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Fulfilling Ageing

Psychosocial and Communicative Perspectives on Ageing

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International Perspectives on Aging

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Marisa Cordella • Aldo Poiani

Fulfilling Ageing

Psychosocial and Communicative Perspectives on Ageing

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To all of us,
travelling along different roads,
on a common human journey.

Preface

Now,
time, I wrap you up,
I lay you inside my
wild box
and I go fishing,
with your long line,
the fishes of my dawn!
Pablo Neruda, *Ode to Age*[1]

Pablo Neruda was not only a great poet (Nobel Prize winner in 1971) but also a great *bon vivant*, lover, and political activist right until the end of his life in 1973, at the age of 69. His poems and life exemplify an optimistic view of old age, a period of new challenges, and never-ending personal growth and fulfillment. This contrasts with a different view of old age as a time for retirement from work, physical and mental decay, personal identity crisis, and financial challenges; rupture of social bonds, potential economic load on the rest of society, and an overall problematic period for both the individual and family. Neruda experienced what we will call in this book a *fulfilling ageing*, or *the ability to effectively express capability and agency, leading to a personally satisfactory level of well-being, contentment, and adaptation within the self and with our surrounding environment as we become older*.

Understanding our elders requires exploring all aspects of old age: the positive and the negative, the psychological, the social, the biological; but in our opinion such exploration should be enlightened by a broader view that digs deep into what

[1] *Ahora,*
tiempo, te enrollo,
te deposito en mi
caja silvestre
y me voy a pescar
con tu hilo largo
los peces de la aurora!
Pablo Neruda, *Oda a la Edad*

makes life worth living. We believe that being fulfilled makes not only our life worth living, but it also makes the inevitable hurdles of our ageing more bearable.

Greater life fulfillment in old age brings greater meaning and satisfaction to our existence despite the inevitable shortcomings of getting old. Life fulfillment is experienced through the development of all our human capabilities, from the cognitive to the emotional, to the existential and the spiritual. It is a dynamic process and one that engages not only the self but also others in social interactions and our broader environment. Fulfilling ageing involves finding personal meaning in the experience of living in the world.

Developing a sense of fulfillment makes life worth living even when not everything runs smoothly or as we wish. Fulfillment also means feeling comfortable with our legacy work, no matter what that might be and how far it might reach.

Life fulfillment should not be equated with "success." Life is not a race, it is not a contest. As we age, we may change, develop, expand, or contract; but for as long as we feel fulfilled, we will be fine. Over time, we may develop a greater integration of the self, a better coherence, a clearer self-identity which may allow us to also develop our wisdom. Through greater life fulfillment, we may even regard ourselves as happy people.

In order to live a fulfilling old age, however, it helps to retain a degree of good physical and mental health, possess some level of material security (whether it is of personal origin or provided by government programs), enjoy positive interactions with others, and be able to engage in personally satisfying activities that give meaning to our life.

Everybody can experience a fulfilling old age. Life fulfillment in old age is a personal experience and so anything goes as far as the specific path towards it is concerned. We may remain cognitively active through using the natural plastic capabilities of our brain in different ways. Building cognitive reserve throughout life (e.g. through education and intellectual curiosity) will certainly help in old age, by supporting our capacity for personal growth. The same is true for broader physical capabilities, but let us not forget that we can also find life fulfillment within the reality of specific physical disabilities and even some mental disorders. A level of optimism will help in all circumstances, as through optimism we may be able to overcome the difficulties encountered throughout our life and incorporate those difficult experiences into our personal growth. Nurturing social relationships with family, friends, and the local community of residence can also promote fulfilling ageing, especially with regard to securing emotional and material support.

Throughout our life, we may often confront important choices. For as long as the choice, whatever it is, responds to strong urgencies rather than superficial whims, it may open a door to fulfillment. Regrets are always possible, nobody is perfect, but it is the overall result that matters.

Our life story can be expressed into a meaningful narrative in old age and such life story will not only help shape our personal identity, from which an integrated self may emerge; but it will also provide the raw material for our legacy and generative work. Meaningful narratives help put the picture of our life into a sharper focus, thus contributing to our ability to develop and transmit the wisdom of our life.

A greater sense of fulfillment and meaning in life should better prepare us to withstand inevitable levels of suffering and, eventually, to face the end of our life with dignity.

