Molecular genetics III

Winter semester

5th week (Nov 3rd – Nov 7th 2008)

Institute of Biology and Medical Genetics 1.LF UK a VFN, Praha

Human DNA polymorphisms used for linkage analysis, direct and indirect diagnostics

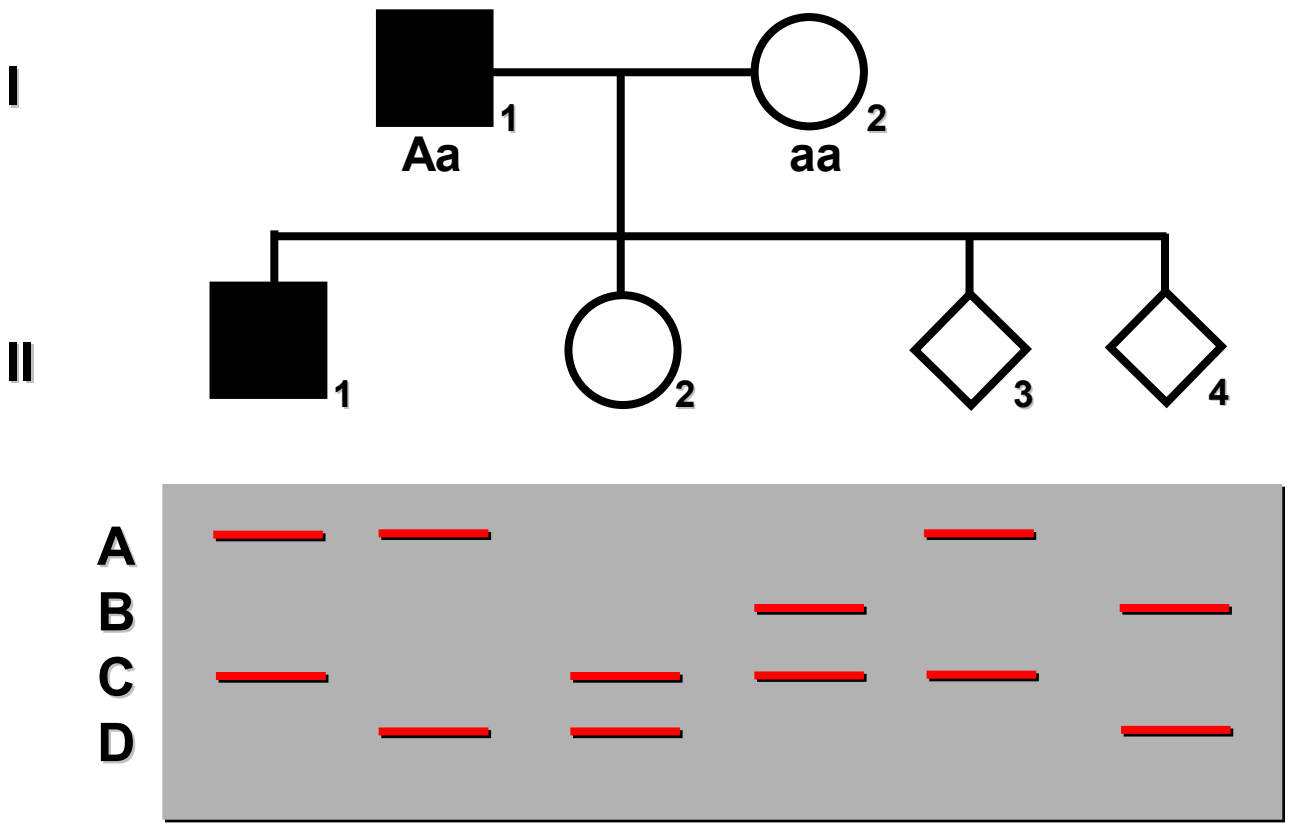
Microsatellites (or STR = short tandem repeats, SSR = simple sequence repeats)

TAGCCATCGGTACACACACACACACACAGTGCTTCAGTAGC

TAGCCATCGGTACACACACACACAGTGCTTCAGTAGCGTAG

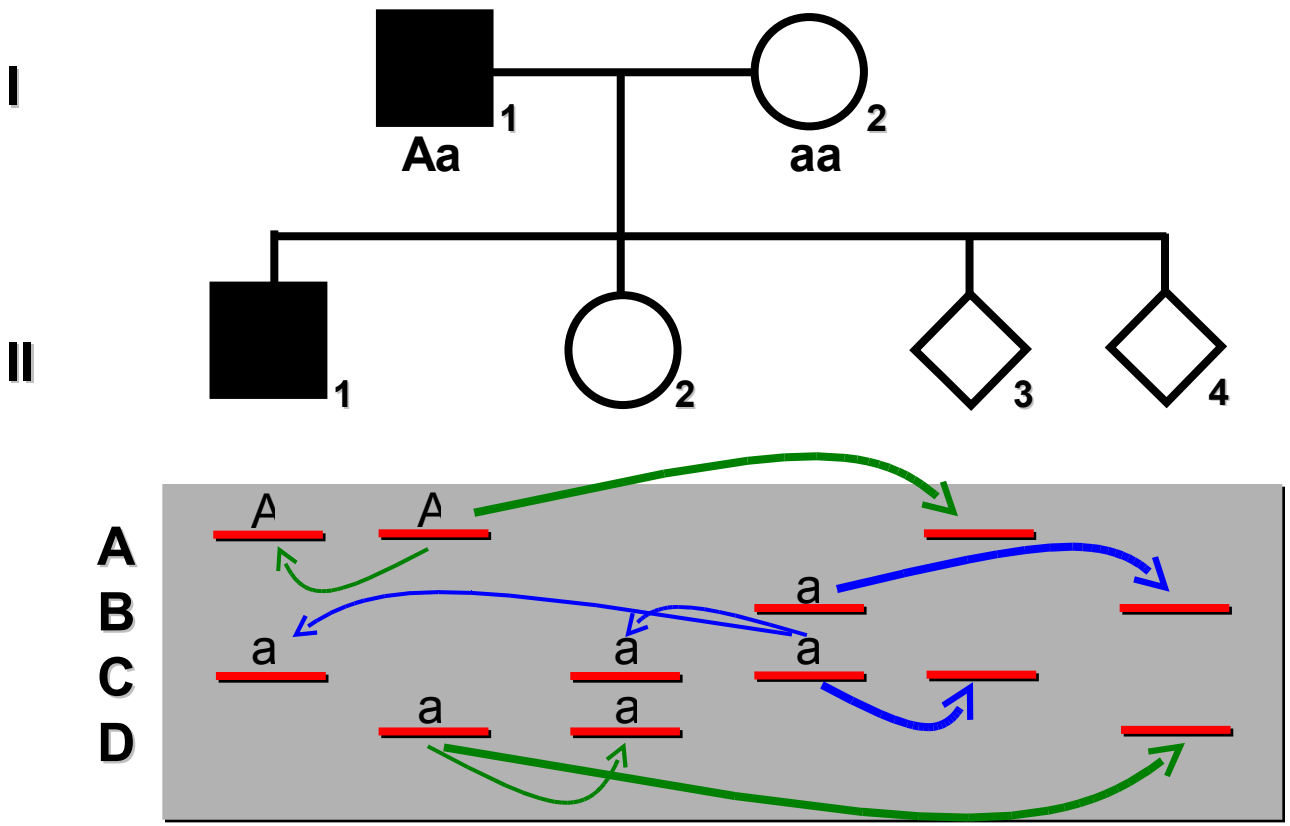
If a *detectable* polymorphism is situated closely enough to a locus, which harbors a causal mutation for the studied disease, the polymorphism will be linked to the mutated allele. In most cases, the polymorphism will be passed together with the mutated allele from the parents to the offspring („cosegregation“). Thus, the polymorphism can be used as a „marker“ for the diesase even without exact knowledge of its molecular basis.

