

Textbook of
Nuclear Medicine
Volume I: Basic Science

JOHN HARBERT
ANTONIO FERNANDO
GONCALVES DA ROCHA
SECOND EDITION

Textbook of Nuclear Medicine

Volume I: Basic Science

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PREFACE

Technologic advances are faster paced in nuclear medicine than in most specialties of medicine—partly because it is a young medical science and partly because so many participants from such other fields as physics, chemistry, engineering, and energy provide us with sophisticated technology needing merely to be adapted to medical use. We have tried in this second edition to reflect these advances while retaining all of the important elements that form the basic science of nuclear medicine.

The numerous changes in the technologic aspects of nuclear medicine that have occurred since publication of the first edition in 1978 (and its companion volume, *Textbook of Nuclear Medicine: Clinical Applications*, in 1979) have been carefully reviewed and constitute most of the changes in the second edition. Noteworthy advances are contained in the chapters on imaging systems, computer systems, and radiopharmaceutical chemistry. New developments are reflected in the complementary imaging disciplines of computed tomography and ultrasound. New chapters covering MR, digital radiography, and the elements of image perception have been added because of substantial developments in these areas. The chapters on counting statistics and production of radionuclides have been completely rewritten. A new chapter on cerebral blood flow studies with Xe-133 has been added. Finally, several useful tables have been added as appendices. The result, we believe, is a more useful general textbook for physicians, residents, and students of nuclear medicine and reference for active laboratory scientists with nuclear counting and radioassay problems.

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Chapter 1

ATOMIC AND NUCLEAR STRUCTURE

ANTONIO F. G. DA ROCHA

MATTER AND ENERGY

Structure of Matter

Although the corpuscular nature of matter had been postulated in antiquity, an understanding of matter was only philosophic and provided no basis for experimental proof. At the end of the eighteenth century, Lavoisier postulated the existence of molecules of definite chemical composition, which could be reduced to simpler substances that were not further reducible by classic chemical methods.

In the following century, Dalton verified that the ratio of elements within molecules varied discretely and that the numeric relationship between elements in molecules represented whole numbers. For example, in the group of hydrocarbons, 12 g of carbon and 4 g of hydrogen form one mole of methane, 24 g of carbon and 6 g of hydrogen form a mole of ethane, and 24 g of carbon and 4 g of hydrogen form a mole of ethylene.

Subsequent developments that reinforced the concept of the atom were contributed by Gay-Lussac (law of gas volumes, 1809), Avogadro (Avogadro's number, 1811), Faraday (electrolysis, 1833), Cannizzaro (atomic weights, 1858), Meyer and Mendeleev (periodic table,

1870), and Perrin (Brownian motion, 1908).

Based initially on atomic weights, Mendeleev's classification of the elements indicated a periodic recurrence of similar chemical properties. This categorization reveals an admirable degree of precision when one considers that Mendeleev was without knowledge of several important facts about matter, particularly data derived from mass spectrometry. Inconsistencies in the periodic chart were later clarified by arraying the elements in order of increasing atomic number rather than weight.

Rutherford's Atom

The understanding of matter further evolved following experiments by Lord Rutherford in 1911. He directed a narrow beam of alpha particles at a thin gold foil and observed that some of the alpha particles passed through in a straight line while others were deflected through large scattering angles. This suggested to Rutherford that matter is discontinuous, that the atom is positively charged, and that the charge is localized to a small volume whose size he was able to estimate from the alpha particle charge and the scattering angle.

The atom imagined by Rutherford was

analogous to a solar system, which is still a useful comparison. The atom may be thought of as having a small, dense, central nucleus consisting of Z protons—each with unit positive charge—and N neutrons, the sum of which equals the *atomic mass number* A . The radii of nuclei are related to the atomic mass:

$$r_N \cong 1.45 \times 10^{-15} A^{1/3} \text{m}$$

The electrons, which contribute negligibly to the atom's mass, are disposed about the nucleus in spherical orbital *shells*, each with unit negative charge and equal in number to the number of protons. The radius of the outer orbital shell of the atom is approximated by:

$$r_a \cong 0.6 \times 10^{-10} (A/\rho)^{1/3} \text{m}$$

where ρ is the density of the material in its solid form. Thus atoms vary in diameter from about 0.6×10^{-10} m for hydrogen to about 1.7×10^{-10} m for the largest atoms, not a great variation in size. With the mass of an electron $1/1836$ that of a proton, an apt spatial analogy would be a golf ball surrounded by a few pinheads circling one kilometer out in space. By far, the greatest volume of matter, even in solids, is empty space, which helps explain why radiation traveling through matter may go a long way before interacting with an atomic nucleus or electron.

