Inverse Problems and Uncertainties in Science and Medicine

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Abstract

Measuring data are always inexact. This truism is frequently disregarded in natural science such as physics, biology or medicine. This may be admissible in "classical" (deterministic and stable) processes. However, unstable or inverse problems are becoming increasingly more practically important. In particular when the body's interior is inaccessible (e.g. gravimetric inverse problems and seismic tomography in geophysics, or X–ray and NMR tomography in medicine), instable or "ill–posed" problems are essential. Rather similar is the case in logic: deduction is a (algorithmic or "deterministic") direct problem, the inverse of which, induction, is essentially more problematic. Uncertainties arise even in deductive logic in the form of Goedel's theorem, and even in deductive physics in the form of Heisenberg's uncertainty. Also behavior problems in biology, psychology and medicine exhibit similar uncertainties.

The present article attempts a synthesis of all these aspects in the form of a unified treatment.

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Introduction

This article considers some general aspects of the relation between theory and experiments in general, and its impact on science and medicine.

The basis will be the theory of inverse problems. Direct and inverse problems are related like deduction and induction. The well–known difficulties of induction are mirrored onto the fact that many problems in science and most problems in medicine are difficult inverse problems. Thus many applications of sciences, technology, and medicine have the proverbial "skeleton in the cupboard". Rather than pretending that this skeleton does not exist, we shall squarely face it and try to examine it. In the use of measurements, we shall try to outline their proper use, their achievements as well as their limitations.

Generally we may make the following remarks:

– Mathematics is the language of physics because, for most physical processes, it allows the formulation of a meaningful description. (This should not scare the reader because all mathematics will be relegated to the Appendix and the main paper can be read without mathematics.)

– Unfortunately, for the complex systems of real nature, there is no unified mathematical systems theory: "Science is patchwork".

– For such systems only certain partial informations can be measured, and practical experience is needed to draw at least some meaningful conclusions from the measured data: "praxis cum theoria".

– Engineering systems are relatively well known and managable. For them, a mathematical systems theory usually exists.

– Biological systems are much more difficult: measurements may not be reliable and meaningful, and mathematical systems theories hardly exist. Thus in medicine practical experience ("ars medica") is particularly important.

– Social sciences are in between: systems theories do exist to a limited extent, and computers can be used with a certain success.

The sections 1 to 3 are a preparation for the central topic (section 4), the relation of man and nature where basic principles of the use of measurements in this context are outlined. The Appendix is only for mathematical readers and may be omitted by the general readers.

1 Inverse problems

An *inverse problem* is the opposite of a *direct problem*. The inverse problem usually is much more difficult than the underlying direct problem.

A few examples will help to understand this.

1. *Weather*. By creating weather, nature solves the direct problem. In forecasting weather, meteorologists have to solve a difficult and notoriously unstable inverse problem.

2. *A broken leg*. By breaking his leg, a person suffers a direct problem, which happens easily. The task of the surgeon is to heal the broken leg, which is the corresponding inverse problem, which is certainly much more difficult.

3. *In medicine* in general, direct problems occur without much effort: the patient falls ill. The task of the medical doctor is to diagnose the illness and find a cure, which may be very difficult, even impossible.

4. *An unknown physical phenomenon* occurs (direct problem). The physicist wants to find a theoretical explanation. This may be easy or difficult, or may lead to a new theory; this is an inverse problem.

5. *Two problems in informatics*. First, someone writes a computer program and makes a mistake. This is direct, and happens all the time. Then one must try to find the mistake, and this may be a very frustrating inverse problem. Second, one writes a source code, having finally succeeded in weeding out all errors. The compiler converts it into a executable file. This is direct: source code (e.g. in the computer language C) is compiled to give an exe–file. The inverse problem, finding the source code from the exe–code, is usually unsolvable. (Commercial software makes money by this fact.)