Task 5, p. 122 – Polycystic kidney disease (AD, p = 5cM)



a) Risk of being affected is 50% for II/3 and II/4.

Task 5, p. 122 – Polycystic kidney disease (AD, p = 5cM)

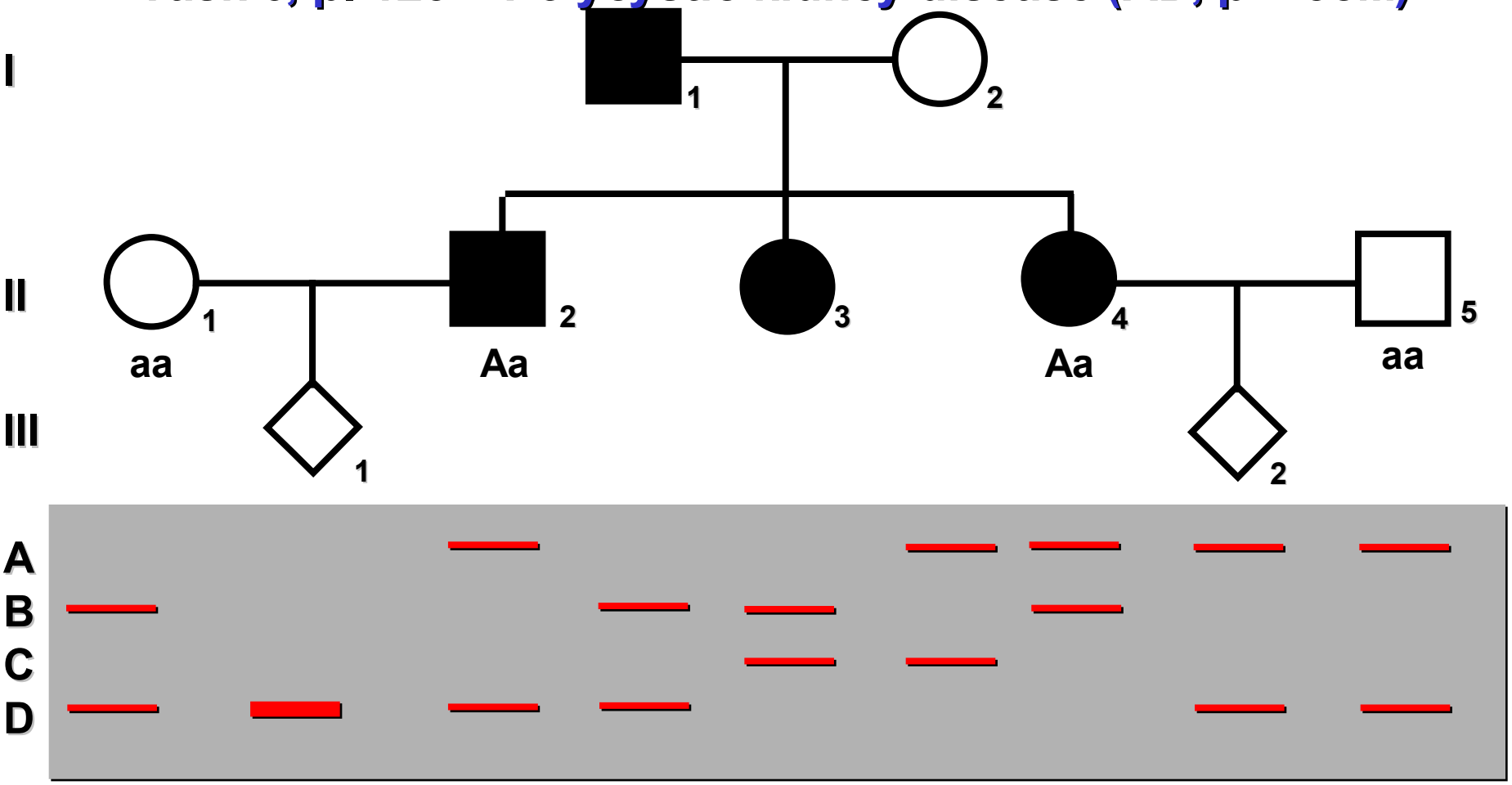


a) Risk of being affected is 50% for II/3 and II/4.

b) Risk of being affected is 95% for II/3.

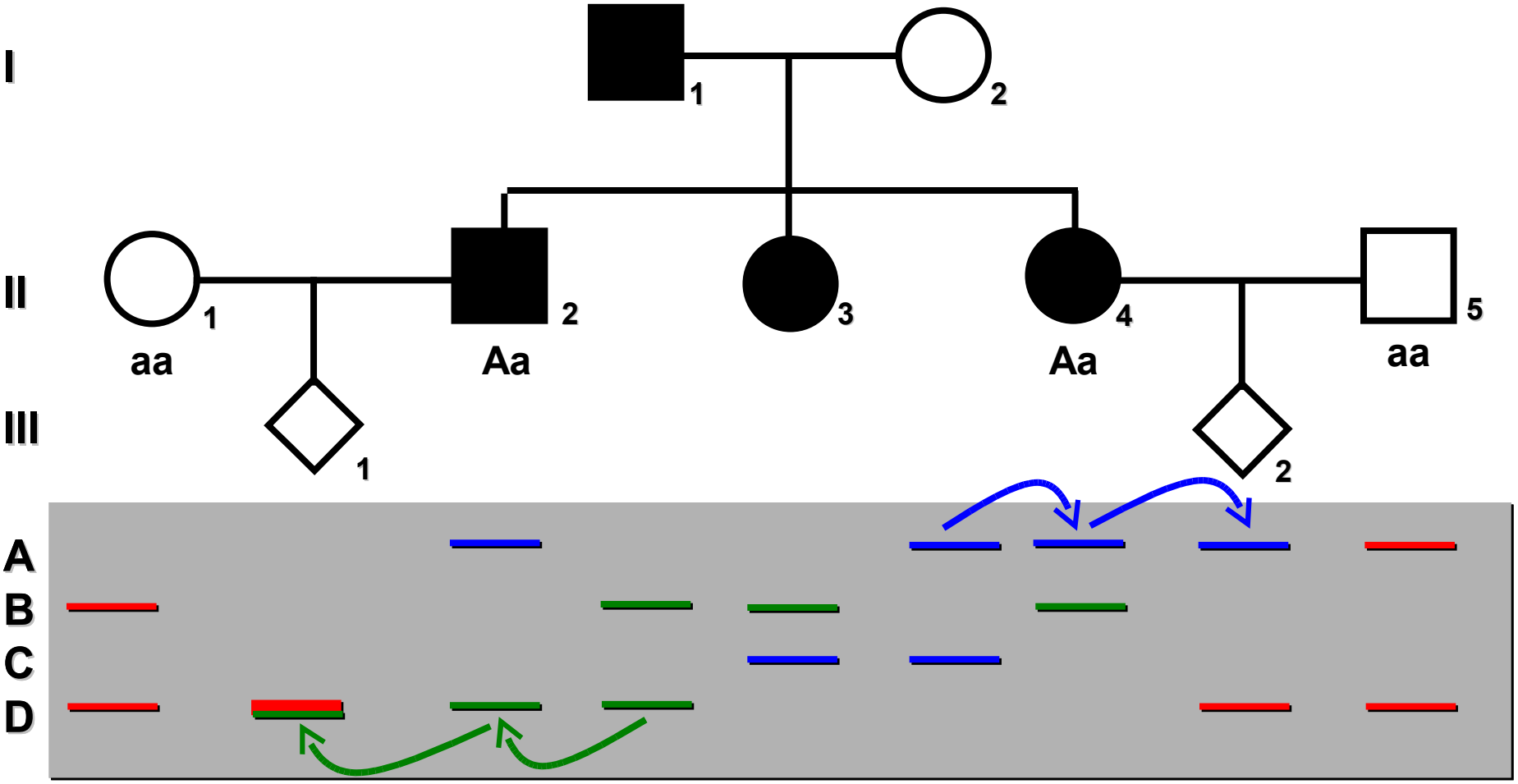
b) Risk of being affected is 5% for II/4.