St.Lucia, QLD, Australia — Marisa Cordella
Clayton, VIC, Australia — Aldo Poiani

Acknowledgments

This book is dedicated to Franco Poiani, who passed away in 2020 at the age of 89. He continues his journey in our memories.

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Contents

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Chapter 1
Introduction

Abstract *Introduction* provides an overview of the book, introducing the major biological, psychological, social, cultural, historical, and existential themes that will be further developed in the rest of the chapters. In particular, the concept of fulfilling ageing is defined and explained here as a central idea that links together the various aspects of ageing addressed in this book.

When should a person be considered "old"? What does define old age, and is it possible to determine a specific point in time for the transition from middle to old age? Even if defining a specific threshold point is possible, would such accepted threshold vary over the years and decades, and would it change across cultures as well?

Regardless of some intuitive views of who should be considered old and who should not, determining a clear set of criteria to distinguish between the two is not easy. Although there is an established twentieth century tradition to identify old age with qualification for the old-age pension or with retirement from work—that is currently variable across countries ranging between 60 and 67 years old, with retirement age for men and women being either the same or women retiring at a somewhat younger age than men—the question remains: What are the criteria to choose those retirement ages rather than others?

In Elizabethan England, the old were identified on the ground of not only age but also the level of deterioration of their body and mind:

> The aged were those who were infirm, frail, and suffering incapacities of body or mind to the extent that they could no longer fully support or take care of themselves, and who also gave the appearance of being old. The assumption was that people could be advancing in years, or they could be incapable of supporting themselves, but it was only when the two conditions came together in one person that that person was considered 'old' by the authorities (Roebuck 1979, p. 417).

The combination of two main factors: "look" and "incapacity" produced a range of ages that even in the eighteenth century could qualify a person as being "old" if she or he was from 40-year-old to 80 plus. The advent of pensions required a stricter

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limit to the beginning of old age that necessarily shifted the threshold to older ages. In the *Friendly Societies Act* of 1875 in England (and its amendment of 1887) old age started after 50, although pensions tended to begin at the age of 65 (Roebuck 1979). In the late nineteenth and early twentieth century Germany, age of pension eligibility started at 70 (Denton and Spencer 2002). Interestingly, in Australian traditional Aboriginal societies a person is also considered old at the age of 55–60, a broad confluence of views with the Western tradition, that is presumably guided by the capacity to perform basic activities of daily living, and also some biological considerations, such as the onset of menopause in women, for instance. In such societies, adult children are expected to support their old and increasingly incapacitated parents in retribution for what they received from them when they were younger, whereas other members of the extended family also contribute to the care of older people (Berndt and Berndt 1992).

According to the *World Health Organization* (WHO), most developed countries currently consider 65 years old as the beginning of old age, although the age of 60 is used by the *United Nations* (Millane 2013). Further distinctions have been introduced within the population of old people based on age. Individuals aged 60–69 are known as the "young-old", those aged 70–79 are the "old-old", whereas those 80 years old and older are referred to as the "oldest-old". Centenarians and ultracentenarians are currently the subject of specific studies, being regarded as categories on their own.

The original introduction of age pensions was a consequence of the difficulties that people of older ages had in finding work. According to Janet Roebuck, in the late nineteenth century people older than 50 who were looking for work had difficulties in finding it and this could vary with the kind of work the person was applying for. However, pensions for those people did cost a significant amount of money to the government, which led to the inevitable push to try to shift the pensionable age to older ages. The argument about the age pension was well alive in the early twentieth century, and it is resurfacing around the world in the twenty-first century, with an ageing population (Denton and Spencer 2002) and in current discussions about what is the best and most sustainable system of pensions (e.g. James 1998). The issue is made even more urgent now given that the ratio of people at work over those in retirement is decreasing, thus raising concerns about the sustainability of pension systems (e.g. Millane 2013). However, there is a counter-argument against this negative view of old age and pensions, as when the rates of unemployment are increasing then it could be better to lower the pensionable age, so that more opportunities are open for the young, an issue that is also relevant at the beginning of this third decade of the twenty-first century. We will see in the next chapter that the conundrum between early retirement to create job opportunities for the young and sustainability of the pensions system can be resolved by the proper taxation of profits from the increasingly mechanised/computerised systems of production.

Older people are currently confronted with additional financial challenges such as their increasing level of debt, that in developed countries may have been accrued in part to finance a better lifestyle, whilst their income after retirement may not be enough to sustain such level of debt in the long term. This has put some pressure on the individual to continue working even when she or he may be officially "retired", although such person may face barriers of discrimination when applying for a job (see Millane 2013).