There is one profession, *engineering*, which thrives on *direct* problems: constructing roads, buildings, engines, computers ... Here, inverse problems are relatively less frequent: finding the reason why a building collapses or why a car suddenly fails. In these "inverse problems", one also speaks of *reverse engineering*, implying that normally, engineering solves direct problems.

In *medicine*, it is the other way round. Every diagnose must solve an inverse problem, so most medical problems are *inverse*. Direct problems in medicine are, e.g., surgery.

The fact that difficult inverse problems are so prominent in medicine, is the result of the use of so much medical technology which again leads to inverse problems of a physical–mathematical nature, from primitive X–rays to sophisticated NMR tomography, which we shall discuss later. Diagnosis is also helped by modern *expert systems* which try to solve inverse problems in logic.

Engineering and medicine, on the one hand, are frequently compared with science, on the other hand. Science is thought of as the *study* of nature, whereas engineering and medicine are intended to *change* nature, hopefully for the better. This is certainly a gross simplification, and we see that engineering and medicine differ by the role of direct and inverse problems. Constructing an automobile may be incomparably simpler than curing a cancer patient or an alcoholic.

The set of all solutions. This is a key concept (Anger 1990). Usually inverse problems have several or even infinitely many solutions. Knowing the set of all possible solutions, we can select out of them a solution that is most suitable for us.

Let us illustrate this by comparing this situation to a simple example. A company needs a new secretary. It advertizes the vacancy and gets a number of applications. From this "set of all possible candidates", the most suitable candidate is selected.

Important as it is, there a few cases in which such a set of all possible solutions of an inverse problem can be found explicitly (cf. Appendix). Nevertheless, this concept is of fundamental theoretical importance.

2 The problem of deduction and induction in science

Let us start with a ridiculously simple reasoning: "If it rains, then the street is wet" is an almost "logical deduction" from basic facts of physics (exceptions are hot desert roads where rain, if it falls, dries up almost immediately). The inverse reasoning: "If the street is wet, it has rained" is less convincing: a watering engine may have passed or a waterpipe broken instead.

The first sentence is a very primitive case of *deduction*, and the second, of *induction*. In this example (and also generally), induction is much more difficult and uncertain than deduction.

As a first preliminary definition, let us speak of the rain as *cause*, and the wet street as *effect*, then *deduction is the reasoning from cause to effect*, and *induction is the reasoning back from effect to cause*. If the first is a direct problem, induction is an inverse problem.

Given the cause, the effect can be deduced *automatically* by pure logic provided the laws of physics are presupposed as *axioms*. For the present context, axioms are simply the starting point of a logical deduction.

Since the procedure is automatic, it can be expressed by a computer program, or in other words, by a computer *algorithm*. (An algorithm is just a mechanized or mechanizable logical–mathematical procedure.) *Deduction is algorithmic reasoning.* (This is already a quite general and useful definition, although logicians and mathematicians are asked to be benevolent and indulgent about our simplemindedness.)

Induction, the inverse problem of deduction, is much less simple, as we have already repeatedly seen. It usually has several or even infinitely many solutions and thus *cannot be directly converted into a computer program.* To get a reasonably correct solution, one must have additional information and include previous experience, which are incorporated using arguments of probability. A good physician performs this complicated reasoning intuitively. Trying to computerize such a procedure leads to medical *expert systems* which are based on logic and data, but should also include the experience of the best medical doctors and some probabilistic reasoning (experts use such incomprehensible terms as non–monotonic reasoning and Bayesian inference; never mind). Still expert systems will be inferior to a physician of the highest class. (In the same way, a chess–playing machine may beat average chess players and even grand masters, but the very best champion will usually beat the best available machine.) The key word in this context is *intuition*, whose logical standing will be discussed later, in the context of artificial intelligence and Goedel's theorem.

Let us thus continue here in the usual informal way. The problem of induction has been one of the most famous and most difficult problems of philosophy, from David Hume (1711–1776) to the present day. Let us start with some simple examples.