Task 6, p. 123 – Polycystic kidney disease (AD, p = 5cM)



a) Risk of being affected is 50% for III/1 and III/2.

Task 6, p. 123 – Polycystic kidney disease (AD, p = 5cM)



b) Risk of being affected is 95% for III/1.

b) Risk of being affected is 5% for III/2.

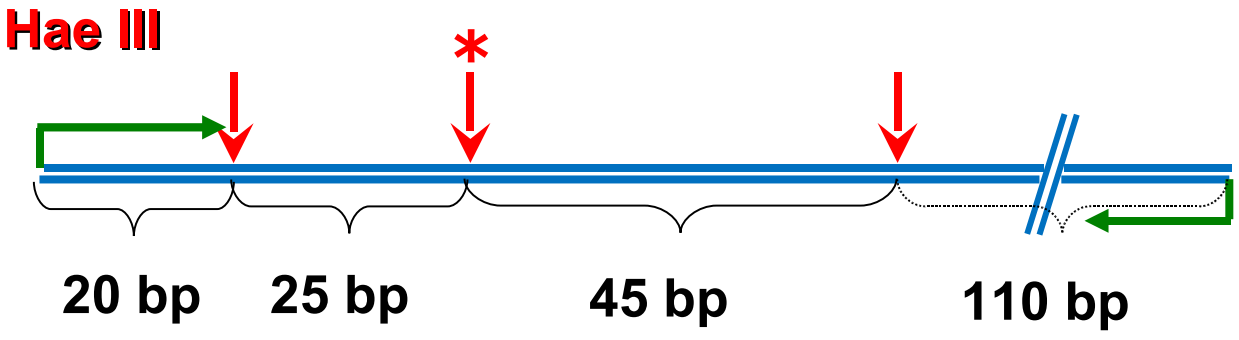
PCR

POLYMERASE CHAIN REACTION

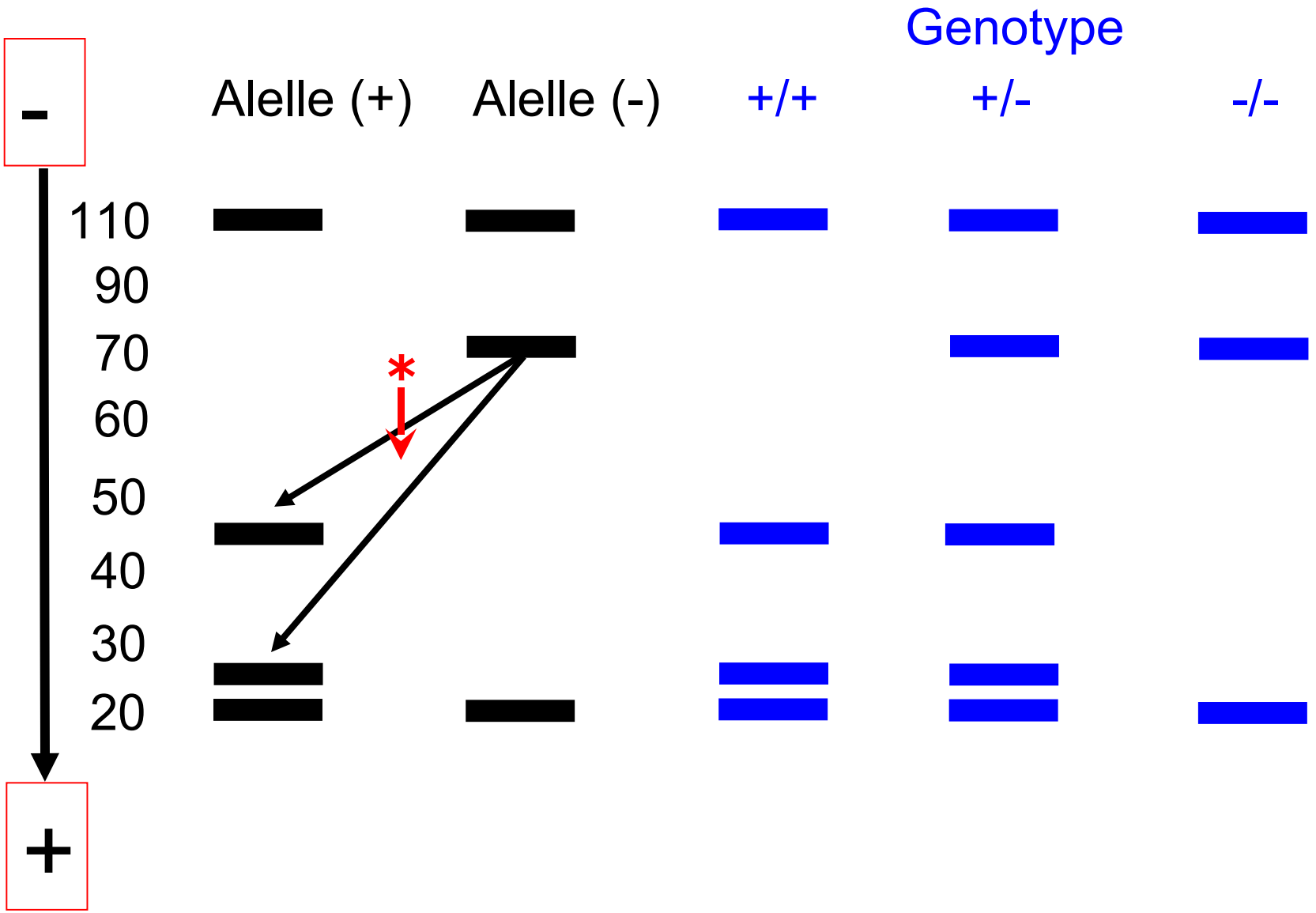
animation at external site:

http://www.sumanasinc.com/webcontent/anisamples/molecularbiology/pcr.html

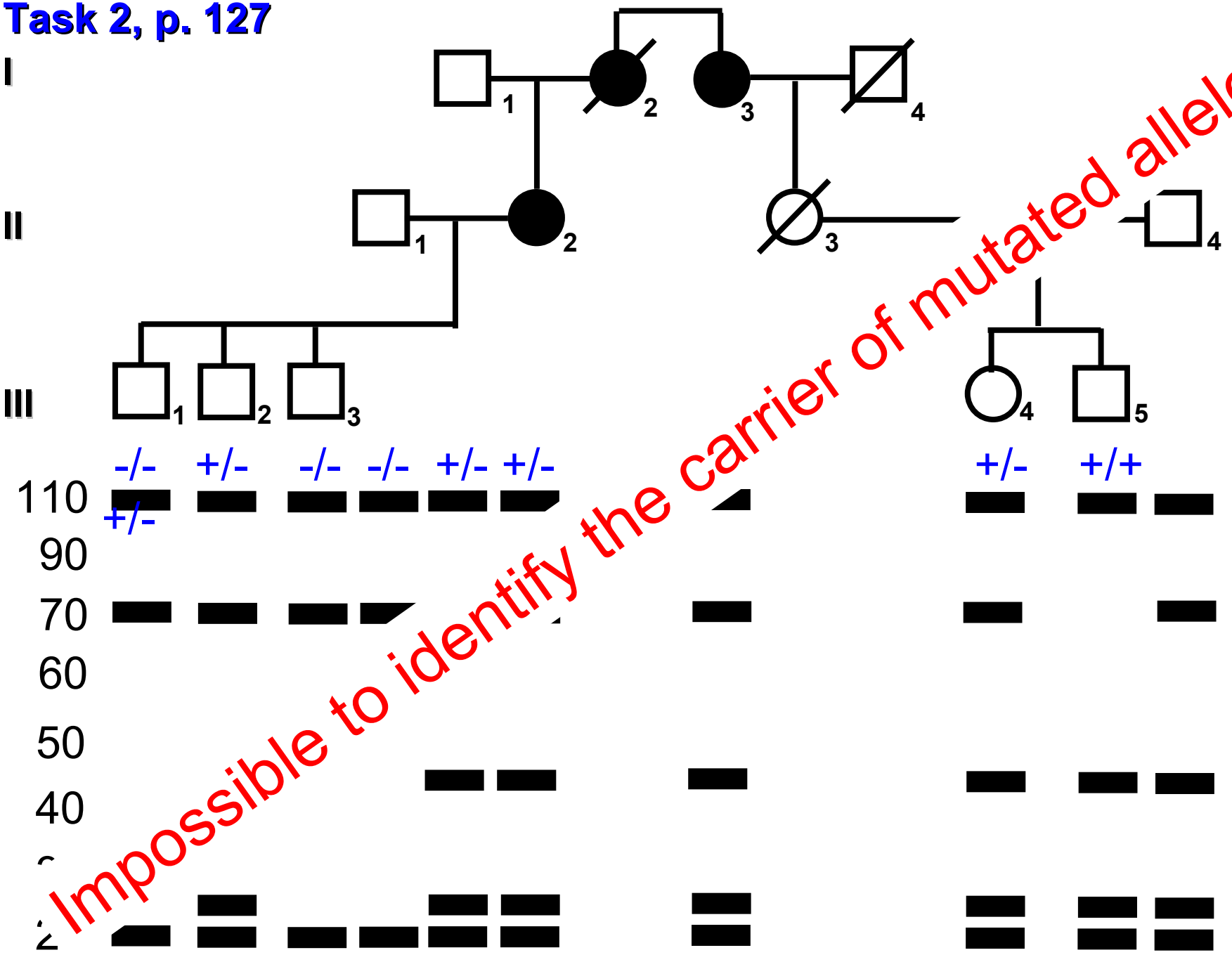
p.125


Hae III
*
Allele +
20 bp
25 bp
45 bp
110 bp
Fragments
20 bp
25 bp
45 bp
110 bp
Hae III
Allele -
20 bp
25 bp
45 bp
110 bp
Fragments
20 bp
70 bp
110 bp

During electrophoresis, smaller fragments migrate quicker than larger ones.