Emily Millane reports the results of a survey carried out by the *Australian Bureau of Statistics* with data for the years 2002–2011 where interviewees were asked about the reasons older people are discouraged from seeking work; the vast majority of respondents (62–78%, depending on the year) was concerned about being considered too old by a potential employer, 10–18% complained about lack of jobs in the area they live in, and 4–8% had issues with lack of qualifications. Such concerns notwithstanding, older people willing and able to work should be given a chance.

The difficulties that older people may confront in their quest to find a job have put to centre stage the issue of superannuation. Given that the recent trend has been to move away from the *defined benefits system* of superannuation where the retirees are expected to receive a predictable income no matter what the fluctuations of the market are, and for as long as they live, and towards a more risky system relying on an amount of accumulated funds that are contributed by the employer—perhaps with some additional voluntary contribution by the employee through salary sacrifice—and that are invested in the stock market or in a secure but usually low-yield cash deposit, the question of whether the retiree will have enough financial means to support him/herself in retirement is also becoming more central than ever. To increase the degree of financial certainty in retirement more and better planning is required as governments reconsider their level of expenditure on age pensions, and superannuation systems are also modified (Feldman and Beehr 2011).

But ageing is first and above all characterised by body and mental changes. Although most of the older people experience a relative decline in their cognitive capacities (e.g. Verhaegen and Salthouse 1997; Skirbekk 2003), the rate of decline can vary considerably across both individuals and specific cognitive skills, and it can be somewhat improved by appropriate interventions. The same variability in decline can be seen in some body changes associated with old age such as wrinkles, grey hair, age spots, health conditions such as arthritis, osteoporosis, and so forth, which can also affect body image in old people (Hurd Clarke and Korotchenko 2011). Deterioration in such variables may be predictive of mortality (e.g. Lee 2000); therefore, recent attempts have been undertaken to include in the definition of old age also the probability of mortality, whereby the limits of what is considered a "young-old", "old-old", and "oldest-old" can change following changes in life expectancy (Denton and Spencer 2002).

In traditional societies the concept of old person is also intermingled with that of "elder". An elder could be defined as "someone who has been sought by their peers for spiritual and cultural leadership and who has knowledge of some aspect of tradition" (Stiegelbauer 1996, p. 39). The elders are the repository of history, beliefs, traditional thoughts, knowledge, and practices that are passed on from one generation to another (e.g. Berndt and Berndt 1992). In a statement produced by an Innu delegation from the *Sheshatshiu Native Canadian Centre* of Toronto, reported by Stiegelbauer (1996, p. 39), elders:

> should be role models for everyone else. Elders should be teachers to the grandchildren and all young people because of their wisdom. Elders should be advisors, law-givers, dispensers of justice. Elders should be open to everyone. Elders should be knowledgeable in all aspects of Innu culture. Elders should be teachers for everyone of the past history of Innu people. Elders should be recorders of history, not only orally but to be preserved in print. Elders

> should be teachers of values important to Innu to be passed on from generation to generation. Elders should be teachers of language and oral history. Elders should be teachers of Innu medicine. We place great importance in our Elders. Their directions for us will guide our lives.

In other words, the elders are "experts on traditional life". In some traditional societies such expertise is kept somewhat secret and it also functions as a way to exert a degree of control over the youth, and to protect useful knowledge from being appropriated by outsiders to the family or the group (e.g. see the *Kpelle* of West Africa described by Murphy (1980), see also Berndt and Berndt (1992)). In these "gerontocratic societies" the level of inter-generational tensions may be particularly high. However, transmission of knowledge from old to young is more often a positive feature of inter-generational relationships across cultures (Maccoby 2007).

In modern societies the traditional cultural role of old people as elders is being compromised by easy access to recorded information from the past and by a fast-changing world that may challenge the capacity of many old people to stay abreast with new developments. Still, they remain living witnesses of a time past and their accumulated life experience may provide useful guidance to the solution of those problems that remain relevant from one generation to the next. We will see throughout this book how older people could continue to contribute to society in various ways, and for that reason, we will use the words *old* and *elder* interchangeably.

