CHAPTER 1

INTRODUCTION

"If anything is worth doing, do it with all your heart."
Buddha

Recently, body composition research has become known as a distinct area of scientific investigation, though the study of human body composition spans from more than a century ago. Information related to body composition is accumulating rapidly and is extended our knowledge of human biology (1). This expanded body of information can be organized into three distinct, interconnected areas: body composition rules, body composition methodology, and body composition alterations (**Figure 1.1**) (1). The first research area describes the rules of human body composition (e.g., the relatively constant relationships between body components and between components and their measurable properties). The second research area studies *in vivo* methods of measuring several body components. The third research area focused upon alterations in body composition caused by various influencing factors (1).

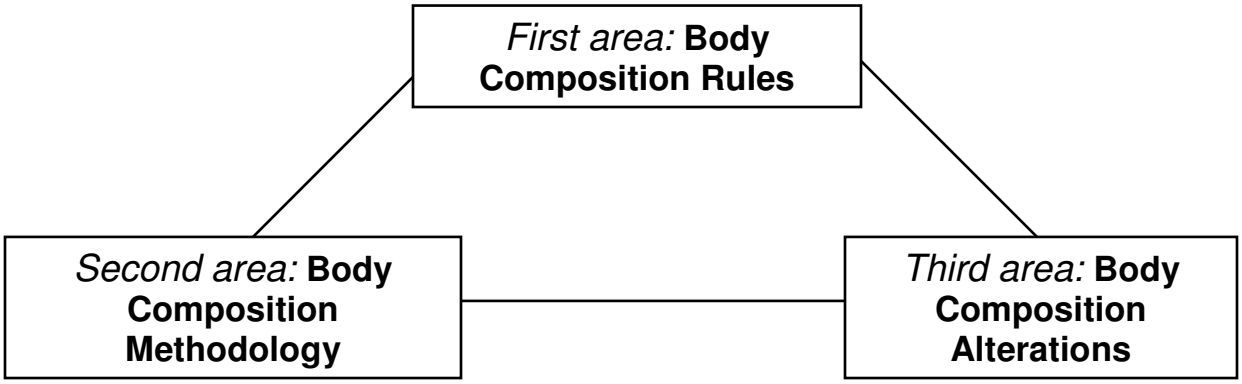

Figure 1.1. The study of human body composition: Three research areas (1).

A brief review of the most relevant Investigators and for their contribution to the study of human body composition is presented in **Table 1.1**.

Considering the lack of *in vivo* methods for measuring several components in the last century, cadaver autopsy was the only procedure to obtain quantitative data on

human body composition. The chemical analysis of tissues and fluids taken from the body can be traced to the mid-19th century. On the basis of limited data from chemical analysis of animal carcasses and human cadavers (2, 3), more detailed densitometric values have been estimated for fat, mineral, and protein. Although Behnke et al. (4) introduced the classic two-compartment (2C) body composition model which divides body mass into fat with a density of 0.9007 kg/L and lean or fat-free mass (FFM) with a density of 1.100 kg/L, the Siri (5) and Brozek et al. (3) 2C models represent the simplest and most common fat estimation formulas. Siri in 1961 (6) derived a three-component (3C) model accounting for variation in subject hydration that added a TBW estimate to Behnke's two-component model (4). According to Clarys et al (7) more chemical and anatomical dissection data are needed, especially in conjunction with *in vivo* body composition methods to help in their validation. However, with the advent of nuclear chemistry in the mid-20th century, direct *in vivo* (nondestructive, noninvasive) chemical assays of the living human body became possible. The basic assumptions for the *in vivo* neutron activation analysis (IVNAA) procedures are solidly based on the chemical analysis of adult human cadavers. Other nuclear based-techniques, such as computerized tomography (CT) and magnetic resonance imaging (MRI) provide information on tissue density or volume based in anatomical analysis of cadavers, for which the work developed by Clarys et al. (8) in the Brussels cadaver analysis studies gave an enormous contribution.