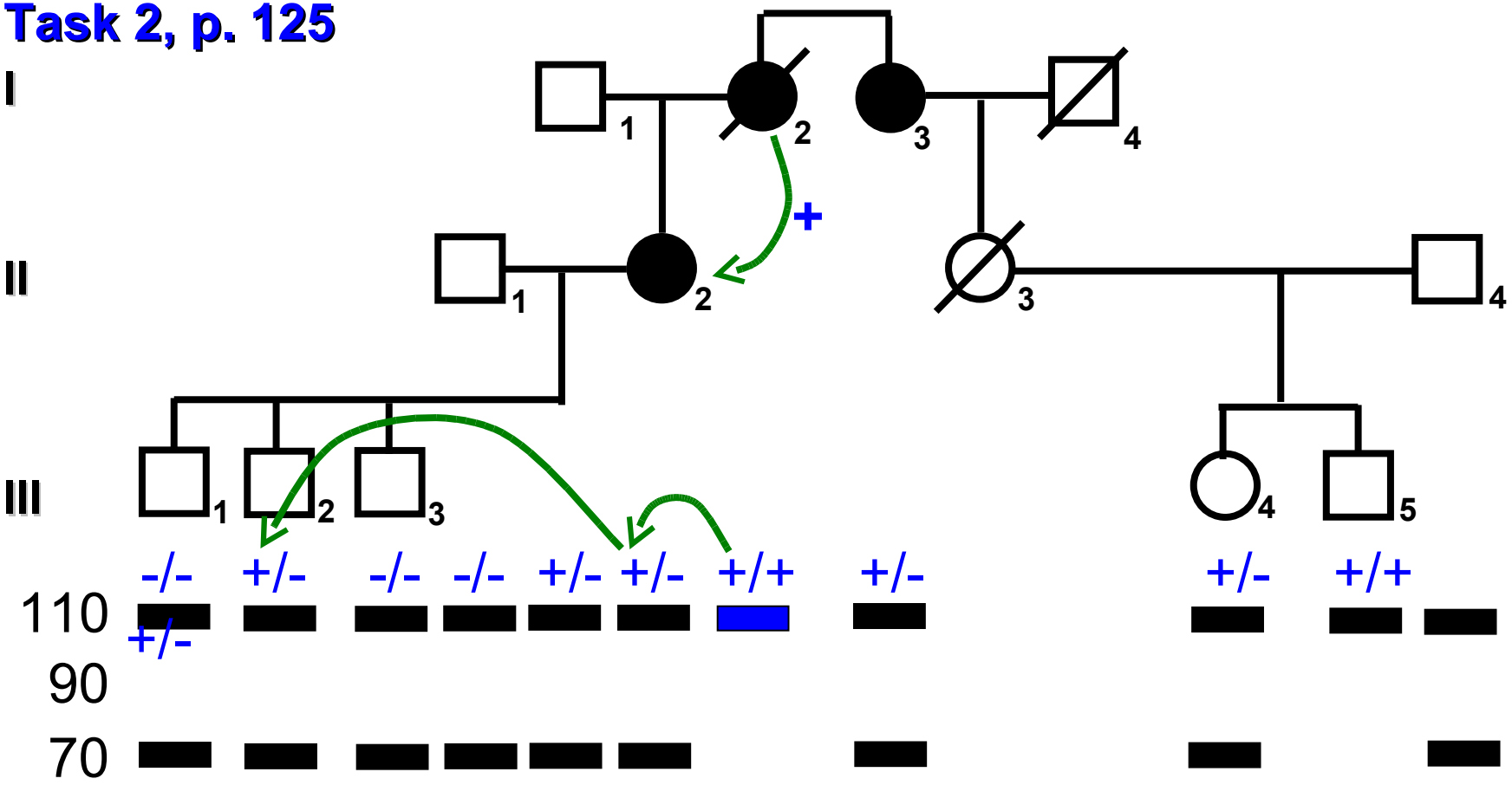


Task 2, p. 127



Impossible to identify the carrier of mutated allele

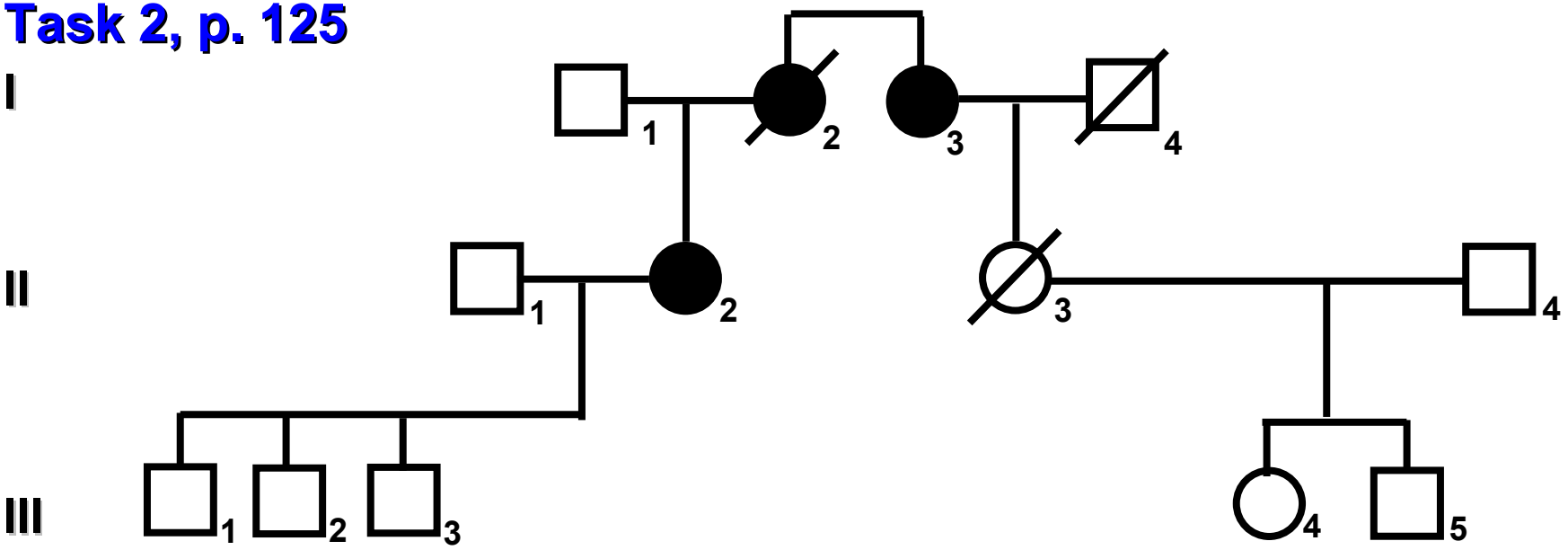
Task 2, p. 125

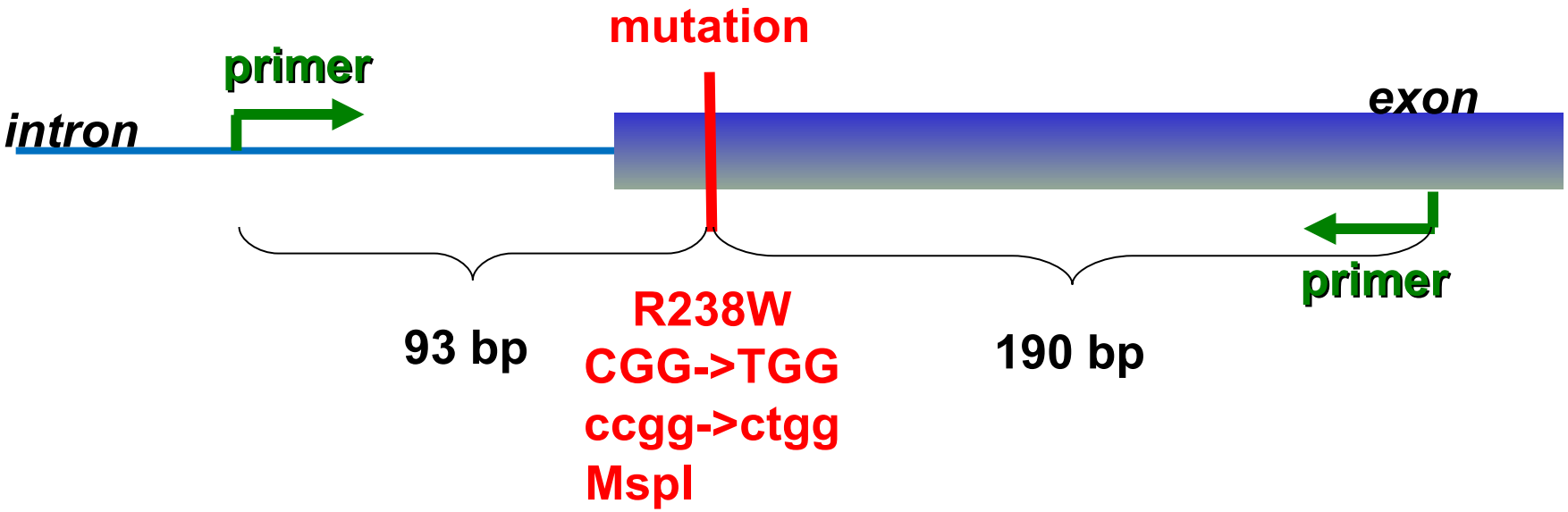


III/1, III/3 unaffected ; III/2 carrier of mutated allele