Rutherford's atom presented two large inconsistencies: 1. According to classical mechanics, negatively charged electrons orbiting positively charged nuclei as Rutherford postulated would spiral inward with ever-decreasing radius, decelerate, and emit energy. Clearly this does not happen. 2. Why did the nucleus not disintegrate by repulsion if it were composed of many particles of like charge?

Bohr's Atom

In 1913, Niels Bohr provided a more satisfactory model of the atom, based on quantum mechanics, wherein the electrons occupy positions at well defined dis-

tances from the nucleus (stable orbits). Changes in energy state are required for an electron to move from one level to another. Energy is required to raise an electron from an inner, more stable orbit to an outer, less stable orbit. These levels are fixed, so that discrete increments of energy are required to move an electron from one level to another. The energy required is equal to the difference in the *binding energies* of the two orbits between which the electron moves. Bohr determined that this energy difference would be equal to $h\nu$, where h is Planck's constant, or 6.62×10^{-34} joule-sec and ν is the frequency of the emitted radiation in hertz.

The orbital shells are denominated by the principal quantum number n , which relates to the energy state of the electron, and by letters for the orbital shells (Table 1-1). Each orbital shell has a number of subshells, denominated by roman numerals, with the electron capacities shown in Table 1-1 and Figure 1-1. When the atom is at *ground state*, i.e., the state with the least energy, all of the inner orbital shells are filled before the outer shells are filled. The maximum number of electrons found in any shell is a function of the quantum number n and is given by $2n^2$. The outer subshell never contains more than eight electrons. These are termed the *valence electrons* and determine to a large extent the chemical properties of the atom. Other quantum numbers are assigned for the angular momentum, magnetic moment, and spin direction of the electron. According to the *Pauli exclusion principle*, no two electrons in any atomic system have identical values for all four quantum numbers.

Energy

Kinetic energy is the energy that a body or particle possesses by virtue of its movement. Classically, this energy is expressed as:

$$T = \frac{1}{2} mv^2$$

This expression applies when the ve-

TABLE 1-1. Denomination and Capacity of Electron Shells

Principle quantum number <i>n</i>	Primary shell	Electrons per subshell							Total capacity
		I	II	III	IV	V	VI	VII	
1	K	2	—	—	—	—	—	—	2
2	L	2	2	4	—	—	—	—	8
3	M	2	2	4	4	6	—	—	18
4	N	2	2	4	4	6	6	8	32
5	O	2	2	4	4	6	6	8	32
6	P	2	2	4	4	x	x	x	32
7	Q	2	x	x	x	x	x	x	32

x These subshells are available to electrons in excited states, but are not needed by atoms in the ground state.

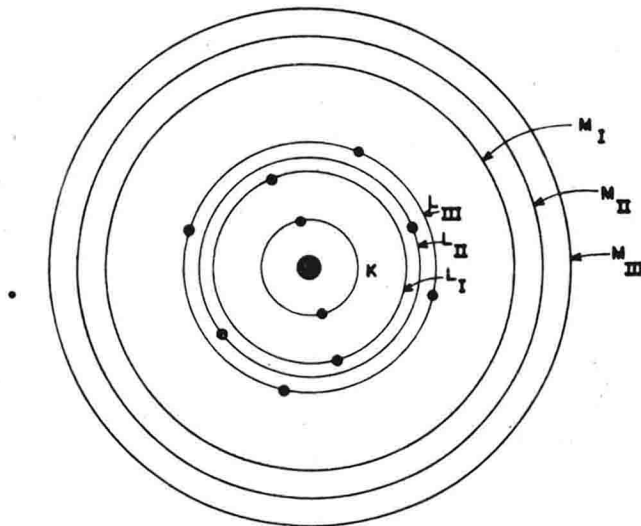


Fig. 1-1. Schematic representation of a neon atom. The M subshells contain only electrons in excited states.

locity v is small compared with that of light. As a particle approaches the speed of light, the variation of mass with velocity becomes appreciable, the mass increasing with increasing velocity:

$$m = \frac{m_0}{\sqrt{1 - v^2/c^2}}$$

where m_0 is the rest mass. Mass and energy are equivalent, related by Einstein's equation:

$$E = mc^2$$

The total energy of a particle, then, is

the sum of the energy that it has by virtue of its mass and its kinetic energy:

$$E = \frac{m_0 c^2}{\sqrt{1 - v^2/c^2}}$$

As the velocity of a particle approaches the speed of light, the mass increases by an amount equal to the increase in T . The variation of mass with velocity is important when dealing with such accelerated particles as protons or deuterons in cyclotrons.