Table1.1. Main contributions for Human body composition research

Main Contribution	References
The international anthropometric measurement - body mass index	Quetelet, 1871 (9)
Body surface area estimation, based on height and weight	Dubois and Dubois, 1916 (10)
Age and chemical development in mammals	Moulton, 1923 (11)
Estimation of the relative proportions of fat and fat-free mass from underwater weighing	Behnke et al., 1942 (4)
The chemical analysis of one male cadaver	Mitchell et al., 1945 (12)
Estimation of fat-free mass by total-body water	Pace and Rathbun, 1945 (13)
The chemical analysis of four cadavers	Widdonson et al., 1951 (14)
The density of body fat	Fidanza et al., 1953 (15)
The chemical analysis of one male cadaver	Forbes et al., 1953 (16)
More detailed densitometric method	Keys and Brozek,1953 (2)
Estimation of total body fat by Potassium-40 content	Forbes et al., 1953 (17)
Body fat estimation from a Three-Compartment model	Siri, 1961 (6)
Total-body water estimation by bioelectrical impedance analysis	Thomasset, 1962 (18)
Revision of quantitive assumptions on densitometric analysis	Brozek et al., 1963 (3)
Quantification of exchangeable body potassium and Body Cell Mass by measuring a radioactive isotope-^{42}K	Moore et al., 1963 (19)
Measurement of total-body Calcium, Sodium, Chloride, Nitrogen, and Phosphorus in man by *in vivo* neutron activation analysis	Cohn et al., 1971 (20)
The Reference Man	Snyder et al., 1975 (21)
Radiographique method of quantifying protein-calorie undernutrition	Heymsfield et al., 1979 (22)
The use of Urinary 3-methylhistidine (3MH) excretion as a marker to study *in vivo* total-body muscle protein degradation	Lukaski et al., 1981 (23)
Body composition from the reference child	Fomom et al., 1982 (24)
Body fat assessment by computerized tomography	Tokunaga et al., 1983 (25)
The anatomical analysis at the tissue level from several cadavers-The Brussels study	Clarys et al., 1984 (8)
Applicability of body composition techniques and constants for children and youth	Lohman, 1986 (26)
Estimation of total body fat by measuring total-body Carbon	Kehayias et al., 1991 (27)
The proposed Five-level model approach to organize body composition research	Wang et al., 1992 (1)

One important advance to build an appropriate structure for body-composition research and hence, to clearly define human body composition as a branch of human biology was the proposed five-level model by Wang et al., in 1992 (1). More than 40 main body components are organized into five distinct levels of increasing complexity: atomic, molecular, cellular, tissue-system, and whole-body (1). If all components at each level are summed, the total is equivalent to body weight. The main components at these body composition levels are illustrated in **Figure 1.2**. As described above, body-composition research includes three interconnecting areas: studying the proportions of various components and their steady-state associations among the atomic, molecular, cellular, tissue system, and whole-body levels (the so-called "rules"), investigating the methods of measuring several components *in vivo*, and studying the influences of biological factors on various levels and components, such as growth and aging.

