(iv) **Penetration resistance** occurs when the cuticle (outer layer of insects) absorb the insecticides molecules much more slowly than the susceptible insects. In addition, the mechanism on thermal stress response has also been proposed by Patil et al. (1996) (42), but its significance has not been well established.

The Biochemical Resistance Mechanisms on the Molecular Level

1) Knockdown Resistance (kdr)

Pyrethroids are one of the most broad-spectrum insecticides and are commonly applied to control virtually all arthropods in terms of agricultural and medically important concern. It is a large class of structurally very diverse, synthetic analogues of natural pyrethrins from the plant of Chrysanthemum spp. extracts. The insecticide resistance mechanism of pyrethroid is known as *knockdown resistance (kdr)* resulting from **mutations in the voltage-gated sodium channel** (the target-site for DDT and pyrethroids).

Although many insecticide resistance mechanisms are hitherto proposed, the **kdr and metabolic resistance** due to insecticide-detoxification are considered to be the most significant mechanisms.

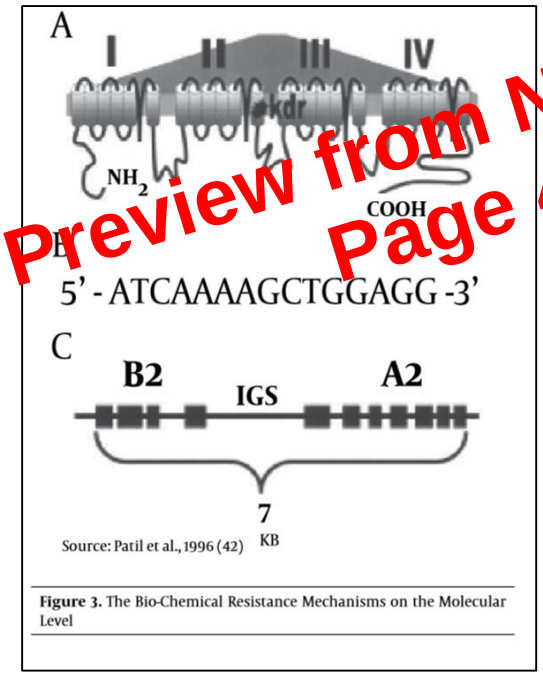

Figure 3. The Bio-Chemical Resistance Mechanisms on the Molecular Level

a. **Single amino acid mutation** in the IIS6 membranes spanning region of the voltage-gated sodium channel gene confers with the target site DDT-pyrethroid resistance in *An. gambiae*. The similar type of mutated codon produces resistance to a number of diversified insects such as mosquitoes, sand flies, cockroaches, and flies (Fig. A).

b. The **regulatory element** termed the Barbie Box al oxidase and esterase resistance genes (Fig. B).

c. **Esterase A2-B2 alleles (amplicons)**. An amplicon is a piece of DNA or RNA that is the source of replication process, which produce one or more copies of a genetic fragment. These resistance esterase genes lie 5' end to 5' end within the same amplification unit. It has been estimated that nearly more than 100 copies of this amplicon may be present within a single species of mosquito (Fig. C)