Units of Mass and Energy

In the *International System of Units* (SI), the basic unit of mass is the kilogram (kg) and the derived unit of energy is the joule (J), or that amount of energy required to accelerate 1 kg to a velocity of 1 m/sec (Appendix A). For events occurring on the atomic scale, however, more appropriate units are used. Energy of particles and of electromagnetic radiation is most often expressed in units of electron volts (eV), which correspond to the energy acquired by an electron accelerated across a potential difference of 1 volt (1.6×10^{-19} J). The basic unit of mass is the *universal mass unit* (u), which by convention is defined as 1/12 the mass of C-12 including its electrons.*

The equivalence between mass and energy cannot be determined by classic chemistry because the variation in mass that occurs in chemical reactions is extremely small. One must observe the larger mass changes encountered in nuclear reactions to appreciate these differences. Thus the classic concept of conservation of matter has been replaced by the law of conservation of energy and the law of the equivalence between mass and energy, which are expressed in Einstein's equation $E = mc^2$ where c is the velocity of light in a vacuum $\approx 3 \times 10^8$ m/sec. The transformation of 1 u into energy yields 931.5 MeV, and an electron at rest is equivalent to 0.511 MeV. Appendix A lists several additional units, constants, and useful conversion formulae.

The energy released by mass conversion occurs most often in the form of electromagnetic radiation, especially *photons*. These are oscillating electrical and magnetic fields without mass, traveling in a vacuum at the speed of light. Electro-

magnetic radiation is characterized by wavelength λ and frequency ν related by

$$\lambda \nu = c$$

where λ is expressed in Angstrom units (10^{-10} m). Photon energy is represented by the following equation:

$$E(\text{keV}) = 12.4/\lambda(\text{\AA})$$

By convention, photons that arise from nuclear transformations are called *gamma* (γ) rays, and photons that arise from extranuclear sources are called *x-rays*.

Electrons

J.J. Thomson demonstrated in 1895 that cathode-ray tubes function by means of a flux of very small particles with a negative electrical charge—now known to be electrons. The mass of the electron is 9.1×10^{-28} g, with a charge of 1.602×10^{-19} coulombs. A similar particle, with equal mass but with a positive charge, was discovered by Anderson in 1932 and called a positive electron, or *positron*. The positron does not exist free in nature, because soon after being formed, it combines with an electron, both of which undergo *annihilation* to produce two photons of 0.511 MeV each.

Electron Energy Levels

Electrons are bound to the atom within their various orbital shells. Each shell and subshell has a characteristic binding energy, which can be determined by nuclear spectrometry. In an atom at the ground state, the electron energy level is at a minimum and said to be stable. In a hydrogen atom, the binding energy of its single electron is given by

$$E_b = \frac{-13.6}{n^2} \text{ eV}$$

where the value -13.6 is the *mean ionization potential* and n is the principal quantum number (Table 1-1). In the case of hydrogen, which has a single orbital

*A slightly different unit, the *atomic mass unit* (amu), is used frequently in chemistry and is based upon the average weight of the isotopes of oxygen. One universal mass unit equals 1.00083 amu.

shell, n equals 1 and E_b equals -13.6 eV. The mean ionization potential I represents the mean energy required to remove an orbital electron (ionization), which forms an *ion pair* consisting of the negatively charged electron and the positively charged atom. Because ionization occurs most frequently in the outer orbital shells of multielectron atoms, where the binding energies are less, any specific ionizing event may require much less energy than the mean potential.