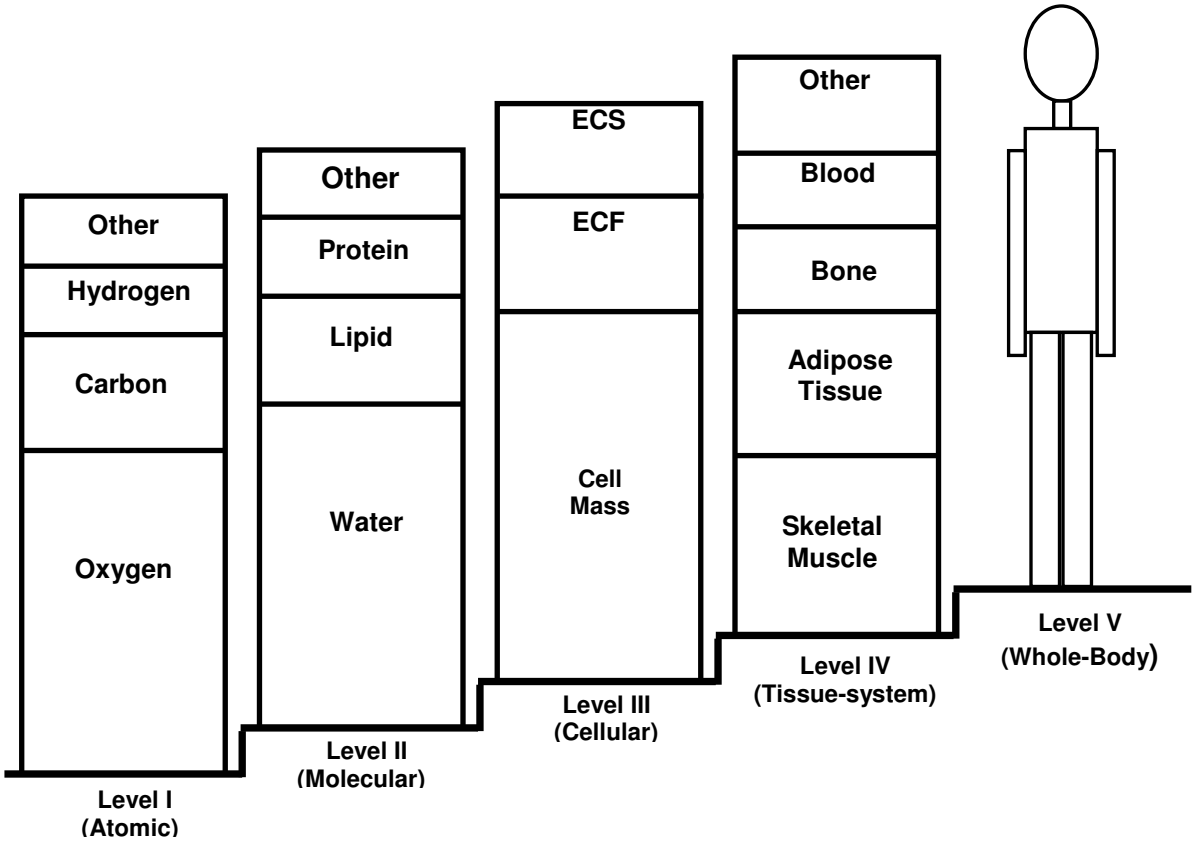

Figure 1.2. The five-levels of human body composition. ECS and ECF, extracellular solids and fluids, respectively (1)

Considering the five-level model, an important feature is that components of successively body composition higher levels are composed of lower-level components. For instances, adipose tissue, a tissue-system level component, includes components such as adipocytes at the cellular level, lipids at the molecular level, and carbon at the atomic level (**Figure 1.2**). A change in adipose tissue during an intervention reflects changes in corresponding components at the cellular, molecular, and atomic levels.

An additional essential concept is the existence of a body-composition steady state. During stable periods, such as the maintenance of fluid homeostasis and body weight, there are relations that are constants or relatively constants within an individual

and between different individuals (28). For example, even though fat and adipose tissue are molecular and tissue-system level components, respectively, there exists a reasonably stable relationship between the two, both within and between subjects (i.e. fat mass = ~0.80 x adipose tissue mass) (21). This is a central concept to the development of body composition methods. According to Wang et al (29), all *in vivo* body composition methods can be summarized into:

$$C = f(Q) \quad (1)$$

This fundamental formula shows that the quantification of an unknown component (C) depends on two distinct but closely connected parts, a measurable quantity (Q) and a mathematical function (*f*) relating Q with C (29). According to the authors (29) two main categories of the measurable quantities were identified in body composition methods, property and component. Therefore, most body composition methods can be organized as property-based and component-based methods (29). In addition, combined methods also exist in which both properties and components are used as the measurable quantities. Hence, the researcher with a measured property or component can estimate an unknown component based on assumed stable property-component or component-component relations (**Table 1.2**).

Table 1.2. Distinguishing characteristics of property-based, component-based, and combined body composition methods (29).

	Methods		
	Property-based	Component-based	Combined
Definition	Allows unknown component to be quantified from measurable property	Allows unknown component to be quantified from known component	Allows unknown component to be quantified from both measurable property and known component
Basic formula	C1 = *f* (PA)	C2 = *f* (C1)	C3 = *f* (PB,C1)
How established	On the quantitative relation between measurable property and unknown component	On the quantitative relation between known and unknown component	On the quantitative relation between measurable property, known component, and unknown component
Role in methodology	Foundation of all *in vivo* methods	Expansion of property-based methods	Expansion of property-based methods

Abbreviations: C, component; *f* mathematical function; P, measurable property.

Two main types of mathematical function (*f*) were also identified in *in vivo* methods. Type I methods share in common mathematical functions derived by statistical analysis of experimental observations. In contrast, type II methods share in common mathematical functions, which are developed, based on well-established models within and between individuals (29).

At the atomic level, using *in vivo* neutron activation analysis, 10.83 MeV γ-ray, a radioactive property of ^{13}N, can be used to estimate the component total-body Nitrogen. At the molecular level, a dilution property, deuterium isotope dilution ($^{2}H_2O$) can be used to estimate the molecular component total-body water. At the cellular level, since there are no direct methods to assess components at this level, a component-based method will

be presented as an example to estimate one of the most important measurable cellular components, the body cell mass (BCM). Therefore, the atomic component total-body Potassium (TBK) can be used to estimate BCM as follows: BCM=TBK(mmol)x0.0083. At the tissue-level component, a physiological property, urinary creatinine excretion using the 24h urine creatinine method can be used to estimate the tissue-component skeletal muscle. Finally, at the whole-body level, an anatomical property, skinfold thickness measurements are utilized to estimate body density.