Our world is undergoing a *demographic transition*; that is, it is changing and ageing as the global population moves from a regime of high fertility and mortality to one of low fertility and mortality. People 65 years old and older represented 8.2% of the global population in 2013; this is expected to increase to at least 19% by 2050 (Lutz and Kc 2010; Draper 2014). From the information available in Table 1.1, it can be seen how all continents, including the two most populous countries in the world: China and India, are trending towards an increased proportion of older people over time, although some continents are ageing faster (Europe) than others (Africa). This trend towards an ageing world population is the result of increased life expectancy, especially since the twentieth century, leading to an increase in the

Table 1.1 Proportion of the population above the age of 65 and projections into the future for the world and various specific areas (UN Scenario of IIASA education projections)

Area	2000 (%)	2010 (%)	2020 (%)	2030 (%)	2040 (%)	2050 (%)
World	7	8	10	13	16	19
Africa	3	3	4	5	5	7
Asia	6	7	9	13	17	21
Europe	15	16	19	23	25	28
Latin	6	7	9	12	15	19
America and Caribbean North America	12	13	16	20	21	21
Oceania	10	11	14	16	18	19
China	7	8	12	17	24	27
India	5	5	7	9	11	14

Simplified from Lutz and Kc (2010)

number of people expected to live to 75 and beyond (e.g. past 100 years), with the oldest-old group expanding rapidly, especially in economically developed countries (Christensen et al. 2009; HelpAge International 2013). In addition, the global ageing population can be also explained by slower overall population growth caused by reduced fertility. Indeed, around the world the section of the population aged 60 years old or older is the one growing the fastest, ranging from 1 to 3.7% annually depending on the region (United Nations, Department of Economic and Social Affairs, Population Division 2013a, b).

Currently, the five countries with the highest percentage of people older than 65 are Japan (21.6% of the population), Italy (20%), Germany (20%), Greece (19.1%), and Sweden (18.3%) (Sokolovsky 2009).

Life expectancy has been dramatically increasing since the mid-nineteenth century in economically developed countries (see Fig. 1.1). In recent decades this increase in life expectancy has been mainly accounted for by increased probability of surviving to old age due to improved general life conditions and medical interventions. Across more than 30 developed countries, probability of survival from age 80 to 90 years increased from 15–16% for women and 12% for men in 1950, to 37% and 25%, respectively, in 2002 (Christensen et al. 2009). This seems to be a result of more people reaching their older ages in better health than it was the case in the past (Vaupel 2010). Women in general tend to live longer than men, with 60-year-old or older women outnumbering men by a ratio of 1.19 in Africa, 1.07 in Asia, 1.56 in Europe, and 1.16 in Latin America and the Caribbean, this is also true for the section of the elderly population aged 70 and older (Lloyd-Sherlock 2000), in spite of the well-known world trend for more males than females to be born (105–107 male for every 100 female births, Hesketh and Xing 2006). In 2008 the sex ratio of the 67–79 years old around the world was 1.31 women/men, whereas for the ≥80 years old it was 2.08 women/men (Cauley 2012). The bias in life expectancy in favour of older women has been consistently increasing throughout the twentieth and the beginning of the twenty-first centuries in most countries, with only few exceptions such as the United Kingdom, Australia, and the USA among developed countries, which in 2007 saw the female bias in life expectancy decrease somewhat in comparison with the 1950s (Kinsella 2009).

Increased ageing, however, also comes at a cost in terms of increased susceptibility to diseases, both infectious and non-infectious, as the immune system becomes more dysregulated. In particular, the oldest-olds may become frailer and less capable of effectively caring for themselves in their daily necessities. Although women are more likely to survive to older ages than men, physical deterioration in old age seems to be more accentuated among women than men (Christensen et al. 2009), although this issue is also ground for much debate (Kinsella 2009, p. 22).

Despite the negative effects of increased age on health, in recent times older people have also become better able to take care of themselves than it was the case in previous generations. This is because they have enjoyed the aid of technology, better housing conditions, and public services, including healthcare services; changing gender roles, better education, better conditions in their workplace, and overall improved economic standards (Christensen et al. 2009).