These concepts are illustrated in Figure 1-2, which depicts the orbital shells of Tc-99m as though they were various levels in a well. The binding energy, given at the right, represents the amount of energy needed to lift an electron at that particular level out of the well. If an electron in the K shell interacts with and acquires the energy of a 20.98 keV photon, it would not

gain enough energy to escape the atom, but would be elevated to the N_I subshell (dotted line). The atom would then be in an *excited* state. Numerous transition patterns exist whereby the atom could "deexcite" and return to its ground state. One possible pattern is depicted in the series of solid arrows showing transitions $N_I \rightarrow M_V \rightarrow L_{II} \rightarrow K_I$. During this process, three photons of 0.18, 2.55, and 18.25 keV, respectively, are given off, representing the energy differences between transitions. This process of deexcitation, in which several photons are emitted in random direction, is called a *cascade* and usually occurs in nanoseconds. Only certain transitions are allowed. Thus if the K electron received only 15 keV, it would not be sufficient to excite the atom. If an L_I electron received this 15 keV, however, it would be ejected from the atom with $15.00 - 3.04$

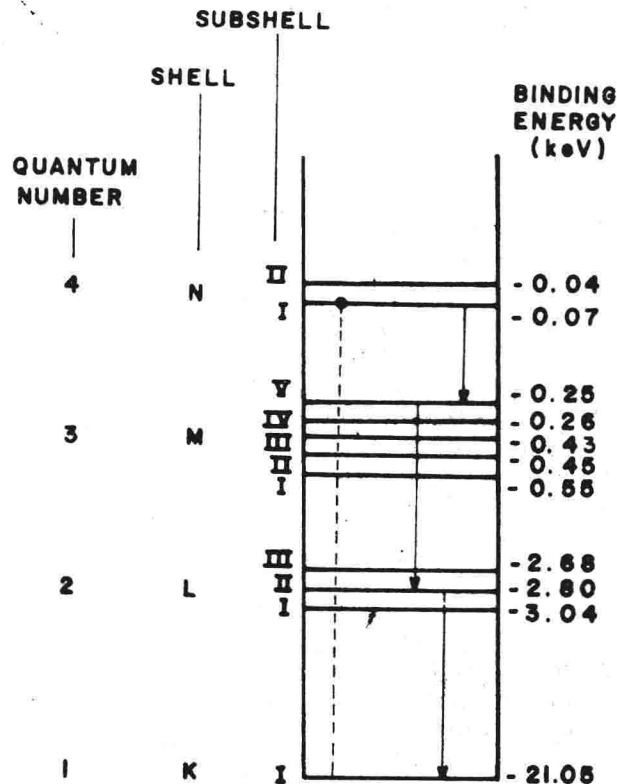


Fig. 1-2. Energy level diagram for Tc-99m.

= 11.96 keV of kinetic energy, which would ionize the atom in the process. Subsequently, this L_I vacancy would be filled by electrons from higher levels, each transition resulting in the emission of a photon equal in energy to the difference between its previous and new levels until the atom deexcites, and emits a total of 3.04 keV energy in the form of photons.

Ionization by removal of an outer electron may require only a few eV whereas to remove an inner electron from a large atom requires many keV (E_b increases with increasing Z). The deexcitation process, however, is the same. Photons emitted in deexcitation between 1.7 and 3.0 eV are in the visible light range. Higher energy photons are called "characteristic" x-rays because their energy identifies the orbital transition that produced them. Characteristic x-rays are also named by the transition process that creates them. If a free electron falls into a K vacancy, a K characteristic x-ray is emitted, and the atom deexcites with a single photon emission. If the K shell vacancy is filled by an L electron, a K_α x-ray is emitted; if filled by an M electron, a K_β x-ray, and so forth. L shell vacancies filled by M and N electrons emit L_α and L_β x-rays, respectively. The outermost shell vacancies are filled by free electrons in the environment.

The excited atom has an alternative means of deexcitation by giving off *Auger electrons*. Part of the energy of excitation may be imparted to an orbital electron (usually in the outer orbits), which, when ejected from the atom, carries with it the energy absorbed minus the binding energy of the vacant subshells:

$$T = E - E_b$$

The Auger process leaves a vacancy, which is filled by an electron from a higher shell or by a free electron, and further emission of characteristic x-rays occurs. The *Auger yield* is the fraction of vacancies that, when filled, result in the emission of Auger electrons versus photons.