(1) *Succession of day and night.* This has been observed since mankind came into existence, and there was never a single exception. Can we conclude that tomorrow the sun will shine again (at least above the clouds) ? Pragmatically we all believe that there will be another day, but this cannot be proved logically. *Induction is not a purely logical problem.* If logical procedures such as deduction are called analytic, *induction is not analytic.* It is a physical problem: there will be no tomorrow if the Earth or the Sun explode during the night, or if the Earth has been destroyed by the impact of a huge meteorite. But still we may consider that with high probability there will be another day.

(2) *All swans are white.* Let us assume, for the sake of argument, that, so far, only white swans have been observed. Can we say (a) that *the next* observed swan will also be white and (b) that *all* swans are white? Obviously we can expect event (a) to occur with much higher probability than the general law (b) to be true. Even if zoology claimed that all swans are white (which it does not), a black swan could still occur: a student might have painted the swan black in order to fool his professor.

It is sometimes said that induction works if there is a certain *uniformity of nature.* This certainly applies to Example 1: the laws of earth rotation guarantee the succession of day and night if there is no perturbation by a collision with a large meteorite or by an explosion as mentioned above. But will these laws also hold tomorrow?

Here we have used the book (Moritz 1995). From this book we also take two quotations:

> To ask whether inductive procedures are rational is like asking whether the law is legal.
>
> Jonathan Cohen

> Induction simply does not exist.
>
> Sir Karl Popper

These extreme statements from two philosophers are typical for the attitude of the philosopher and the scientist towards induction.

Verification and falsification. Scientists, especially physicists, don't like induction. They try to reduce induction to deduction.

To understand this, let us reformulate the definitions. *Deduction* proceeds from the general to the particular, using a general law to compute particular observable quantities which then may be compared with actual observations. *Induction* is said to proceed from the particular to the general, using particular observed data to derive the general law.

In simple cases in science, induction may indeed be used. For formulating the grand theories of physics, however, such as Newtonian classical mechanics, Einsteins theory of relativity, or the quantum mechanics of Heisenberg and Schroedinger, physicists proceed quite differently. They first formulate a provisional theory, based on experiments, experience, mathematics, physical intuition, and good luck. They use this provisional theory as a working hypothesis, and try to derive, by deduction, *possible* outcomes of experiments. If they are in agreement with many different *actual* experiments, and no instance to the contrary is found, scientists consider the theory as correct. This is *verification* of theory by experience.

Note that all above–mentioned theories, from Newton to Heisenberg, have been found in this way. All these theories are very simple and beautiful to the mathematician. Discoverers, from Kepler to Schroedinger, have thus been guided also by esthetic considerations. Usually, great theories are also beautiful. The converse is not true: there have been beautiful theories which have not been found to explain the observed facts.

Thus a theory must be thoroughly verified. The excellent philosopher Sir Karl Popper, has maintained, however, that no amount of verification can ensure the validity of a theory, whereas a single *falsification* is sufficient to overthrow it. Therefore, falsification is logically more important than verification.

However, this holds for pure mathematics and pure logic. Actual data are almost always affected by uncertainties and errors. Thus even Popper's falsification is not absolute: the falsification may only be *apparent*, caused by a measuring error, whereas in reality, the theory is true. This is not a theoretical speculation: many modern experiments operate in the gray zone between error and reality: it may be difficult to decide whether a certain small effect is "real" or due to measuring errors.

In practice, there is no big difference between verfication and falsification. If a new interesting theory is presented, the discoverer (or inventer) of this theory need not worry about verification or falsification: his experimental friends will try to verify it and his opponents will be most happy to falsify it.

In all these cases, measuring errors play an essential role; so they will be discussed in the next section.

3 Uncertainties in science

3.1 Measuring errors

Measurements are inexact. If I measure the length of my desk, I may get 1.41 meters. Is this true?

If we apply the logician's alternative, true or false, then the answer must invariably be that the measurement is *false*. A more careful measurement may give a length of 1.407 m. Is this mathematically true? It is also false because the length is certainly not 1.407000000... but perhaps 1.40723....