Although women tend to live longer than men, a pattern that, as we have seen, is broadly common around the world, they also tend to have less material protection

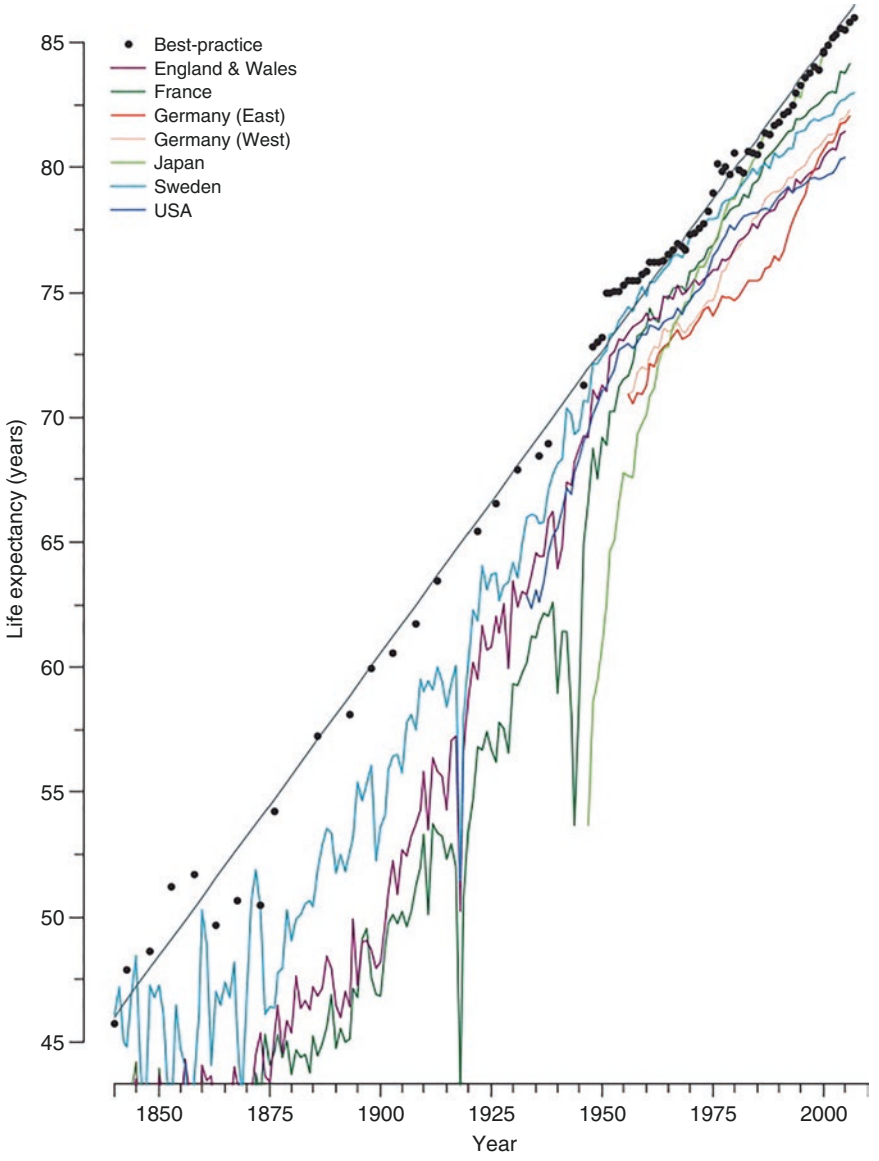

Fig. 1.1 Increase in life expectancy in various economically developed countries since the mid-nineteenth century (from Christensen et al. 2009)

than men in old age, but they tend to enjoy greater social support from a broader network of family and acquaintances than men do.

In terms of the capacity of various countries to secure the well-being and to provide good quality of life to their older citizens, the *Global AgeWatch Index* (HelpAge International 2013) opens a window into the ability of 91 countries to afford their older citizens enough income, ability to maintain good health, and access to quality

healthcare services, along with a capacity to participate in various activities within their communities. Northern European and North American countries top the list, along with New Zealand in number 7, Japan (number 10) and Australia (number 14). The best South American country is Chile (number 19) and, not surprisingly, at the bottom of the list are poor countries ravaged by war and civil unrest. It should be noted that although the ranking reflects to a great extent the material wealth of the country, it is also dependent on the specific policies and social factors affecting the well-being of older people, that can be modulated by historical processes and specific political priorities. For instance, although Chile ranks number 19, the much wealthier Brazil (as measured through the country's gross domestic product (GDP): https://data.worldbank.org/indicator/NY.GDP.MKTP.CD), also a South American country, ranks 31. Incidentally, as we revise the text of this chapter in November 2019, we have to note that Chile is in the grip of significant social unrest that was initially motivated by a broad dissatisfaction with the costs of living and wealth inequality in that country: not all that seems to shine is actually gold.

