Hodgkin- Huxley.

<u>Idealised Channel</u>, which is open when a gating particle with charge ze is in the open position.

y = fraction of open channels

$dy/dt = \alpha(1-y) - \beta y = \alpha - (\alpha+\beta)y$ Eq 1

In the steady state $y = y_0 = \alpha/(\alpha+\beta)$

We can rewrite Eq 1 as $dy/dt = (y_0-y)/\tau$. Eq 2

Both Eqs 1 and 2 are equivalent, some authors use rate constants , some use time constant and y_0.

If we make a step change in either or both of the rate constants, as in a voltage clamp experiment (H & H assumed that V determines the rate constants, in a manner to be discussed below), the temporal evolution of y is given by the solution of eq 1 or eq 2:

$y = y_{\&} -(y_{\&}-y_0)\exp-(\alpha+\beta)t$

(I have used & to represent the infinity sign. $y_{\&}$ and y_0 are just the fraction of channels open at the end of the step and before the step.

The V-dependence of $y_{\&}$ or y_0 can be calculated using the Boltzmann formula, since the energy increase of the gating particle moving from the closed to open positions is $ze\delta V$ where δ is the fraction of the membrane potential through which the gating charge moves. The result is $y_{\&} = 1/(1+\exp(C - ze\delta V/kT))$ where C is the chemical energy difference between the closed and open states. This is a sigmoidal function of V, with $z\delta$ governing the steepness of the curve and C governing its position along the V axis.

Similarly, the V-dependence of the rate constants can be calculated assuming that the barrier is half way between the closed and open positions. The results are

$\alpha = \alpha_0 \exp ze\delta V/2kT$ and $\beta = \beta_0 \exp - ze\delta V/2kT$

where α_0 β_0 are the rate constants at V = 0. The factor 2 in the denominator arises because the peak of the energy barrier is midway between the open and closed positions of the gating charge .

From these equations it can be seen that τ will have a bell-shaped dependence on V. Because we assumed a symmetrical barrier, the peak of the bell will occur at the voltage corresponding to the midpoint of the Boltzmann y_0 sigmoid.

Real HH channels

To account for the sigmoidal conductance activation 4 identical independent gating particles behaving as above were postulated, with all 4 required open to open the channel. Thus $G_k = G_{k,max}\, n^4$

where $G_{k,max}$ is the maximum K-conductance, with all the K channels open. For Na channels, to account for inactivation, an additional h gating particle was postulated. This is in the *open* position at negative potentials. So $G_{Na} = G_{Na,max}\ m^3h$

For the "space clamped" or isopotential condition, the current equation is

$$I_{stim} = I_l + I_{Na} + I_k + C\ dV/dT$$

with $I_{Na} = G_{Na}\ (V\text{-}E_{Na})$ etc. I_l is the leak current.

For the propagating spike, the cable equation must be used, modified to include active conductances:

$$d^2V/dx^2\ (1/\ r_a) = I_l + I_{Na} + I_k + C\ dV/dT$$

Since the spike advances as a nondecrementing wave, one can replace x by θt where θ is the (unknown) velocity. Although θ is unknown, it will be close to the observed velocity, and in simulating the equations on a computer, one starts with a "guessed" value of θ similar to the observed value. This will not be exactly right for the H-H model, and because of this internal inconsistency, the calculations will soon "blow up", leading to infinities. Trial and error will yield successively better values of θ, which should (if the HH equations provide a good description of spike propagation) still be quite close to the experimental values.

In reality, H and H also slightly modified the above equations for the rate constants to better fit the data.