Antibodies

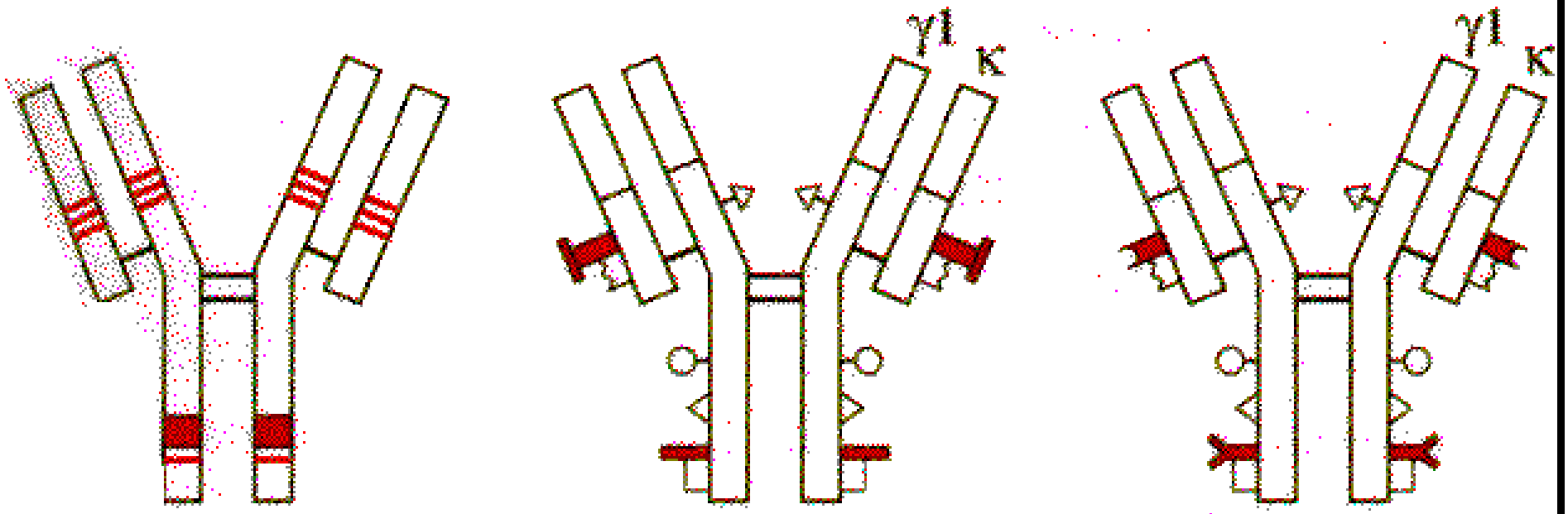
Other proteins except for T-cell Receptors do not show these kinds of variations and are not immunogenic in this way