The *Human Development Index* (HDI), an indicator of social progress, is linearly associated with the values of the *Global AgeWatch Index*, but countries such as Canada, Switzerland, The Netherlands, Germany, and Sweden perform much better than the expected from the linear trend due to their national social policies in favour of the elderly.

An important issue to consider when we study older people is that not all cohorts of, say, 60–70 years olds are the same. Even within a single country, each cohort will have experienced different historical processes throughout their lifetime that may mark the way in which they reach and live their old age (Millane 2013). For instance, old people in the 1980s–1990s had been young adults at the time of World War II and the fall of European colonialism that followed across the world; on the other hand, in the 2010s old people had been young adults in the 1970s, when the world was dominated by the Cold War, social unrest, unseen-before levels of consumerism, the rise of feminism, and the emerging conscience of the human impact on the environment. This phenomenon is known as *generational imprinting* (Dorfman et al. 2004). Therefore, both similarities and differences between cohorts of equally aged old people can be explained by a combination of biological, psychological, cultural/social, and historical factors. For instance, the decrease in the number of children per family observed in recent decades may produce a cohort effect in future generations of elders, by decreasing the probability that younger generations may directly help their ageing parents, thus shifting the responsibility of aged care for future cohorts of elderly to the individual (through savings and lifetime investments) and society at large (pension systems and public aged care initiatives) and away from the direct family.

Older generations are better able of taking care of themselves after retirement and enjoy a greater level of well-being the more they have built their capabilities over their lifetime. Following the views of Amartya Sen, capabilities in old age should not only be seen in terms of financial backup, although this is certainly an important issue, but also in terms of the mental, existential, social, and physical scaffolding that allows individuals to build a personally satisfactory level of functioning in their later life:

> The capability of a person reflects the alternative combinations of functionings the person can achieve, and from which he or she can choose one collection. The approach is based on a view of living as a combination of various 'doings and beings', with quality of life to be assessed in terms of the capability to achieve valuable functionings (Sen 1993, p. 271).

> The functionings relevant for well-being vary from such elementary ones as escaping morbidity and mortality, being adequately nourished, having mobility, etc., to complex ones such as being happy, achieving self-respect, taking part in the life of the community, appearing in public without shame ... The claim is that the functionings make up a person's being, and the evaluation of a person's well-being has to take the form of an assessment of these constituent elements (Sen 1993, p. 276).

We agree with Sen that the ability to effectively express personal capabilities and agency is at the core of human freedom and the achievement of a satisfactory level of well-being, this remains true throughout the life of an individual, but it is especially so at older ages. We will introduce and develop later in this chapter our concept of *fulfilling ageing* that encapsulates such notions as those mentioned by Sen and others into a comprehensive view of ageing. The concept will be further developed throughout the book and synthesised in the last chapter.

Personal capabilities may be also translated into material productivity. Material productivity is dependent on many specific factors such as physical and mental abilities, formal education, experience. Although experience is likely to increase with age some abilities that are currently of use in many jobs may in fact decline as technology changes (Skirbekk 2003).

Capabilities that do not require constant retraining and updates, but just maintenance and reinforcement of well-established routines (*crystallised abilities*) may not decline with age; whereas *fluid abilities*—or the capacity to solve new problems and identify new patterns—are relatively more susceptible to age-dependent decline (Horn and Cattell 1967). Whenever constant adaptation to a fast-changing world is required, some older workers may find themselves at a relative disadvantage, leading to higher levels of unemployment or sub-employment, and decreased income (Skirbekk 2003). At that point in their life they may hope to have real choices: going ahead alone if they have sufficient personal resources, fully relying on the support from a good welfare system if they lack personal resources, or enjoying the benefits of a combination of both kinds of resources. Not having any adequate choice is the worst situation an elderly person can expect.

In what follows we provide a general overview of some major areas of interest in ageing studies that will be analysed in greater detail in the remaining chapters.