Well, this is logical hairsplitting because everyone knows that a length of 1.41 meters is only approximate. We thus must, in some way, take measuring errors seriously.

After earlier attempts by R. Bošković and A.M. Legendre, C.F. Gauss (1777–1855) created a theory of errors in a perfect and comprehensive form which is valid even today, in spite of the great progress of statistics since then. The principle is that *every* measurement or empirical determination of a physical quantity is affected by measuring errors of random character, which are unknown but subject to statistical laws.

Error theory has always been basic in geodesy and astronomy, but has been less popular in physics. Here it is frequently thought that, at least in principle, the experimental arrangements can always be made so accurate that measuring errors can be neglected. This is, usually implicitly, assumed in any book on theoretical physics. You will hardly find a chapter of error theory in a course of theoretical physics.

In medicine, assume that I (H.M.) measure my own blood pressure with one of these popular home instruments. I may get 135/85, which probably is fine at my age. Half an hour later I get 145/95, which is less acceptable. I am getting frightened, so I measure again and get 160/105. The next measurement gives a reassuring 140/85. Is there a real change of my blood pressure, or is the outcome simply the incorrect reading of my cheap blood–pressure instrument which, furthermore is operated by a layman, namely myself? Such questions can be of vital importance.

The answer given already by Gauss is that every measurement should be accompanied by a measure of its accuracy, which is called *standard error* or *r.m.s.* (root mean square) *error*. In the first case, the result may be

$$\text{length} = (1.41 \pm 0.004) \text{ meters},$$

in the second case, say,

$$\text{blood pressure} = 150 \pm 8/90 \pm 8$$

which explains all measurements to be the same within a prescribed accuracy. (If the standard error is 1.0, then a measurement of a quantity of value 45.1 may well be

$$44.2 \quad \text{or} \quad 46.5 \quad ,$$

but also

$$43.0 \quad \text{or} \quad 47.1 \quad ,$$

or even slightly smaller or larger values are possible, but with smaller probability.)

In fact, if a medical expert system receives as input not only certain measuring data, but also their accuracy, then the outcome would be better and more reliable.

Taking inaccuracies into account, rather than glossing over them, is in a way a matter of honesty and wisdom.

Effect on verification and falsification. In the present section we have seen that a theory must be verified or falsified by experience. Popper considers falsification to be better because a theory can be falsified by *one* counterexample, whereas *any number* of measurements cannot completely verify a theory: the next measurement may already contradict it. This is true in principle; because of measuring errors, even the falsification may only be apparent: the theory may still be true, the measurement being in error. In the language of statistics, this is an *error of second kind*: rejecting a hypothesis although it is true. Verification is subject to *errors of first kind*: a hypothesis is accepted although it is false.

3.2 Heisenberg uncertainty in quantum physics

Unavoidable observational errors came to the attention of physicists first around 1925 when W. Heisenberg established his famous uncertainty relation (if you don't like the mathematics, forget it!)

$$\Delta p \Delta q \doteq \frac{h}{2\pi}$$

where h is Plancks constant basic in quantum theory. It states that a coordinate q and a momentum p (mass times velocity) cannot *both* be measured with arbitrary precision. If q is very accurate ($\Delta q \to 0$), then the error Δp in p will be very great:

$$\Delta p = \frac{h/2\pi}{\Delta q} \to \infty \quad ,$$

that is, an accurate measurement of position q makes the momentum p very uncertain.

Heisenbergs uncertainty relation is of fundamental conceptual importance and thus has become justly famous. In fact, Heisenbergs relation is much more popular with natural scientists and natural philosophers than Gauss' error theory, although the latter, as Jeffreys (1961, pp. 13–14) remarked, is certainly more important in everyday experimental practice than Heisenbergs uncertainty relation. Ordinary observational errors are usually much larger than Heisenbergs quantum uncertainties.