(a) Isotypic determinants



Isotype.pcx
Figure 5-11a
Kuby, 2nd Ed

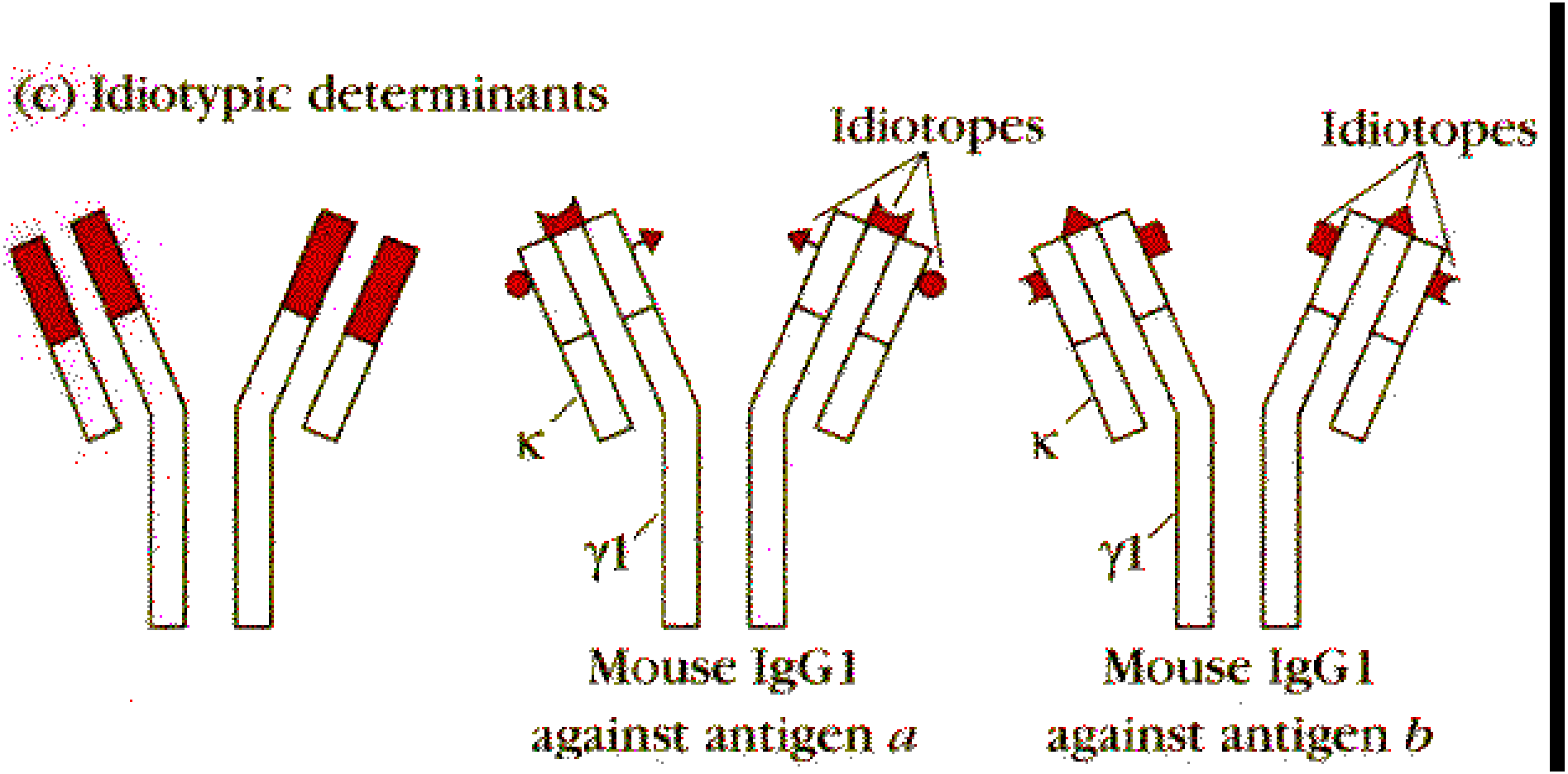
(b) Allotypic determinants



Mouse IgG1
(strain A)

Mouse IgG1
(strain B)