The description of the body composition levels and a general idea of measurement methods and component relationships are presented in the next sections.

Atomic level

Atoms or elements are the basic constituents of the human body (**Table 1.3**). About ~50 of 106 elements are found in the human body and their distribution in the various tissues and organs are well documented (21). Oxygen, Carbon, Hydrogen, Nitrogen, Calcium, and Phosphorus account for more than 98% of body mass (BM) while the remaining 44 elements represent 2% of BM (21).

Table 1.3. Body composition on the atomic level (I) for the 70-kg Reference Man

Element	Amount kg	body mass %
Oxygen	43	61
Carbon	16	23
Hydrogen	7	10
Nitrogen	1.8	2.6
Calcium	1.0	1.4
Phosphorus	0.58	0.83
Sulfur	0.14	0.20
Potassium	0.14	0.20
Sodium	0.1	0.14
Chlorine	0.095	0.14
Magnesium	0.019	0.027
Total	69.874	99.537

Information adapted from Snyder et al. (21)

Traditionally, elemental analysis of humans is performed in cadavers or in biopsy specimens from selected tissues and organs.

At present, the whole body content of most essential elements can be measured directly using *in vivo* techniques: Potassium by whole-body counting, Sodium, Chlorine and Calcium by delayed-γ neutron activation analysis (20), Nitrogen by prompt -γ neutron activation analysis (20, 30), and Carbon by inelastic neutron scattering (31). More than 98% of BM can now be reconstructed from elements that can be estimated *in vivo*, largely by neutron activation techniques. According to Wang et al. (1), the atomic level is the basis of body-composition and is the starting level point for the five levels.

The lack of accurate *in vivo* methods to assess some components, such as protein explains the uncertainty of some body composition assumptions (6), namely its relation to total body mineral in living humans. The development of *in vivo* neutron activation analysis provides an opportunity to accurately estimate those body components and

therefore to test the constancy of widely used rules at the molecular level, namely the stability of the mineral to protein ratio, not yet studied.

Molecular Level

Body composition components at the molecular level are essential to research in many nutrition areas; including energy, protein, and lipid metabolism, bone mineral homeostasis, and water balance. The 11 principal elements are incorporated into molecules that form more than 100,000 chemical compounds found in the human body. It is not possible to measure all of these chemical compounds individually in living human. Therefore, an alternative is to consider chemical compounds in categories of closely related molecular groups. The several compounds can be classified into five main groups: water (TBW), lipid (L), protein (TBPro), mineral (M), and glycogen (G) as indicated in **Table 1.4**.

Table 1.4. Body composition on the molecular level (II) for the 70-kg Reference Man (21)

Component	Amount Kg	Percent of body mass %
Water		
Extracellular	18	26
Intracellular	24	34
Lipid		
Nonessential (fat)	12	17
Essential	1.5	2.1
Protein	10.6	15
Mineral	3.7	5.3
Total	69.8	99.4

Glycogen, normally ~400 g, is not included in the reference Man. Information adapted from Snyder et al. (21)

Water is the most abundant chemical compound in the human body, comprising 60% of BM in the Reference Man (21). Water is distributed into the extracellular water (ECW) and intracellular water (ICW) compartments, and the ECW includes five subcompartments: interstitial, plasma, connective tissue, bone, and gastrointestinal tract (29, 32). The water distribution can be assessed based on total Potassium and water (24). Previous studies reported similar intracellular Potassium concentrations (*m*) in mammals: 150-160 mmol/kgH_2O (33), 150 ± 7.2 (SD) mmol/ kgH_2O (19), 152 mmol/kgH_2O (33), and 159 mmol/kgH_2O (34). Hence, it is known that almost all body Potassium exists in intracellular water (ICW) and extracellular water (ECW), and given *m* and *n* as the potassium concentrations in intracellular and extracellular fluid, ECW and ICW can be derived as ECW = (*m* x TBW – TBK)/ (*m*-*n*) and ICW = (TBK – *n* x TBW)/(*m* - *n*), respectively, where TBW is in kilograms and TBK is expressed in millimoles (35). However, it is important to note that there are other methods to assess ECW such as the bromide, radiobromide, and thyosulfate methods, which might estimate a slightly different ECW volume even in the same subjects (32). An appropriate interpretation of ECW in the clinical setting is critical as this compartment varies widely in volume both in health and disease (36-41). Since the work of Moore et al.(19) that presented the only simple approach in estimating ECW based on body weight, other potential factors that moderate fluid distribution, including sex, race, age, height, and body composition were not further investigated. In addition, a lack of normative values is unavailable to serve as reference values when evaluating ECW in individuals or groups with clinical conditions.

