

## THE ALLOSTERIC MACROMOLECULE FOR SODIUM CHANNEL

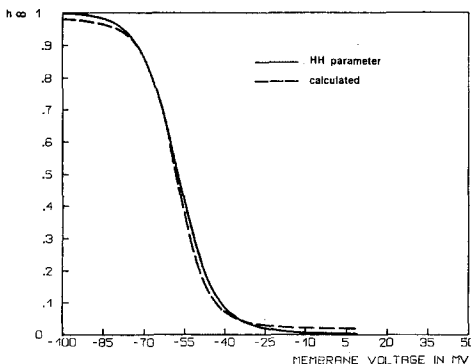
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While the existence of that elusive object ( the sodium channel protein ) might be considered as proved beyond any reasonable doubt, its structural and functional properties remain completely unspecified to date.

In this regard one of the most auspicious concepts is the allosteric and oligomeric protein molecule of Monod, Changeux and Wyman (MWC) (1). It is based on assumptions of utmost generality, such as elementary molecular interaction and principles of symmetry. Enlarging this model's scope so as to encompass a prospective membrane bound channel protein implies replacing ligand specificity by electrospecificity. This modification is thought not to be at variance with principal model assumptions.

Possible reaction mechanisms sensitive to the electric field are discussed by Hill and Chen(2) as well as used for an approximate description of the Hodgkin and Huxley (HH) parameters  $n_\infty$  and  $m_\infty$ . Neglecting all terms of second order the present approximation is admittedly cruder than the above. But assuming only first order reaction kinetics the activity parameter of MWC and membrane potential become equivalent quantities and the formalism of MWC may be applied. One result (3), the reproduction of the parameter  $h_\infty$  is shown in the figure.

The close relation between the HH formalism and the MWC model is further demonstrated by an identity of the reaction schemes for either the HH sodium channel as deduced by T.L.Hill (4) or of the MWC oligomeric ligand binding protein. The principal difference consists in correlating the transition activating-inactivating the channel to the change from tense to relaxed conformation ( and vice versa ) rather than to a fourth subunit. The antagonism of long standing, additive independence versus sequential multistate kinetics, thus might be settled and a fairly large amount of experimental findings, hitherto considered incompatible with HH kinetics, can be understood.



## References:

- (1) J.Monod, J.Wyman and J.-P. Changeux: J.Mol.Biol. (1965) 12, 88 - 118
- (2) T.L.Hill and Y.Chen: Proc. Nat.Acad.Sci.USA (1972), 69, 7, 1723 - 1726
- (3) Th.Lorenz and I.Schmiedel-Jakob, submitted for publication
- (4) T.L.Hill in D.P.Agin ed.: Perspectives in Membrane Biophysics, (1972), 187 - 203