1.1 The Multiple Dimensions of Ageing: An Overview

Many theories have been proposed over the years to explain the process of ageing at several levels of analysis. Table 1.2 summarises some of the main biological theories that consider mechanisms spanning from the evolutionary to the more proximate molecular, cellular, and systemic ones. Such theories encompass two main broad perspectives of the biological processes of ageing: the "programmed ageing"

Table 1.2 Classification and brief description of the main biological theories of ageing

Biological level/theory	Description
Evolutionary	
Mutation accumulation	Mutations that affect health at older ages are not selected against
Disposable soma	Somatic cells are maintained only to ensure continued reproductive success; after reproduction, soma becomes disposable
Antagonistic pleiotropy	Genes beneficial at younger age become deleterious at older ages
Molecular	
Gene regulation	Ageing is caused by changes in the expression of genes regulating both development and ageing
Codon restriction	Fidelity/accuracy of mRNA translation is impaired due to inability to decode codons in mRNA
Error catastrophe	Decline in fidelity of gene expression with ageing results in increased fraction of abnormal proteins
Somatic mutation	Molecular damage accumulates, primarily to DNA/genetic material
Dysdifferentiation	Gradual accumulation of random molecular damage impairs regulation of gene expression
Cellular	
Cellular senescence–Telomere theory	Phenotypes of ageing are caused by an increase in frequency of senescent cells. Senescence may result from telomere loss (replicative senescence) or cell stress (cellular senescence)
Free radical	Oxidative metabolism produces highly reactive free radicals that subsequently damage lipids, proteins, and DNA
Wear and tear	Accumulation of normal injury
Apoptosis	Programmed cell death from genetic events or genome crisis
System	
Neuroendocrine	Alterations in neuroendocrine control of homeostasis results in ageing-related physiological changes
Immunologic	Immune function dysregulation with ageing results in increased incidence of autoimmunity

From Weinert and Timiras (2003), with slight modifications

view, whereby intrinsic molecular clocks regulate the timing of biological events that describe the ageing process, and the "error accumulation ageing" view that includes inputs from the external environment (stresses, for instance) that can progressively damage aspects of our biology, eventually leading to ageing (see Weinert and Timiras 2003 for a review).

From a genetic perspective, genes that affect phenotypic traits that are damaging to the organism at old ages, and that underlie the process of senescence, are usually expressed after the individual has already reproduced, and therefore they escape the filtering process of *natural selection*; this allows those genes to remain in the population from one generation to the next (Medawar 1946, 1952). In addition, the longer an individual survives, the more likely it is that it may accumulate mutations in the DNA of cells in various tissues (*somatic mutations*), that could eventually lead to genomic instability and eventually ageing, as first suggested by Leo Szilard (1959, see also Trifunovic et al. 2005). Therefore, ageing is likely to be a combination of "programme" and "error accumulation".

Studies carried out on human centenarians support a degree of heritable variation in the ability to survive to oldest ages (Weinert and Timiras 2003). Heritability, however, tends to be lower than 50% as seen in studies of identical twins (Finch and Ruvkun 2001). One gene that has been shown to have clear effects on ageing is the *apolipoprotein E* (*APOE*) gene. Apolipoprotein E, the gene product, is a major cholesterol carrier that is involved in the transport of lipids and injury repair in the brain, along with being involved in the repair of arterial lesions and protection against atherosclerosis. In particular, the *APOE2* allele is especially prevalent among centenarians (Finch and Ruvkun 2001), whereas *APOE4* is associated with dementia. Caloric restriction also increases longevity in a variety of mammals, this could be mediated by insulin and it could therefore be affected by mutations in genes of the growth factor system. The growth factor system includes the hormones insulin, insulin-like growth factor-I (IGF-I) and IGF-II. Recent studies have identified an insulin-like signalling pathway that can regulate lifespan in both invertebrates and vertebrates (Cheng et al. 2005).

Apart from heritable genetic aspects of ageing, there are also modes of inheritance that can affect ageing but that do not involve any change in the primary structure of the genetic material, the DNA. These are known as *epigenetic mechanisms*. Such epigenetic mechanisms include random events in gene expression that affect the phenotype, and DNA methylation. In this case older people may display a variable degree of methylation in diverse regions of the DNA of various cells, which affects the expression of the genes involved (Fraga and Esteller 2007).

Other specific molecular mechanisms have been also proposed that could affect the process of ageing. Ageing at the cellular level can be affected by the accumulated effects of repeated cell replications and stresses suffered by the cell, alongside the effects of the shortening of telomeres following cell replications when telomerase becomes less active. Telomeres are repetitive sequences of DNA found at the tips of the chromosomes that protect the integrity of chromosomes. They are shortened by each cell replication but are reconstituted thanks to the action of the enzyme telomerase. The longer the telomeres are, the more likely it is that the person can survive beyond the age of 60 years old (Muller et al. 2007). Telomeres can be shortened by life events such as long-term chronic psychological stresses and infections (e.g. Effros 2011).