Protein includes almost the compounds containing nitrogen, ranging from simple amino acids to complex nucleoproteins. There are several different families of proteins,

though noninvasive body composition methods are available only for estimation of total protein (42) and muscle and non-muscle proteins (43).

Glycogen is the principal storage form of carbohydrate, which comprises less than 1kg in healthy adults; the remaining carbohydrates are considered negligible (21, 44). The main distribution is in skeletal muscle and liver, which contain ~1 and 2.2 % of their respective wet weights in the form of glycogen (21, 30). The growing availability of nuclear magnetic resonance spectroscopy systems for human use is providing new no invasively obtained information on the amount of and dynamic changes in intracellular glycogen (45).

Mineral describes a category of inorganic compounds containing an abundance of metal elements (e.g., Calcium, Sodium, and Potassium) and nonmetal elements (e.g., Oxygen, Phosphorus, and Chlorine). Minerals comprise nearly 5% of BM in healthy adults and are distributed in two major components: bone minerals and non-bone or soft-tissue minerals. The largest constituent of bone minerals (Mo) is Calcium hydroxyapatite (21), with small contributions made by Na, K, Mg, and Cl. Soft tissue minerals include well-known ions such as Na^+, K^+, Cl^-, $HPO_4^{2-}$and HCO_3 (21).

Lipids are defined as a group of chemical compounds that are insoluble in water and soluble in organic solvents such as diethyl ether, benzene, and chloroform (44, 46). From the five molecular components above described, lipid is the most confusing because the terms lipid and fat are used, inaccurately, interchangeably. The term fat is synonymous with triglycerides and therefore fat is clearly a subcategory of total lipid (44, 46). The non-fat lipids include phospholipids, sphingolipids, and steroids. In humans, triglycerides or nonessential lipids are energy storage compounds, while the remaining

lipid groups are essential in various physiological and biochemical processes. In the Reference Man, about 90% of total body lipid is nonessential, while nearly 10% is essential (21).

The several compounds at the molecular level are illustrated in **Figure 1.3**.

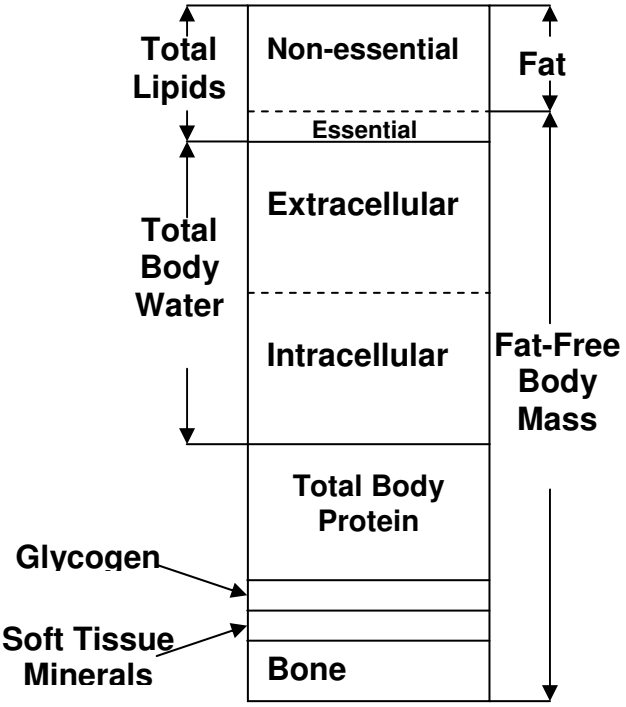

Figure 1.3. Molecular level components

Molecular Models

Several stable relationships recognized for the molecular level are fundamental to the body composition methodological area. Physical density of the molecular level components is central for methodological development. This is because whole-body density is relatively easy to measure accurately in most children and healthy adults (47), and several molecular level models are based on body density or closely related body volume (BV) (48, 49).

From a body composition view, water, triglycerides (i.e., fat), and glycogen are homogeneous or approach homogeneous chemical moieties. Therefore, their densities at body temperature were easily established by early investigators using conventional gravimetric methods (28). Protein, bone mineral, and soft-tissue mineral are heterogeneous with respect to composite amino acids, minerals, and electrolytes and their densities were more difficult to estimate (28). The density of combined components, such as FFM can be calculated by assuming relatively stable proportions among the various constituent chemical components (4). The calculated and assumed constant densities of combined molecular level models are the basis of the multicompartment molecular level models, which are formulated on body density or volume measured with underwater weighing (UWW) (4) or, recently, air displacement plethysmograph (ADP) systems (50). In addition, other important stable relationships include the hydration (13) and Potassium content (32) of the FFM.

