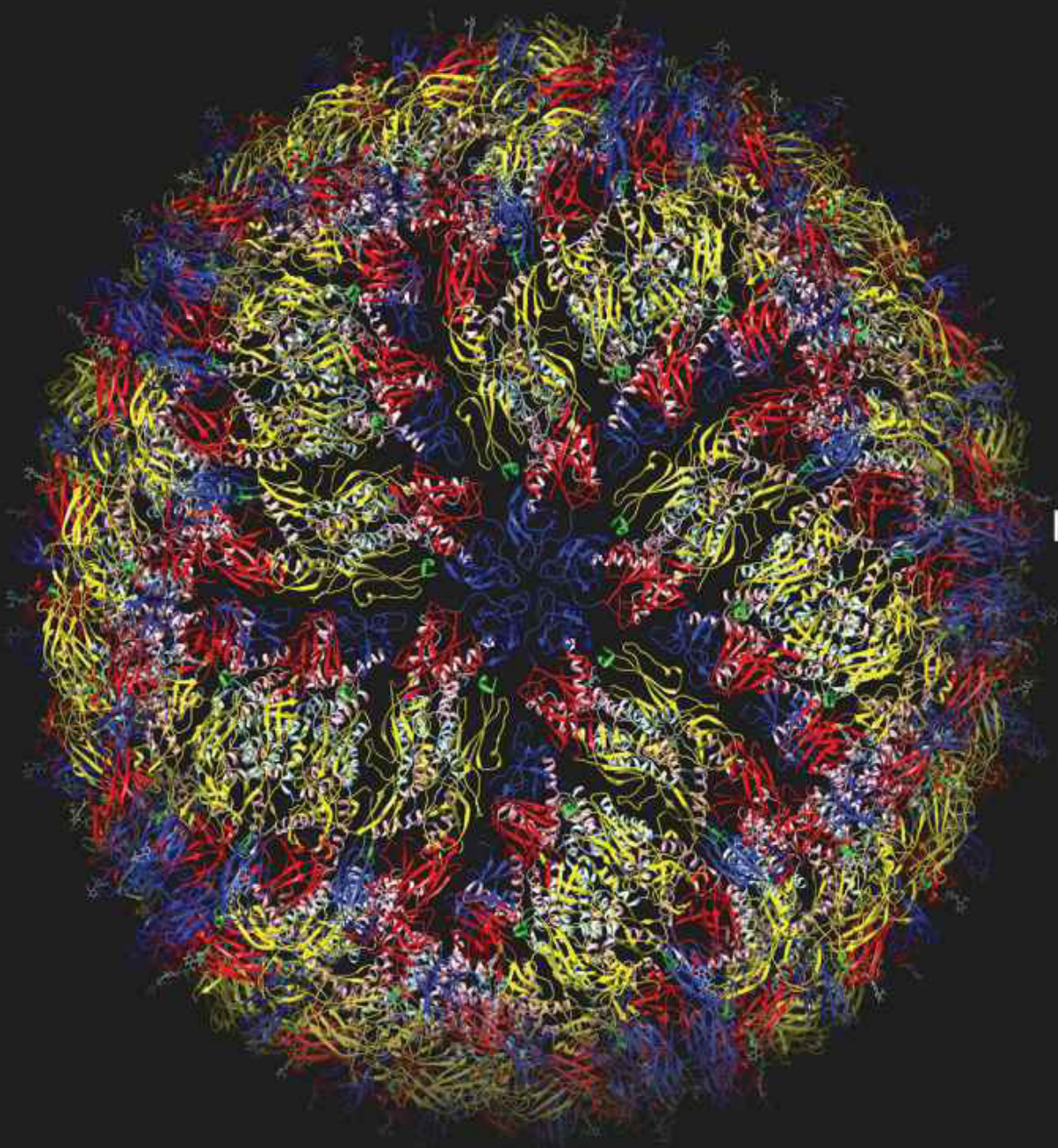

Victor W.
RODWELL

David A.
BENDER

Kathleen M.
BOTHAM

Peter J.
KENNELLY

P. Anthony
WEIL

31ST EDITION

HARPER'S ILLUSTRATED BIOCHEMISTRY

Mc Graw Hill Education
LANGE®

(transferases), subclass 7 (transfer of a phosphoryl group), sub-subclass 1 (alcohol is the phosphoryl acceptor), and “hexose-6” indicates that the alcohol phosphorylated is on carbon six of a hexose. While EC numbers have proven particularly useful to differentiate enzymes with similar functions or similar catalytic activities, IUB names tend to be lengthy and cumbersome. Consequently, hexokinase and many other enzymes commonly are referred to using their traditional, albeit sometimes ambiguous names.

PROSTHETIC GROUPS, COFACTORS, & COENZYMES PLAY IMPORTANT ROLES IN CATALYSIS

Many enzymes contain small molecules or metal ions that participate directly in substrate binding or in catalysis. Termed **prosthetic groups**, **cofactors**, and **coenzymes**, they extend the repertoire of catalytic capabilities beyond those afforded by the functional groups present on the aminoacyl side chains of peptides.

