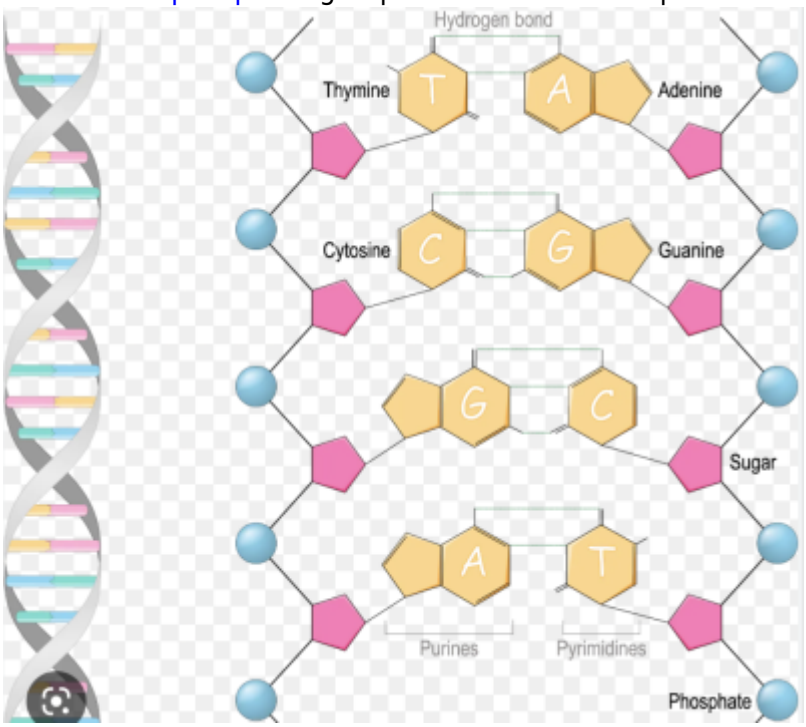
Nucleotide

Nucleotides are organic molecules that serve as the monomers, or subunits, of nucleic acids like DNA and RNA. The building blocks of nucleic acids, nucleotides are composed of a nitrogenous base, a five-carbon sugar (ribose or deoxyribose), and at least one phosphate group. Thus a nucleoside plus a phosphate group yields a nucleotide.



Most DNA molecules consist of two biopolymer strands coiled around each other to form a double helix. The two DNA strands are known as polynucleotides since they are composed of simpler units called nucleotides. Each nucleotide is composed of a nitrogen-containing nucleobase—either guanine (G), adenine (A), thymine (T), or cytosine (C)—as well as a monosaccharide sugar called deoxyribose and a phosphate group. The nucleotides are joined to one another in a chain by covalent bonds between the sugar of one nucleotide and the phosphate of the next, resulting in an alternating sugar-phosphate backbone. According to base pairing rules (A with T and C with G), hydrogen bonds bind the nitrogenous bases of the two separate polynucleotide strands to make double-stranded DNA.

Nucleotides serve to carry packets of energy within the cell in the form of the nucleoside triphosphates (ATP, GTP, CTP, and UTP), playing a central role in metabolism.

In addition, nucleotides participate in cell signaling (cGMP and cAMP), and are incorporated into important cofactors of enzymatic reactions (e.g. coenzyme A, FAD, FMN, NAD, and NADP+).

The genetic code defines how sequences of nucleotide triplets, called codons, specify which amino acid will be added next during protein synthesis.

In experimental biochemistry, nucleotides can be radiolabeled with radionuclides to yield

radionucleotides.

Long non-coding RNAs (long ncRNAs, lncRNA) are non-protein coding transcripts longer than 200 nucleotides.

Since the discovery of nucleotides over 100 years ago, extensive studies have revealed the importance of nucleotides for homeostasis, health, and disease. However, there remains no established method to investigate quantitively and accurately intact nucleotide incorporation into RNA and DNA. Herein, we report a new method, Stable-Isotope Measure Of Influxed Ribonucleic Acid Index (SI-MOIRAI), for the identification and quantification of the metabolic fate of ribonucleotides and their precursors. SI-MOIRAI, named after Greek goddesses of fate, combines a stable isotope-labeling flux assay with mass spectrometry to enable quantification of the newly synthesized ribonucleotides into r/m/tRNA under a metabolic stationary state. Using glioblastoma U87MG cells and a patient-derived xenograft (PDX) glioblastoma mouse model, SI-MOIRAI analyses showed that newly synthesized GTP was particularly and disproportionally highly utilized for rRNA and tRNA synthesis but not for mRNA synthesis in glioblastoma (Glioblastoma) in vitro and in vivo. Furthermore, newly synthesized pyrimidine nucleotides exhibited a significantly lower utilization rate for RNA synthesis than newly synthesized purine nucleotides. The results reveal the existence of discrete pathways and compartmentalization of purine and pyrimidine metabolism designated for RNA synthesis, demonstrating the capacity of SI-MOIRAI to reveal previously unknown aspects of nucleotide biology [1].

1)
Ikeda Y, Hirayama A, Kofuji S, Hirota Y, Kamata R, Osaka N, Fujii Y, Sasaki M, Ikeda S, Smith EP, Bachoo R, Soga T, Sasaki AT. SI-MOIRAI: A new method to identify and quantify the metabolic fate of nucleotides. J Biochem. 2021 Jul 9:mvab077. doi: 10.1093/jb/mvab077. Epub ahead of print. PMID: 34244779.