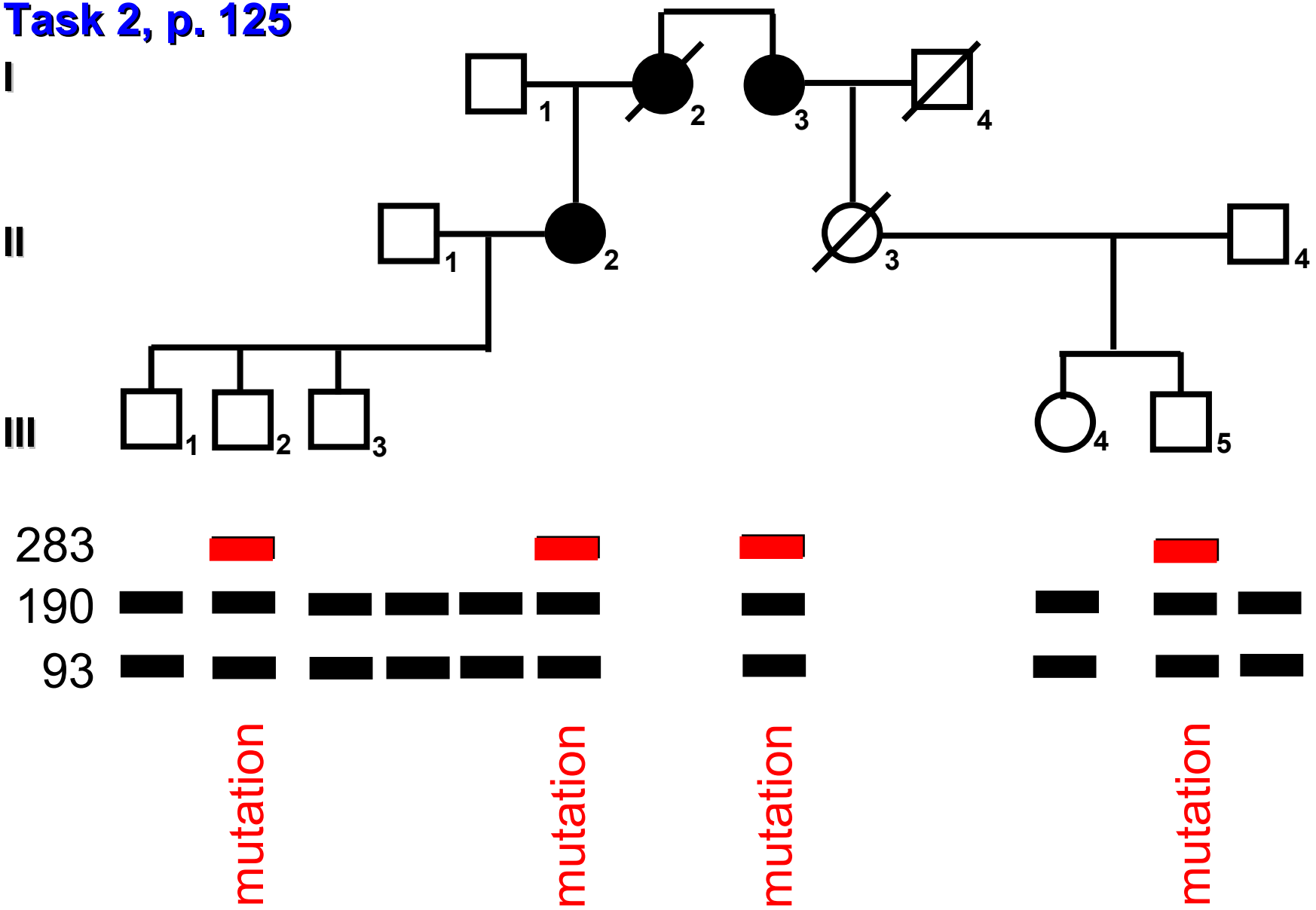
III/4, III/5 impossible to determine

Task 2, p. 125


I
1
2
3
4
II
1
2
3
4
III
1
2
3
4
5

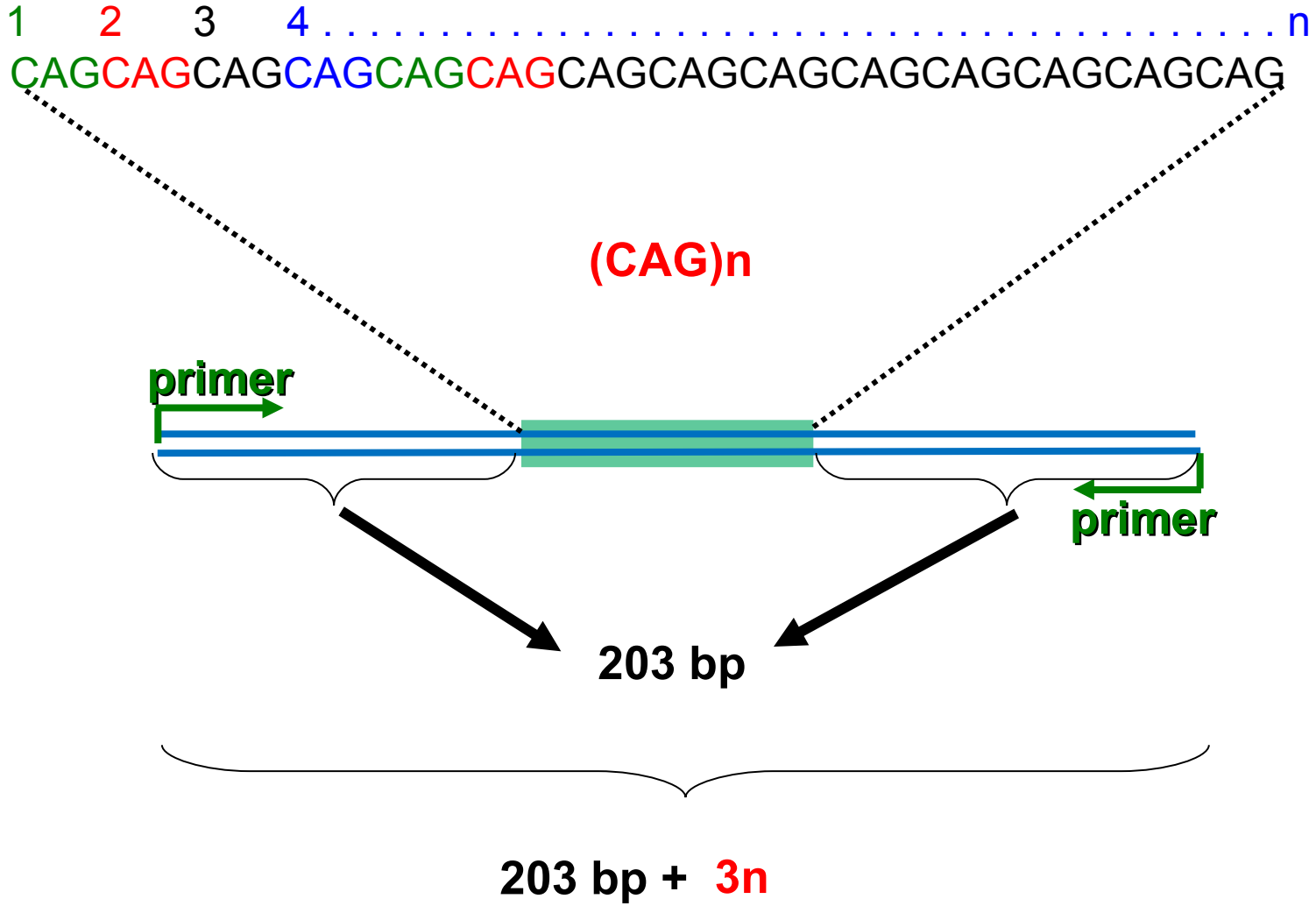

mutation
primer
intron
exon
primer
93 bp