Several multicompartment models have been published (**Table 1.5**). Generally, these models were developed from simultaneous equations, which may include two or more unknown components, and/or the measurable property. Total body water by isotope dilution, total body protein by *in vivo* neutron activation (45), and bone and soft-tissue minerals by *in vivo* neutron activation analysis (51-53), whole-body ^{40}K counting (32), and dual-energy x-ray absorptiometry (DXA) (54). The molecular level can be described as any of the following combinations: a two-compartment model, BM = fat + fat-free mass and BM = lipid + lipid-free mass; a three-compartment model, BM = fat + water + residual (i.e. the sum of protein, minerals, and glycogen) (29), BM = fat + Minerals + residual (i.e. the sum of protein, water, and glycogen) (26), and BM = fat + bone mineral

+ lean soft tissue; a four-component model, BM = fat + water + minerals + residual (i.e. the sum of protein and glycogen) (29); and finally a five-component model, BM = fat + water + Bone mineral + Soft tissue mineral + residual (i.e. the sum of protein and glycogen) (55, 56).

However, some uncertainties in these models may still remain about the inclusion of the essential lipids component (Le). Wang et al. (1) suggest that Le should be included in the residual FFM, as long as the terms of the molecular level are consistent with each other. Hence, FFM or even the widely used lean body mass terms refer to the sum of Le plus lipid-free mass (1).

Table 1.5. Models for estimating total body fat mass based on measured body weight and volume (28)

Model	Measurable Properties	Known component(s)	Reference
2-Compartment Fat=4.95xBV-4.50xBM	BV, BM	None	Behnke et al 1942(4)
3-Compartment Fat=2.057xBV-0.786xTBW-1.286xBM	BV, BM	TBW	Siri, 1961(6)
Fat=6.386xBV+3.961xmineral-6.09xBM	BV, BM	Mineral	Lohman, 1986(26)
4-Compartment Fat=2.75xBV-0.714xTBW+1.148xmineral-2.05xBM	BV, BM	TBW, mineral	Baumgartner et al. 1991(57)
Fat=2.75xBV-0.714xTBW+1.129xmineral-2.037xBM	BV, BM	TBW, Mo	Selinger, 1977(58)
Fat=2.513xBV-0.739xTBW+0.947xmineral-1.79xBW	BV, BM	TBW, Mo	Heymsfield et al. 1996(48)
5-Compartment Fat=2.748×BV-0.715×TBW+1.129×Mo+1.222xMs - 2.051×BM	BV, BM	TBW, Mo, Ms	Wang et al. 2002(55)

Abbreviations: Bv, body volume; BM, body mass ; TBW, total body water; Mo, bone mineral; Ms, soft-tissue minerals.

However, multicompartment models are costly, time-consuming, not allowing wide implementation for most laboratories. For instances, to assess FM, a typical four-compartment model study requires many hours for completion, normally starting with isotope dilution for TBW and measurement of BM. Then, UWW and DXA techniques for BV and Mo assessment are used, respectively. A total of four measurable variables, TBW, BM, BV, and Mo are used to calculate FM (**Table 1.5**). FM could be assessed by the conventional two-compartment model, using UWW or ADP to estimate body volume, but the assumed stable FFM density would not be accurate to examine physiological or other processes on several compartments.

Therefore, less expensive and laborious techniques have been used in clinical settings to estimate molecular level components. Some of these methods are described elsewhere (59), such as surface morphology, bioelectrical impedance analysis (BIA), ADP and DXA. The biological variability of human body composition and the lack of well-established methods (e.g., the 4C molecular model) to validate the most useful techniques, namely ADP and DXA, are critical issues to improve the accuracy of these practical methods.

Originally designed to determine bone mineral density (BMD), DXA technology has subsequently been adopted for the assessment of whole-body composition. DXA has been considered one of the most used methods at the molecular level for its low radiation exposure, cost and rapidly, which has explained the several studies conducted using this technique (60). DXA also has the advantage of being a 3C molecular model that quantifies FM, LST, and BMC and also yields regional as well as total body values. However, more research is needed to improve its utility in body composition assessment

(60-65). Validation studies of DXA against well-established molecular models have been conducted (66, 67) which have resulted in new calibrations of this technique, specifically in the identification of the soft tissue constituents (fat mass and fat-free mass).