What makes Heisenberg uncertainty so interesting is that it reflects the influence of the observer on the observed quantity: if you observe an electron under a powerful light microscope (say), then the measurement involves a collision of the measuring photon (the particle equivalent of a light wave) with the observed electron, which usually disturbs the electron unpredictably.

Quantum effects are very small; they belong to the world of molecules, atoms, electrons, protons etc. Nevertheless mental processes in the brain may be quantum effects rather than effects of classical physics, so that the simplistic materialism of "neurophilosophers" and neuroscientists such as Churchland (1988) or Edelman (1989) is most certainly inadequate. Mental activity and quantum phenomena seem to be interrelated in a very remarkable way, see (Lockwood 1989), (Margenau 1984), (Moritz 1995), (Penrose 1989), (Squires 1990), or (Stapp 1993).

Classical physics (including relativity theory) claims that *the material world is essentially independent of the observer*: a train moves through the countryside in the same way whether it is observed or not (except by the engine driver). An apple falls from a tree without the least regard to its being observed or not.

Quantum physics claims that the observer interacts with the material microworld, changing it by the very act of observation.

3.3 Heisenberg–type uncertainties in psychology, medicine, and biology

Physicists are justfied in considering quantum physics, together with the Heisenberg uncertainty relations, as highly relevant philosophically.

Curiously enough, disturbing of the surrounding world by observation, has been a well–known fact in life–sciences, long before the arrival of quantum theory, but its philosophical implications have hardly been noted.

If a man observes a girl, the very act of observation changes the "object": the girl blushes, touches her hair, comes closer or walks away. In medicine, this is the *placebo effect* which is so important that great care is needed to take it into account (or rather to eliminate it) in testing a new medicament. The very fact that the patient thinks that a new medication being tested on him may relieve his symptoms, makes the medication possibly effective even if it is only a placebo (a medically inactive substance).

If you observe a dog, he may wish to play with you or bite you. He will certainly not remain passive under observation. If you dont know the dog, you may suffer from a very unpleasant "Heisenberg uncertainty" concerning the behavior of the dog in the next second. Dogs may be as dangerous as quantum theory!

3.4 Uncertainties in logic: the logical paradoxes

Around 1900, the German logician Frege tried to derive mathematics from logic, thus putting mathematics on a firm and exact logical basis. Unfortunately, his (at that time the only) follower, the British philosopher Bertrand Russell, discovered a paradox which made Frege so unhappy that he considered his life work useless. Russell tried to minimize the damage by finding a way to avoid his paradox, which led to the monumental work "*Principia Mathematica*", by B. Russell and A.N. Whitehead, published around 1910.

What is this paradox? It concerns the set of all sets which do not contain itself as a member. Most people, including the present authors, have great difficulties understanding this abstract formulation. Russell himself gave it a popular formulation which anybody can understand. In a small village there is only one barber, but a remarkable one: he shaves all male persons in the village who do not shave themselves. Does the barber shave himself? Yes, if he does not belong to the persons who do not shave themselves. The opposite is also true. Thus the barber shaves himself if and only if he does not shave himself ...

A ridiculous logical children's play? Not quite, it has shattered the very foundations of logic and mathematics, a shock from which these "most exact" sciences have not recovered to the present day, and no way is seen for recovery in the foreseeable future. The very fundament of logic and mathematics, *set theory*, remains in doubt. Probably it works, nobody has found a devastating failure yet, but this is not excluded in the future. As a mathematician said: "God exists because mathematics is consistent, and the devil exists because we cannot prove it".

A second paradox is known from classical antiquity: the *paradox of the liar*. Someone writes a sentence on the blackboard: "This statement is false". Is it correct? Yes, if the sentence is correct, then the statement holds and says it of itself. The opposite can also easily be seen. Thus, this sentence is correct if and only if it is false. If we call the statement L, then L *is correct if and only if it is false*. This paradox is used by the logical and mathematical genius, the Austrian Kurt Goedel, to prove a highly important statement, which throws doubt not only on the absolute, all–embracing and provable exactness of mathematics, but is also basic for understanding artificial intelligence.

