Chapter 1
GENERAL CONCEPTS AND HYPOTHESES IN THE STUDY OF CARDIOVASCULAR NEURAL REGULATION

Concepts are tools, useful for thinking. Hypotheses are also tools, useful for investigating.

In the field of cardiovascular neural regulation, general concepts and hypotheses are only but a few. The term *homeostasis* is the inescapable incipit.

In its intuitive terms it probably pertains to human wisdom and, as such, surely precedes the birth of experimental physiology. There is, however, a general agreement in regarding the *milieu intérieur* of Claude Bernard (1878) as the matrix of Walter Cannon’s (1932) *homeostasis*. “La fixité du milieu intérieur est la condition de la vie libre, indépendante: le mécanisme qui la permet est celui qui assure dans le milieu intérieur le maintien de toutes les conditions nécessaires à la vie des éléments” (Bernard 1878). The sentence suggests that stability and freedom are linked as fundamental attributes of life. Stability being an obvious concept, freedom must refer to the range of worlds and activities which an organism may enter and survive (Yamamoto 1965). However, the interpretation of the relationship between stability and freedom is not so transparent: one way to achieve stability might be giving up freedom to invade certain areas or curtailing the range of activity. Moreover, the stability that appears intuitively highly desirable for intracellular or extracellular fluids cannot indiscriminately be considered as useful for other controlled variables. As is the case of arterial blood flow and pressure, the sudden changes of which are so crucial to permitting performances like strenuous exercise, fight or
flight, which often ensure the very threshold for freedom, i.e. survival. In fact, Cannon’s interpretation of “Wisdom of the body” (1932) largely based on homeostatic principles seems to underestimate the fact that in emergencies the sympathetic nervous system promotes the changes, rather than compensating for them (Recordati 1984). Yet, not surprisingly, Cannon wrote (1932) that “responses of the organism itself to situations in the external environment, are associated with disturbances of the internal environment”. Thus instability as well appears to be part of the same biological planning. In general, homeostasis, i.e. stability and its loss, i.e. instability, are likely to be but the extremes of a continuum spectrum.

In addition, and from another point of view, it is clear that organisms are thermodynamically open systems and that living processes are homeodynamic and not homeostatic (Rose 1998). Thus, the metaphor of homeostasis in a sense constrains our view of living systems.

An additional concept that has to be included in these basic premises is feedback. This term proves that along the last decades there has been a striking similarity between ideas in engineering and in the study of regulatory mechanisms in physiology. The term “arose in the engineering context to denote a type of connectivity in which the consequences (output) of an action produced by a machine are returned in some fashion to participate in the causes (input) of the mechanical action” (Yamamoto 1965). In the traditional biological reasoning while homeostasis implies stability, the term feedback deals with the organization of this process. That is to say that feedback mechanisms have been exclusively assigned to the biological strategy searching for stability (Sagawa 1983).

THE NEGATIVE FEEDBACK

When Heymans and his coworkers, at the end of the twenties, observed the hypotensive reflex elicited by increasing the arterial pressure in a recipient dog carotid sinus perfused with the blood of a donor dog, they were probably the first ones to witness the operational characteristics of a circuit with negative feedback characteristics (Heymans 1929). Electronic devices were still to come.