Prosthetic Groups

Prosthetic groups are tightly and stably incorporated into a protein’s structure by covalent or noncovalent forces. Examples include pyridoxal phosphate, flavin mononucleotide (FMN), flavin adenine dinucleotide (FAD), thiamin pyrophosphate, lipoic acid, biotin, and transition metals such as Fe, Co, Cu, Mg, Mn, and Zn. Metal ions that participate in redox reactions generally are bound as organometallic complexes such as the prosthetic groups heme or iron–sulfur clusters (see Chapter 10). Metals also may facilitate the binding and orientation of substrates, the formation of covalent bonds with reaction intermediates (Co^{2+} in coenzyme B_{12}, see Chapter 44), or by acting as Lewis acids or bases to render substrates more **electrophilic** (electron-poor) or **nucleophilic** (electron-rich), and hence more reactive (see Chapter 10).

Cofactors Associate Reversibly With Enzymes or Substrates

Cofactors serve functions similar to those of prosthetic groups. The major difference between the two is operational, not chemical. Cofactors bind

weakly and transiently to their cognate enzymes or substrates, forming dissociable complexes. Therefore, unlike associated prosthetic groups, cofactors must be present in the surrounding environment to promote complex formation in order for catalysis to occur. The most common cofactors also are metal ions. Enzymes that require a metal ion cofactor are termed **metal-activated enzymes** to distinguish them from the **metalloenzymes** for which bound metal ions serve as prosthetic groups.

Many Coenzymes, Cofactors, & Prosthetic Groups Are Derivatives of B Vitamins

The water-soluble B vitamins supply important components of numerous coenzymes. **Nicotinamide** is a component of the redox coenzymes NAD and NADP (**Figure 7–2**); **riboflavin** is a component of the redox coenzymes FMN and FAD; **pantothenic acid** is a component of the acyl group carrier **coenzyme A**. As its pyrophosphate **thiamin** participates in the decarboxylation of α-keto acids while folic acid and cobamide coenzymes function in one-carbon metabolism. In addition, several coenzymes contain the adenine, ribose, and phosphoryl moieties of AMP or ADP (Figure 7–2).

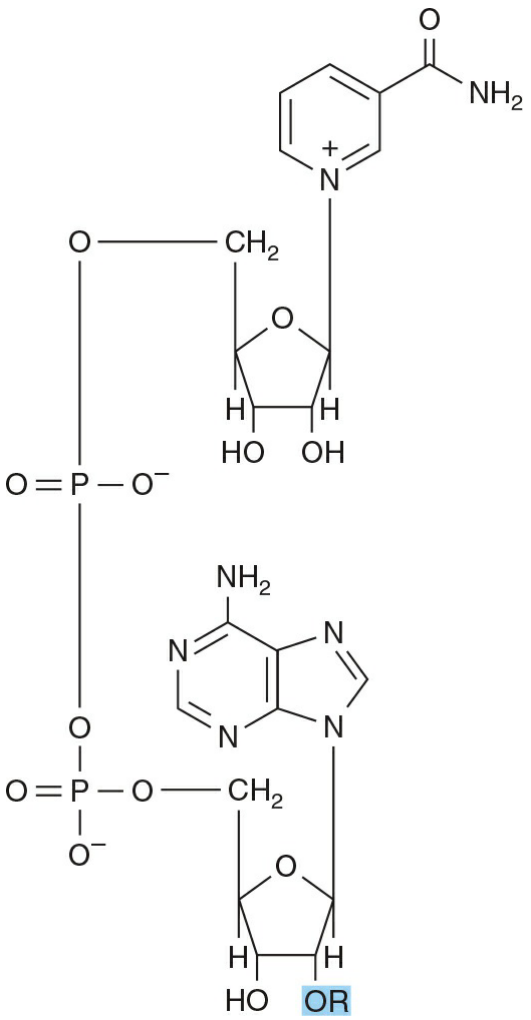

FIGURE 7–2 Structure of NAD+ and NADP$^+$. For NAD^+, OR = —OH. For $NADP^+$, —OR = —OPO_3^{2-}.

Coenzymes Serve as Substrate Shuttles

Coenzymes serve as recyclable shuttles that transport many substrates from one point within the cell to another. The function of these shuttles is twofold. First, they stabilize species such as hydrogen atoms ($FADH_2$) or hydride ions (NADH) that are too reactive to persist for any significant time in the presence of the water, oxygen, or the organic molecules that permeate cells. Second, they increase the number of points of contact between substrate and enzyme, which increases the affinity and specificity with which small chemical groups such as acetate (coenzyme A), glucose (UDP), or hydride (NAD^+) are bound by their target enzymes. Other chemical moieties transported by coenzymes include methyl groups (folates) and oligosaccharides (dolichol).