It is also known that oxidative damage to DNA—and to proteins and lipids—by reactive oxygen species (ROS, such as hydroxyl radicals, hydrogen peroxide, and superoxide anions that are mainly produced by mitochondria) accumulates with age. This can have a direct effect on the ageing process (Martin et al. 1996; Finkel and Holbrook 2000; Weinert and Timiras 2003; Beal 2005; Muller et al. 2007), a suggestion that was first made by Denham Harman in the 1950s (Harman 1957). Genes which products can defend tissues against the effect of free radicals, as it is the case of superoxide dismutase (SOD), can delay the process of ageing. In addition, reduced availability of calories can reduce the capacity of mitochondria to produce ROS, thus also delaying cellular ageing (Finkel and Holbrook 2000; Wallace 2005).

ROS can be produced endogenously within the cell by organelles such as mitochondria or peroxisomes. They can have physiological functions in homeostasis, helping in normal growth and metabolism, but they can also have damaging effects on the organism through their roles in ageing, cell death and disease if they are in

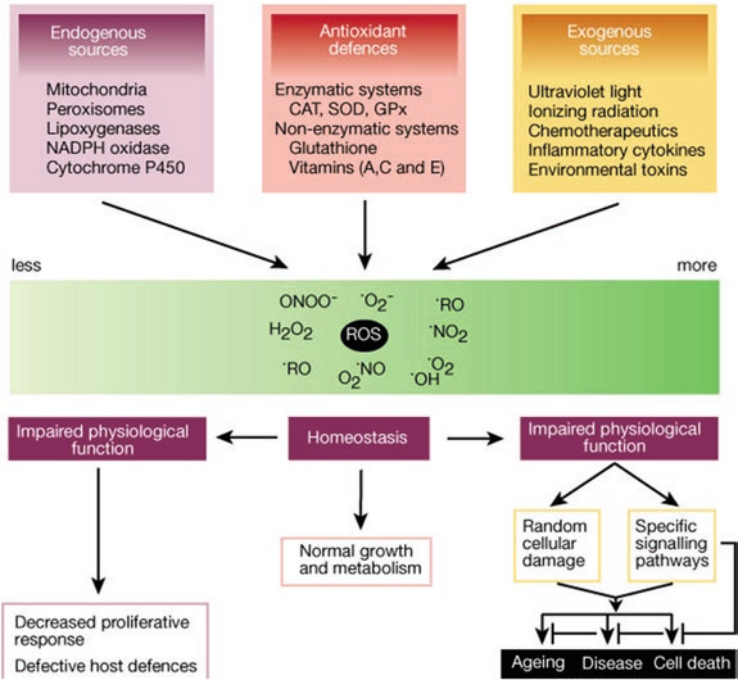

Fig. 1.2 Various sources of reactive oxygen species (ROS) and antioxidant defences, along with effects of ROS on the organism's physiology, including ageing (from Finkel and Holbrook 2000)

high concentration. At lower concentrations than normal, they can impair the immune response. Production of ROS is regulated by antioxidant molecules such as SOD and various vitamins as summarised in Fig. 1.2.

Intracellular degradation of macromolecules occurs in the lysosomes as part of the normal functioning of cells. This happens through a process known as *autophagy*, which literally means "eating itself", but autophagy decreases in effectiveness with age. Age-dependent failure in autophagy leads to waste accumulation within cells and a decrease in the normal functioning of such cells. In turn such malfunction will affect the tissues those cells are part of and the physiological processes the tissues are involved in (e.g. immunity, brain activity), leading to altered health, physiological performance, and behaviours (Cuervo et al. 2005). *Proteasomes* are intracellular multi-subunit assemblies of proteases that can specifically contribute to the ageing process through this autophagy mechanism in the cells of the nervous system (Keller et al. 2002).

Apoptosis, an internal mechanism of cellular self-destruction, that can be very adaptive in the defence against cancer, can also have the negative side effect (*antagonistic pleiotropic* effect) of promoting tissue senescence (Campisi 2003).

At the systemic level, ageing can be expressed in changes to endocrinological, immunological, and neurological functions that in fact form a closely integrated and interacting biological network, thus what affects some parts of this neuro–immune–endocrine system may also affect others.