R238W
CGG->TGG
ccgg->ctgg
MspI
190 bp

Task 2, p. 125

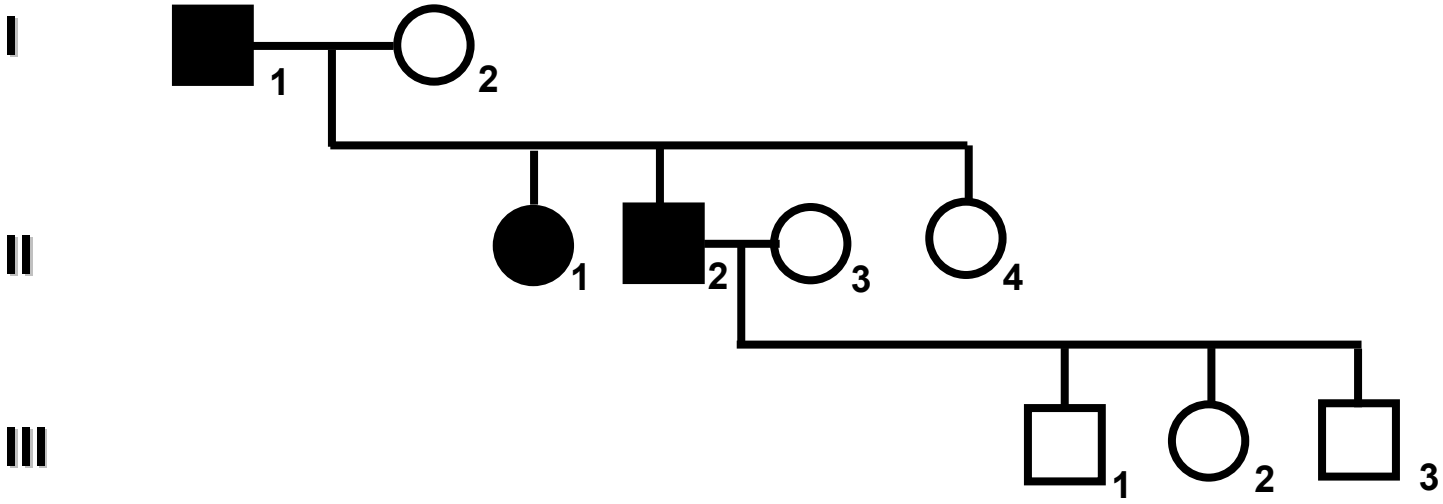


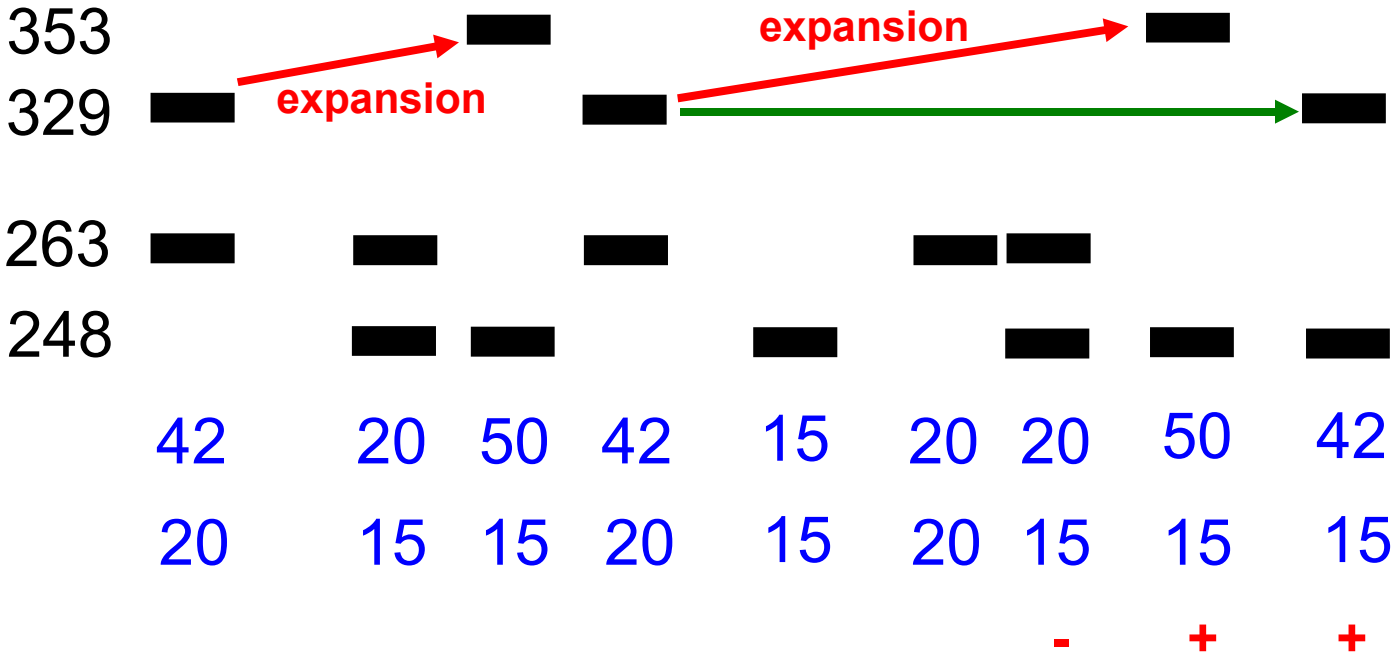
Direct diagnostics of causal allele, the diagnosis is fully informative even in family with incomplete data.