Cellular Level

To create the living organism, the combination of the different molecular components into cells is fundamental. Functions and interactions between cells are critical to the study of human physiology in health and disease. Three main components are central at the cellular level: cell mass, extracellular fluid, and extracellular solids (**Figure 1.4**).

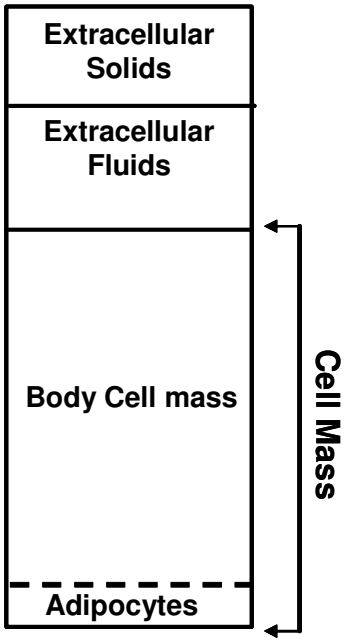

Figure 1.4. Main components at the cellular level.

The extracellular solids are a nonmetabolizing portion of human body composed by organic and inorganic chemical compounds. Calcium, Phosphorus, and Oxygen are

the main elements of dry bone matrix in the Reference Man (21). Organic ECS includes three types of fibers: collagen, reticular, and elastic fibers (1).

The extracellular fluid consist of nonmetabolizing fluid surrounding cells that provides a way for nutrients transportation, gas exchange, and excretion of metabolic end products. ECF can be divided into two major compartments: Plasma in the intravascular space and interstitial fluid in the extracellular belong space (21).

The cells mass component is of interest primarily for the metabolically active protoplasm that includes cytoplasmatic organelles and mitochondria found within the intracellular space (28). It is important to note that triglycerides are stored in the intracellular compartment of adypocites and to a less extent other cells. Therefore, the concept of body cell mass (BCM) emerged as an approach of quantifying the metabolically active fat-free portion of the intracellular space (19). Currently, a generally equation that characterizes the cellular level of body composition analysis is given by BM = fat + ECF + ECS + BCM. Regarding the difficulty in estimating *in vivo* most of the cellular components, this general equation emerges as an alternative method to determine BM at the cellular level. The use of many relatively stable cellular-level relationships is fundamental to assess body composition at the cellular level. One of those stable relations is made with the atomic level, namely the total-body Potassium to BCM (TBK = 0.00469 x BCM g/kg) proportion.

Tissue-system level

The cellular level is organized into tissues, organs and systems, composing the tissue-system level. Adipose tissue, skeletal muscle, bone, visceral organs, and brain are the principal tissue-system level components.

A practical alternative to describe the tissue-system level is given by BM = adipose tissue + skeletal muscle + bone + viscera + blood + residual, where the first five components account for about 85 % and the residual accounts for the remaining 15 % of BM in the Reference Man (21).

It is important to note that the tissue-system level presents interactions with other areas of human biology, such as histochemistry and histology along with the anatomy and physiology of the organs. Therefore, this level has been widely investigated by physicians, nutritionists and exercise physiologists.

Some reasonably stable relations at the tissue-system level include: Skeletal muscle/adipose tissue free body mass = 0.54 (men) or 0.49 (for women) and fat/adipose tissue =0.8 (21).

At this level, estimation of tissue-system components was accomplished with relatively inaccurate methods such as anthropometry. Recently with the advent of the imaging techniques, a few *in vivo* direct methods can be used to determine the most important components. Computerized axial tomography (CT) and magnetic resonance imaging (MRI) can directly estimate the volume of subcutaneous and visceral adipose tissue (68, 69). Additionally, a few indirect techniques at this level, such as estimation of skeletal muscle mass from 24-h urinary creatinine excretion or from TBK and nitrogen content by neutron activation analysis (70, 71) can be used.

Whole-body level

Similar body composition between humans and primates are found at the atomic, molecular, cellular, and tissue-system levels. Nevertheless, the complex characteristics that differentiate humans from all the other primates are found at the whole-body level of body composition. The presence of distinct morphological features namely body size, shape, and exterior physical characteristics are presented. Stature, segment lengths, body breadths, circumferences, skinfold thickness, body surface area, body volume, BM, body mass index, and body density are some of the suggested dimensions that can be directly determined at the whole-body level. For example, skinfold thickness measured at specific anatomic sites, triceps, subscapular, calf, abdominal, provides a simple method of estimating fatness and the distribution of subcutaneous adipose tissue. Most of the type I mathematical function are developed at this level. Hence, it is possible to find several equations for the prediction of body fat using skinfold thickness as the measured property. Additionally, body density is also widely used to indirectly estimate total body fat and FFM (32, 72) and is defined at the molecular level as:

$$1/Db = fFat/D_{Fat} + fFFM/D_{FFM}.$$

Where, Db, D_{fat}, and D_{FFM} are the densities (kg/L) of the total body, fat, and FFM, respectively, and *f* represents the fractions of BM as fat and FFM, respectively (6).