3.5 Uncertainties in mathematics: Goedel's theorem

Of all sciences, mathematics has always been the most exact. All valid mathematical theorems must, and can, be derived from a finite set of axioms. Crudely speaking, axioms are fundamental truths which are immediately recognized as correct, even self–evident. For instance, statements such as "1+1=2" or "Through two given points there passes one and only one straight line". Euclidean geometry is based on the historically first set of axioms, which were formulated already in the 3rd century B.C.

It is necessary that the axioms be *consistent*. For instance, possible axioms "1+1=2" and "1+1=1" are inconsistent. *From inconsistent axioms, all propositions, even logically contradictory ones, could be derived*. For instance, "2+2=4" and "2+2=3" could be derived as follows

To	1+1=2		To	1+1=2		
add	1+1=2		add	1+1=1		
to get	2+2=4	(true)	to get	2+2=3	(false)	

This, of course, is nonsense because the axioms are inconsistent and the "axiom" "1+1=1" is manifestly false.

There are, however, more complicated instances of this general principle.

In 1931, the young mathematician and logician Kurt Goedel, then living in Vienna, published a paper with the formidable title "On formally undecidable propositions of *Principia Mathematica* and related systems". The paper is extremely difficult and very few people understood its importance. Nevertheless it soon became famous among specialists.

Principia Mathematica is the work by Russell and Whitehead mentioned in the preceding section, which claimed to furnish a complete system of axioms, by which all mathematics can be derived from logic.

What did Goedel do? He considered a proposition similar to (L) above:

(G) This statement is unprovable.

He then proved that G is derivable from the axioms if, and only if, its contrary, not–G, is also derivable! Thus, with "provable" being the same as "derivable from the axioms",

(GG) G is provable if and only if not–G is provable.

The reader will note the similarity to the paradox of the liar, discussed in the preceding section, about a proposition L: "This statement is false". We saw that L is true if and only if it is false, or in other terms,

(LL) L is true if and only if not–L is true.

Clearly, the sentence (LL) is ridiculous and pretty useless. Not so, if we consider Goedel's sentence (GG) which differs only in replacing "true" by "provable".

If G were provable, then not–G would also be provable. If a proposition is derivable together with its contrary, then the axioms of Principia Mathematica would be inconsistent. Hard to swallow, but possible.

There is, in fact, another possibility: neither G nor non–G are provable. Then (GG) would also be true because it does *not* say that G is provable, but *only* that G is provable *if* not–G is also provable. If neither G nor non–G are provable, fine.

At present it is generally assumed that the axioms of mathematics *are* consistent. Then the second alternative says that there is at least one proposition, namely G, which can never be derived from the axioms, but neither is its contrary, non–G, derivable. The proposition G is *undecidable* (see the title of Goedel's paper).

But now comes the sensation: though neither G nor non–G can be derived, it can be seen by higher–level "informal thinking" that G *must be true*. In fact, let us rephrase what we have just said:

– neither G nor non–G can be derived,

– hence, trivially, G cannot be derived,

– hence, G is unprovable.

This means that the proposition G above, which says exactly this, *must be true* (provided, of course, that our axiom system is consistent). Clearly, this proof is not a simple derivation from the axioms but involves "metamathematical" reasoning.

This proof is tricky indeed, but the reasoning, though oversimplified, is basically correct. From the darkness of undecidability there arises, at a higher level, the light of truth!

Thus there is at least *one* true proposition that cannot be derived from the axioms.

This is admittedly a somewhat difficult argument. (Never mind, Goedel's paper with all the details is even incomparably more difficult. The best "popular" presentation is still (Nagel and Newman 1958).)

As we have seen, deduction from the axioms is a typical activity of a computer working "algorithmically" by fixed axioms and rules of deduction. The way by which G is seen to be *true* is a typical flash of *intuition*, no less rigorous than algorithmic deduction. However, this kind of rigorous intuition is typical for the human mind able to *reflect* "from a higher level" on the algorithmic work of the computer.