Task 3, p. 129 – direct presymptomatic diagnosis of Huntington chorea

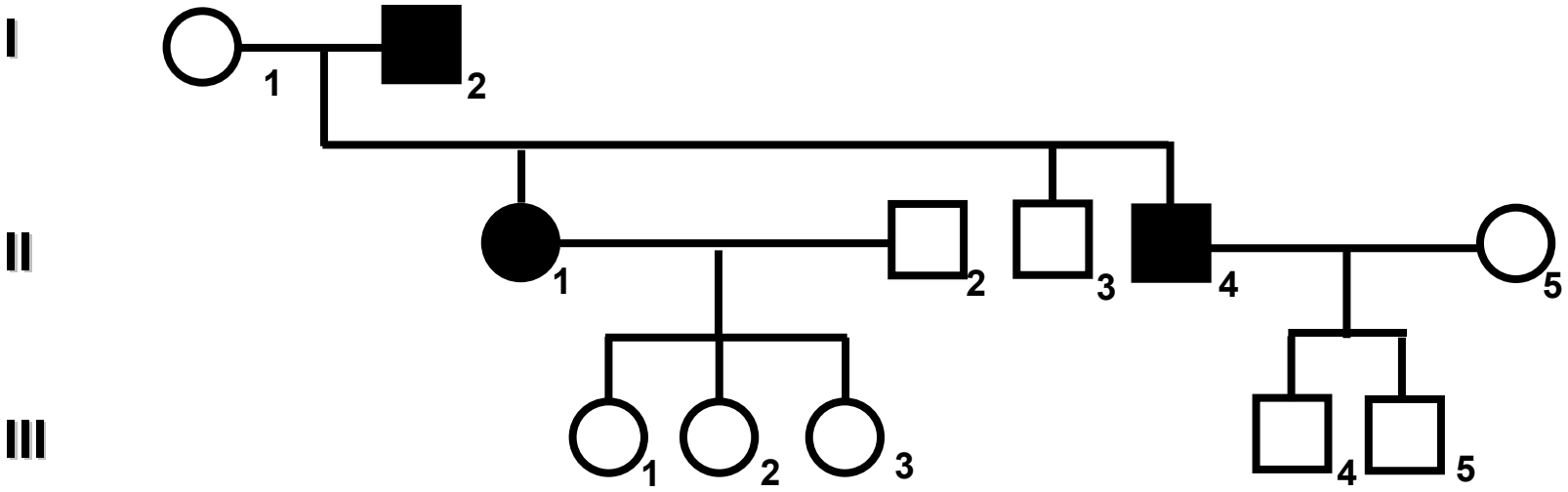


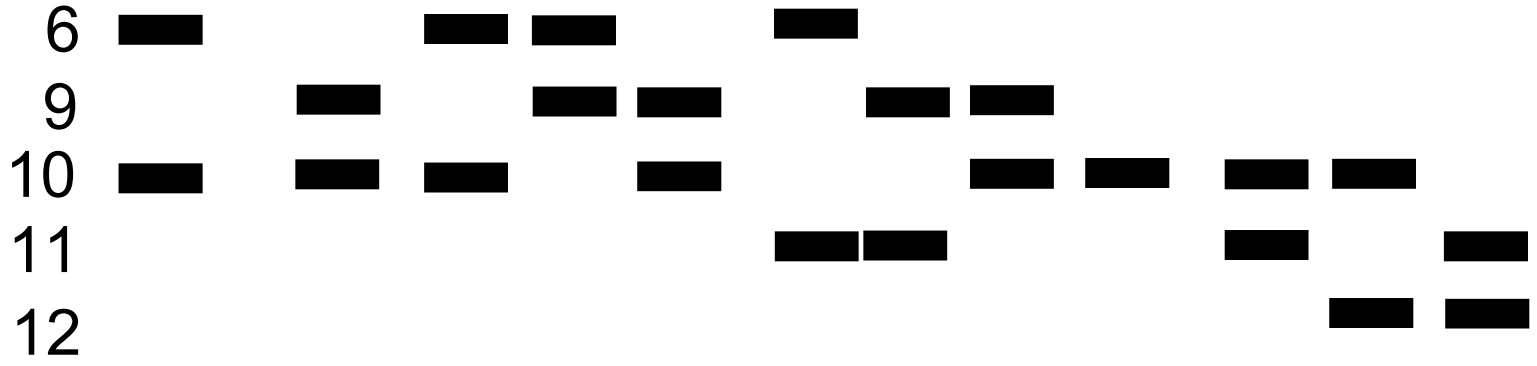
Task 3, p. 129 – direct presymptomatic diagnosis of Huntington chorea



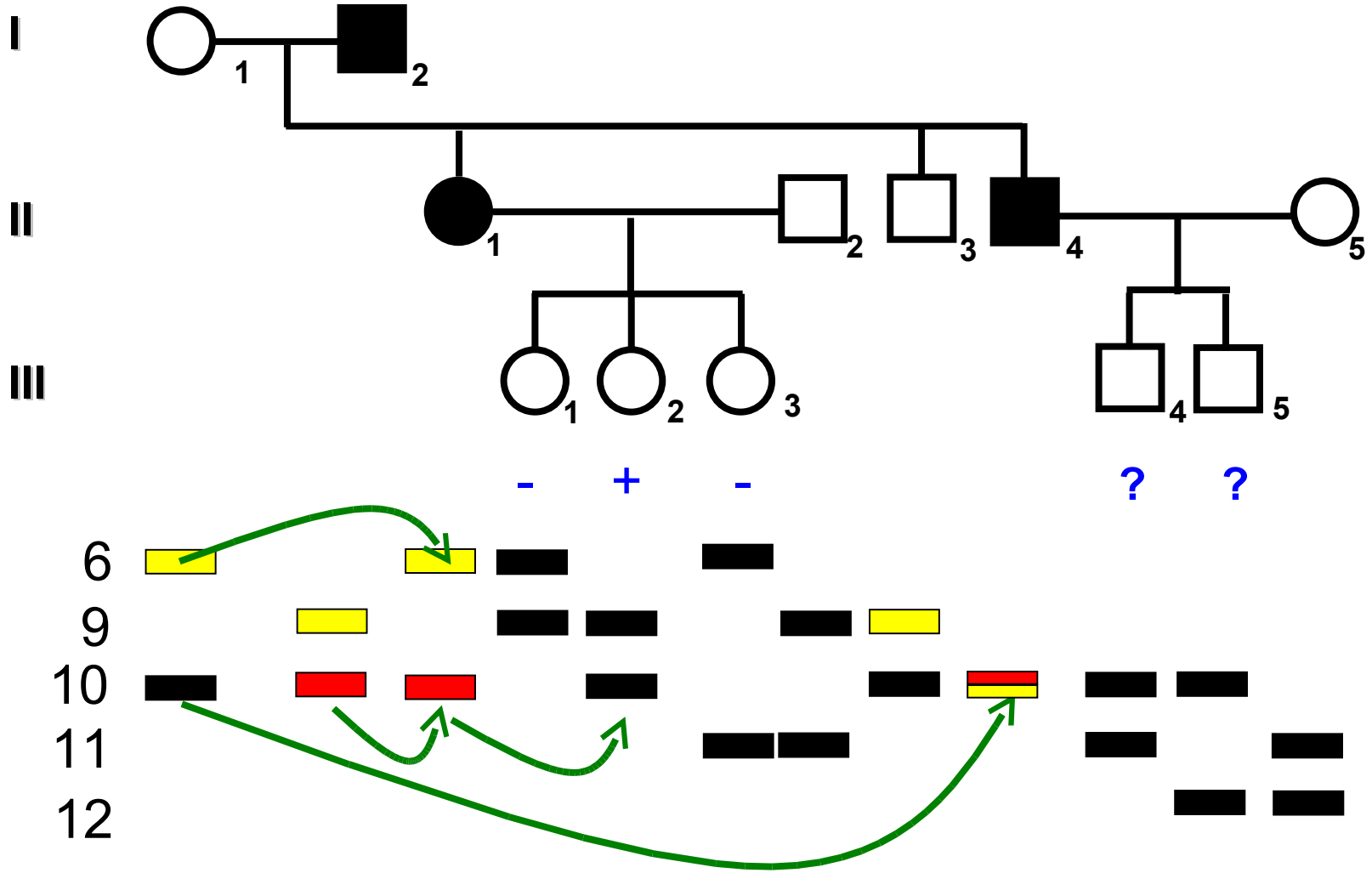


Task 4, p. 130 – indirect diagnostics of familiar adenomatous polyposis





Task 4, p. 130 – indirect diagnostics of familiar adenomatous polyposis



FAP is linked to allele 10.

b) Analyze another polymorphism, in which the II/4 is heterozygous or use direct diagnostcs – detection of APC gene mutation.