I. In the first half of the nineteenth century physiological chemistry drew level with developments in organic chemistry. Observational evidence was mostly defined in terms of the results of elementary and proximate analysis. The dualistic radical theory of molecular constitution served as the dominant theoretical framework, sometimes in its electrochemical formulation.

G.J. Mulder systematically elaborated a physiological-chemical methodology which was not elucidated abstractly but as the outcome of previous experience. Applying dualism as a theoretical context, he aimed at the elucidation of the molecular constitution and properties of proteins and at combining these results with micro-chemical investigations in order to reach ultimately chemical understanding of animate processes.

Mulder's theories came under attack when the radical theory underlying his line of argument and definition of observational support began to decline. The theories were shielded effectively from attacks but had to lose much of their direct impact in the field.

II. Theories on fermentation and metabolism similarly kept in line with the development of organic chemistry. Berzelius's theory of catalysis was a special application of his electrodualistic theory of molecular constitution and action.

Liebig rejected the 'dynamic' line of argument (handling the notion of 'force'), and drafted a theory in which empirical evidence was defined 'statically' (in terms of balances). His theory of fermentation was based on the balance between 'affinity' and 'difference' of the atoms in a molecule. His meta-
bolic theories were based on the balances of elementary composition. In order to formulate theories on this statical basis, he applied classical particle mechanics as a conceptual and argumentative framework or paradigm.

Mulder attacked Liebig's system by pointing out that the arguments were not supported by sufficient empirical evidence to forestall the introduction of chimeras and the deviation of physiology from what he conceived as the true course of science.

Lehmann maintained the classical tenet of Liebig's system which, in his opinion, provided the indispensable rational framework for scientific physiology, but claimed only empirical research along the lines of Mulder's methodology was to bring forth its substantial contents. This was the opinion also of other renowned physiologists not unsympathetic toward Liebig.

III. If considered against the background of contemporaneous philosophical thought, Liebig appears to have been on the side of rationalism. He strove after 'clarity and distinctness' as marks of scientific truth by defining the observational basis of his system quantitatively (elementary analysis) and reasoning along a number of apriori, undubitable mechanistic principles.

On the other hand, Mulder was on the side of empiricism and positivism. He recognised that deterministic theories are well possible without necessarily having to define the state of a system in the way of classical particle mechanics. He considered causality a suggestion of human understanding induced by inductive reasoning: a 'cause' is merely a representation of a universal as it is derived from a number of particulars. He considered as the greatest and most dangerous heresy in science the arbitrary definition of a force and attributing to it properties as required for the explanation of the phenomena in question. It has been demonstrated that this was the very strategy applied by Liebig.

It has been pointed out that neither the methodologies nor the metaphysical attitudes they imply must be analysed on their own ground, but only in connection with actual scientific practice. It is quite understandable that, lacking scientific devices and data, scientists had to appeal to metaphysical guidelines while setting up conceptual and argumentative frameworks for their enterprises. Many of Liebig's and Mulder's successors recognised that such regulative beliefs should be susceptible to critical discussion in the light of the progress of the science, notably the success or prospect of partial reduction.

IV. With the emergence of structural organic chemistry by 1850 organic chemists recognised the impossibility of tackling the problems of protein structure and action with the contemporaneous potential of their discipline. In the doctrine of the living substances a gradual transition has been demonstrated from an
'atomistic' to a 'thermodynamic' research programme, in which the conception of
'colloids' played a crucial role. This development drew level with developments
in physics, such as the kinetic theory, Hess's thermochemical law, the prin-
ciple of energy conservation, the equivalency of mechanical and thermal energy
(supplying important clues as to the essential energy balances in organisms),
thermodynamics (alternative state descriptions), etc.

V. In Germany Liebig's rational system continued providing the framework for
investigations in scientific physiology. By 1860 the theories were virtually
rid of their falsifiable contents, but were not discarded. Rather were the me-
taphysical guidelines gradually replaced by sound scientific arguments derived
from thermochemistry and energetics, which resulted in sound theories of energy
metabolism. By 1900 these developments, combined with the colloid science of
live substances, resulted in a scientific physiology based on the continuous
(in contrast to atomistic) state description.

In France, Bernard had linked up with Mulder's line of investigation, but
his positivism was to deviate from Mulder's in apriori defining a line of de-
marcation between the domains of chemistry and physiology. Fermentation, e.g.,
almost apriori was placed under the heading of a 'chemical process', a 'pheno-
menon of death'.