This yield is higher with lighter elements. The *fluorescence yield* is the fraction of vacancies that, when filled, result in photon emission. The fluorescence yield increases with increasing Z .*

The Nucleus

In its simplest conceptualization, the nucleus is composed of neutrons and protons, collectively known as *nucleons* (Table 1-2). The nucleus is described in terms of its mass number A , which corresponds to the sum of its neutrons and protons, and its atomic number Z , which is equal to the number of protons and to the number of orbital electrons in the non-ionized state. The atom is called a *nuclide* and is symbolized



where X is the element symbol. For example, hydrogen is expressed as ${}^1_1\text{H}$, and deuterium, which has a proton and a neutron, as ${}^2_1\text{H}$. In the medical literature and by convention in this book, the mass number follows the elemental symbol, e.g., H-2 , as the nuclide is pronounced. The subscript is often deleted since the atomic number can be determined from the chemical symbol. Nuclides with the same Z but different A are called *isotopes*. Since chemical properties depend upon the atomic number, which determines the number of orbital electrons, isotopes have identical chemical properties. Most elements found in nature have more than one isotope. Some examples of natural isotopes are listed in Table 1-3. Note that the mass units u are different from the *atomic weight* used in chemistry. The latter refers to the average weight in g/mol of an element's isotopes in their natural state.

*Auger electrons are denoted by e_{abc} where a denotes the shell with the original vacancy, b denotes the shell from which the vacancy was filled, and c denotes the shell from which the Auger electron was emitted. For example, an Auger electron denoted e_{KLM} arose from the M shell in response to a K-shell vacancy filled by an L-shell electron.

TABLE 1-2. Mass and Energy Characteristics of Nucleons and Electrons

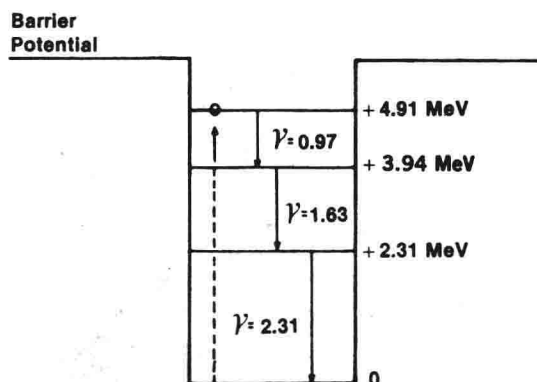
Particle	Symbol	Charge	Mass (u)	Energy (MeV)
Proton	p	+1	1.007593	938.211
Neutron	n	0	1.008982	939.505
Electron	e	-1	0.000548	0.511
α -particle	α	+2	4.0028	3727

TABLE 1-3. Examples of Natural Isotopes

Element	Isotopes	u	% Abundance
H	${}^1_1\text{H}$	1.008145	99.98
	${}^2_1\text{H}$	2.014741	0.02
O	${}^{16}_8\text{O}$	16.00000	99.759
	${}^{17}_8\text{O}$	17.00453	0.037
	${}^{18}_8\text{O}$	18.00488	0.204
Cl	${}^{35}_{17}\text{Cl}$	34.98006	75.4
	${}^{37}_{17}\text{Cl}$	36.97767	24.6
U	${}^{234}_{92}\text{U}$	234.1129	0.006
	${}^{235}_{92}\text{U}$	235.1156	0.712
	${}^{238}_{92}\text{U}$	238.1241	99.282

The arrangement of nucleons within the nucleus is not yet fully understood. One model, called the *shell model*, depicts the nucleons moving in orbits about one another in a manner similar to the movement of electrons about the nucleus in Bohr's model of the atom. The most stable arrangement for the nucleons is the ground state. When the energy level is raised above the ground state, the nucleus is said to be either *excited* or *metastable*. Excitation is a transient state lasting less than 10^{-12} sec; metastability is an excited state lasting longer, i.e., minutes or hours.

Another way of conceptualizing nuclear energy levels is provided by the energy "well" shown in Figure 1-3. The nucleus has an internal organization of energy levels that are in some respects analogous to, though much higher than, the energy levels of orbital electrons. The nucleus can be excited when a nuclear constituent is raised above its ground energy level. When it falls back to the ground state, en-


Fig. 1-3. Energy level diagram representing nuclear energy excess.

ergy is liberated in the form of photons with energy equal to the difference between the two nuclear energy levels. Radioactive nuclei may be naturally unstable, or they may be made radioactive by bombardment with high-energy photons or accelerated particles. Figure 1-3 shows N-14 after photon bombardment, which