THE THERMODYNAMIC BASIS OF COOPERATIVE ASSEMBLY: RELATION OF ASSOCIATION CONSTANTS, BOND ENERGY, AND SUBUNIT ENTROPY

Cooperativity means that the association of subunits is enhanced as their number increases, i.e., that larger polymers are more favorable than smaller. The reason is that subunits in the interior, which are relatively more numerous in larger polymers, have more bonds than subunits at the edge, so the average bond energy per subunit increases as the polymer grows larger. For a quantitative description of cooperativity we need to know the free energy change for subunits associated by different numbers and combinations of bonds. The basis of the theory is illustrated most simply by considering the relation of the three association constants

for polymerization of a subunit into a 2-D lattice (Fig. 1). It can attach (*a*) to the side of the sheet, forming a lateral bond of energy e_a; (*b*) to the end of a protofilament, forming a longitudinal bond of energy e_b; or (*c*) into a niche or "cozy corner," forming both a lateral and a longitudinal bond, with total bond energy $e_c = e_a + e_b$.

The key point in the analysis is to separate the free energy of association into two parts. One component, which opposes association, is the free energy required to immobilize a subunit in the polymer. We assume that this free energy, which we designate e_s, is the same regardless of whether the subunit forms a lateral bond, a longitudinal bond, or both at once. The other component, which favors association, is the free energy associated with the interface or bond between subunits, either e_a, e_b, or $e_a + e_b$, depending on the type of bonds formed.