Allotype.pcx
Figure 5-11b
Kuby, 2nd Ed



Idiotype.pcx
Figure 5-11c
Kuby, 2nd Ed

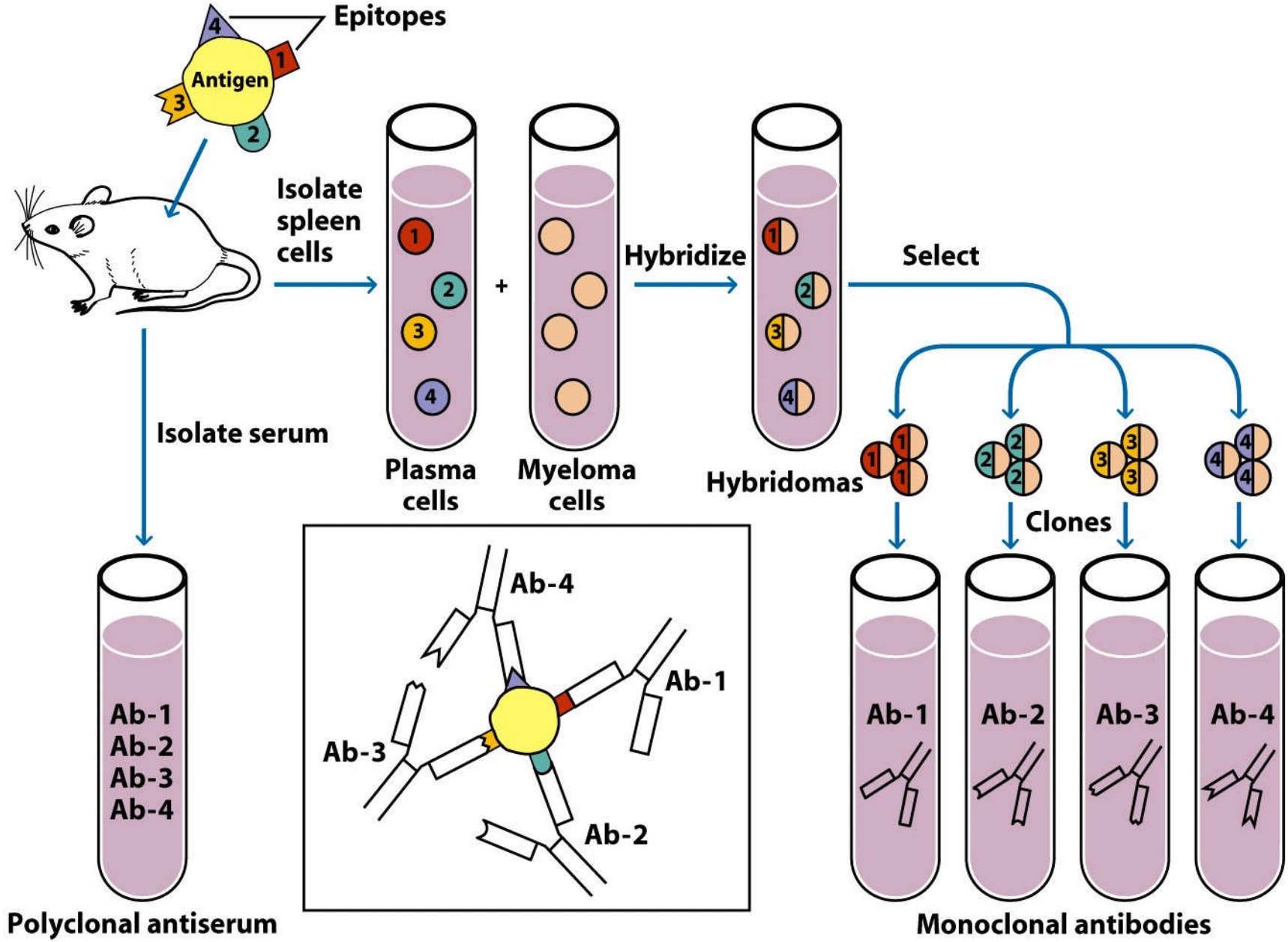


Figure 4-25
Kuby IMMUNOLOGY, Sixth Edition

View from CD OnLine at Textbook Web-site:

Molecular Animation of Immunoglobulin Structure

Molecular Visualization of Immunoglobulin Structure

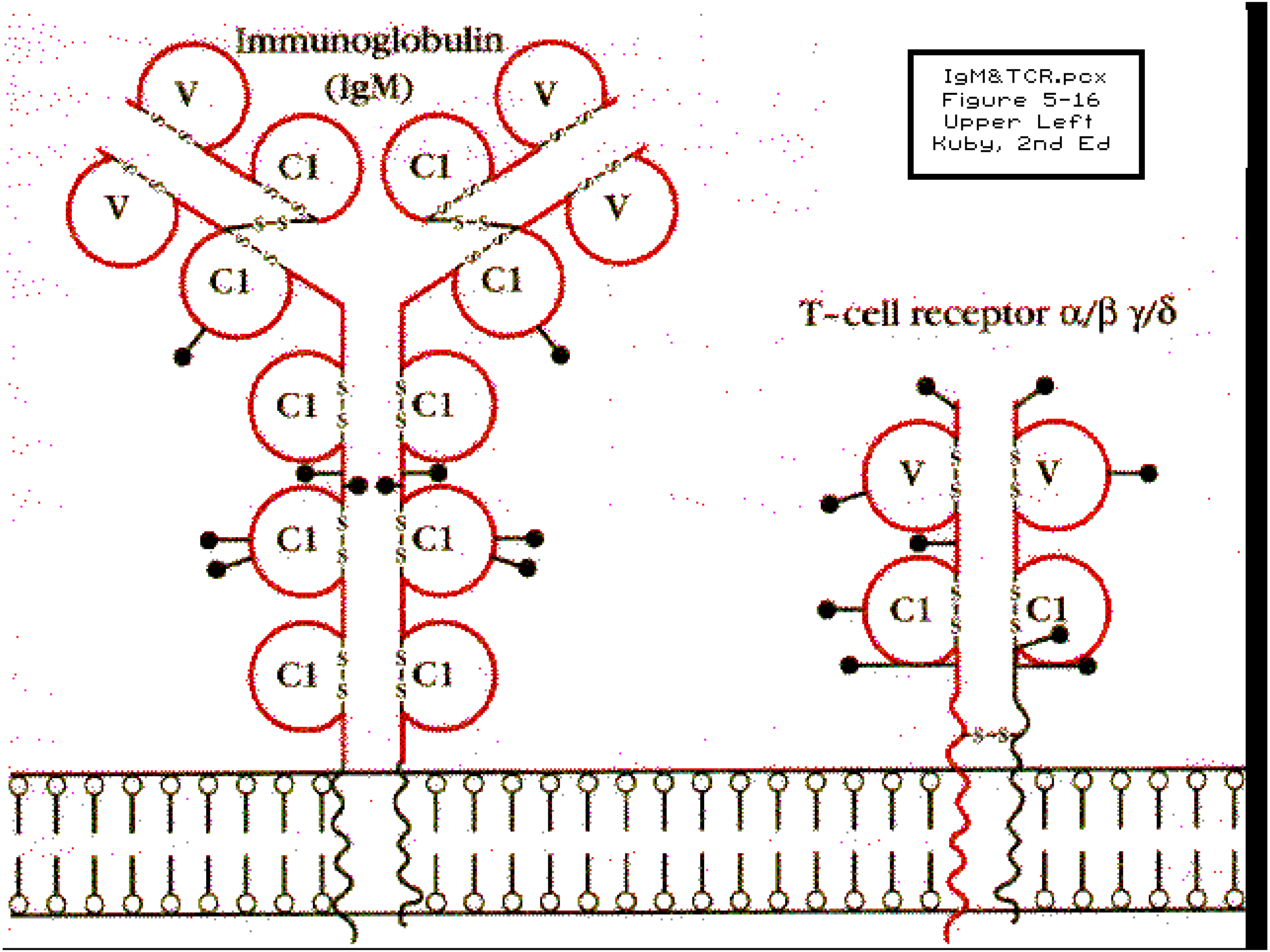
Molecular Visualization of Antigen-Epitope Interactions

For the Turning Point Quiz Questions Following:

1. Put away ALL notes.
2. No devices other than ONE XR transmitter
3. No talking or consulations

Avastin for Breast Cancer: Possible withdrawal of FDA approval. Sept. 16, 2010

http://www.cnn.com/video/#/video/health/2010/09/17/dnt.cohen.breast.cancer.cnn?iref=allsearch


Immunoglobulin
(IgM)
V
V
V
V
C1
C1
C1
C1
C1
C1
C1
C1
C1
C1
S-S
IgM&TCR.pcx
Figure 5-16
Upper Left
Kuby, 2nd Ed
T-cell receptor α/β γ/δ
V
V
C1
C1
S-S

I am here!

(Testing your XR Transmitter)

1. Yes
2. No

TCR&MHC.pcx
Figure 5-16
Upper Right
Kuby, 2nd Ed