Against the deceptive clarity of Liebig's, and the doctrinaire schematism
of Bernard's system, Pasteur posed his empirical investigations which demon-
strated the vectorial nature of fermentative processes and both specificity
and plurality in regard of the by- and end-products of such processes, obstruct-
ing any 'simple' chemical or mechanical explanation.

Besides the predominantly biological lines of research initiated by Pas-
teur, there were French chemists who continued to study the chemical aspects
of enzyme action and fermentation. By 1900 this development gave rise to a doc-
trine in which the nature and 'mechanism' of such actions was conceived in the
conceptual system of the chemistry of oxidative and reductive reactions.

VI. The general transition from an atomistic to a thermodynamical research
programme induced modifications also in philosophical thinking. The main cur-
rents were neo-positivism and neo-Kantianism, both aiming to answer to the
phenomenalist tendency in the contemporaneous natural science: the replacement
of explanatory mechanisms by subsumption of phenomena under general phenomenal
laws of nature.

Examples have been produced of debates between neo-vitalists and materia-
lists which have mainly taken place within the context of phenomenalist science
and either neo-positivist or neo-Kantianist methodology. Again the subservience
of philosophical arguments to the urgent issues of methodology has been argued.
At about the beginning of the twentieth century a number of specialties existed, each elaborating vital phenomena in its own traditional conceptual context: biology, anatomy, physiology, immunology, bacteriology, histochemistry, organic chemistry, pharmacology, etc. Their interplay was largely determined by the general doctrine of colloid science, but subsequently molecular protein chemistry was to compete for this function.

VII. Owing to Buchner's discovery of cell-free fermentation the study of metabolic pathways developed fruitfully and rapidly. Protein chemistry saw a revival of ideas reminding of the older system of Mulder, both in respect of methodology and results. It became particularly successful owing to the contributions of Fischer who, simultaneous to Hofmeister, formulated the peptide theory.

With metabolic theory providing knowledge of 'what' happened, and protein chemistry supplying information on the material substrates of vital processes, the fundamental conceptual framework could arise in which the various specialties were to become pulled together to form 'biochemistry'. Although colloid science ceased to be the general framework for these investigations, it has been pointed out that many originally colloidal notions have been incorporated into the conceptual system of modern biochemistry.

Characteristic of biochemistry has been the constant attempt to supersede the immunity of conceptual and argumentative frameworks, with the aid of partial reductions as elaborated and provided by colloid science, energetics, thermodynamics, protein chemistry, etc. It was inevitable that initially chemists had to appeal to metaphysical arguments in justifying their choice of a conceptual and argumentative system. These inevitable metaphysical attitudes induced dogmatic polarities. Yet such polarities have increasingly become liable to scientific criticism in the light of partial reductions, providing criteria for 'violating' their immunity by furnishing indications about how vital phenomena are to be abstracted to reach various levels of (inorganic) science.

Examples of such superseded dogmatic polarities are the following:
- is the living substance 'just' a molecular edifice, or is it 'irreducible to a molecular construction?  
- is biotic energy a form of energy 'sui generis', or is it 'just' a form of physicochemical energy?  
- is the form of protoplasm 'unique', or is it 'just' a physicochemical structure?  
- have vital processes 'no' material substrates, or are they 'just' material rearrangements?
In the context of discovery, metaphysical arguments have been valuable sources of ideas and creative contributions to understanding in physiological chemistry. In the context of justification, appraisal essentially was based on the levels of abstraction of the conceptual and argumentative systems. They showed somewhat the character of Lakatos's research programmes, but degenerating systems were not just replaced by progressive ones. Rather, they all tended to lose empirical meaning if not timely forged together with other systems. Such syntheses of conceptual systems concerned their very metaphysical cores, as is revealed by a reconstruction of the mostly implicit metaphysical positions of the scientists concerned. Critical discussions on the metaphysical foundations of various conceptual systems was possible, as has been argued, on the basis of insight into their abstractive relations, in the light of the success or prospect of partial reduction. At this level a fruitful interplay with general philosophical thought has been demonstrated.

On the whole our study has made a plea for the combined research into the history, methodology and philosophy of science. There is an intricate communication between these aspects of science, philosophy being both a fruit of scientific developments and a higher-level frame of reference for discussion on the inevitable metaphysical issues in science. As such philosophy can be very useful to science, but should never impose its ideas on the conduct of scientists.