Differences found at this level are related to changes in composition from the other levels and vice versa. This relation is the basis for determining the components of the other four levels by using measurements at the whole-body level, which are simpler and easy to perform.

The biological variability of human body composition at the five described levels has obvious effects in the rules and methodological research areas, as described in **Figure 1.5**. Several gaps generated from these implications have to be solved and will lead us throughout the current dissertation.

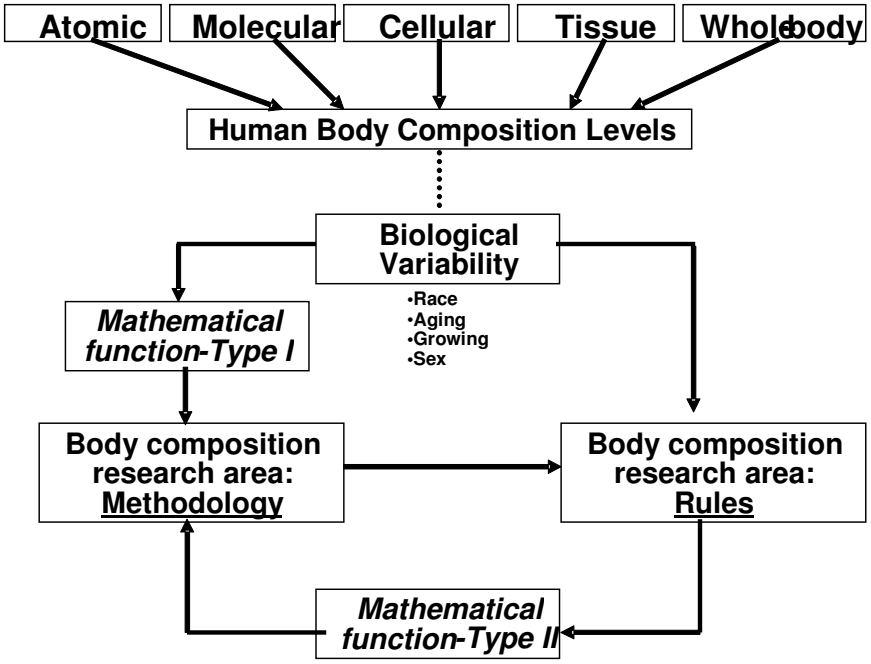

Figure 1.5. Research pathways throughout the present dissertation.

The aim of this investigation

The study of body composition has two related research aspects, theoretical and experimental. Under the direction of the theoretical research, the present dissertation studies some practical problems related with two important body composition research areas, rules and methodology. Race, sex, aging, and growing, are the main issues in promoting the biological variability in human body composition at the atomic, molecular, cellular, tissue-system, and whole-body levels. Therefore, the exploration of body composition models (rules), mediated by the relatively constant relationships between body components and between components and their measurable properties (mathematical function type II) and the development and evaluation of body composition methods (methodology) and the development of Type I mathematical functions, will be studied, as the principal research pathways (**Figure 1.5**).

A detailed review of the methodology used in the present dissertation is showed in **Chapter 2**.

In the area of body composition rules, the magnitude and constancy of the relationship between two molecular level components, mineral and protein, is studied (**Chapter 3**). In the area of body composition methodology, based on the theoretical approach, models to establish the cross-sectional relationship between ECW and age are developed controlling first for other biological factors (**Chapter 4**). A simple and safe method, using a recent statistical procedure, is developed yielding an approach for ECW reference values for healthy adults to be used at the clinical setting (**Chapter 5**). The performance of two widely used body composition methods to assess body fat, DXA and

air displacement plethysmography (ADP) were compared against a reference multicompartment molecular model (**Chapter 6**). Accuracy of DXA-system to estimate bone mineral, lean soft tissue and fat mass was tested and calibrated for a specific population (**Chapter 7**).

Finally, based on these studies, **Chapter 8** discusses, in general, the areas of body composition rules, methodology, and the interrelations between these two areas.

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