Perhaps a medical example can serve to illustrate the situation. A patient suffering from compulsory neurotic thinking always repeats to himself a certain argument. (It is said that an antique "philosopher" got such a compulsory neurosis by taking the antinomy of the liar too seriously, day and night repeating: L implies non–L implies L implies non–L ... Had he been able to think about this *from a higher level*, he would have recognized that this argument is really nonsense, and he would have regained his normal thinking.) In fact, one way of curing a neurotic is raising his thinking to a higher level to make him recognize the futility of such an "infinite loop" of thinking.

We have used this word purposely because also in a computer there are *infinite loops*, which must be avoided by good programming and having built–in mechanisms that stop the computer before an infinite loop occurs. Alas, all programmers know that computers nevertheless fall quite frequently into an infinite loop, and often it may be necessary to stop the computer and start it again ...

Whereas the loop (LL) is deadly but irrelevant, Goedel's formula (GG) is logically acceptable and incredibly fruitful.

Two results of Goedel's theorem should be pointed out.

1. Mathematics cannot be completely derived "algorithmically", although computer algorithms are very useful, not only in numerical computation but also in computer algebra and computer logic (e.g., theorem proving). Hopefully, mathematics is consistent; to the present day no case to the contrary seems to have been found. However, we can never be absolutely certain; an element of "Goedelian uncertainty" remains, as we have mentioned in the preceding section.

2. Computers working algorithmically can never be intelligent as humans are, because they cannot reflect about themselves, about their own thinking: they cannot display "creativity" or "intuition". To repeat, "intuition" in the sense used by Goedel is to recognize as true a proposition that cannot be derived from the axioms. There is nothing mystical in this, and it is as rigorous as algorithmic thinking.

Thus, computers can think only "algorithmically". Man, in addition, can think "nonalgorithmically". ("Nonalgorithmic thinking" is but another expression for "intuition" or "creativity", but it sounds less mystical.) Since computers cannot think nonalgorithmically, they can never replace human thinking.

Goedel's proof shows something which is absolutely remarkable: in contrast to a machine, man can think "at two levels": a lower level, "algorithmic thinking", is accessible to computers as well as to humans, but a higher level, "nonalgorithmic thinking", is reserved to man only.

Other terms for "nonalgorithmic thinking" are "reflexive thinking", "self–referential thinking", as well as "selfconsciousness" or "creativity", even "metathinking".

This thinking in two levels is not a useless hairsplitting, but the basis of Goedel's proof, which has been seen to have enormous theoretical and practical importance for artificial intelligence. By replacing "true" by "provable", Goedel has tamed the destructive energy of the paradox of the liar, turning it into a highly sophisticated logical proof (some people regard Goedel's proof as the most important achievement of mathematical logic and Goedel himself as the greatest logician of all time, with the possible exception of Aristotle).

Such a thinking "at two levels" occurs, whenever I reflect about the possible value or insignificance of my latest scientific work. Such self–critical thinking is impossible to a computer (unfortunately also to some human persons ...). A computer will never spontaneously write on the screen "Thank you, dear programmer, your program has really been great" or "It is a shame that I must work with such a stupid program".

Multilevel thinking is quite common in philosophy. One of the most famous philosophical statements is "Cogito, ergo sum", "I think, therefore I am". This conclusion is *not* a deduction of *formal* logic, which could be done algorithmically by a computer. Instead, the conclusion follows by reflecting on the *meaning* of the fact that I am thinking, by reflecting on thinking at a higher level. This cannot be done by a computer! By the way, this is perhaps the simplest example of "nonalgorithmic thinking" and thus may help understand Goedel's argument. In fact, we may say: With Descartes, from low–level thinking or even doubting ("cogito" or "dubito"), there follows high–level certainty of existence ("sum"). With Goedel, from low–level undecidability there followed high–level truth.

Another example, perhaps less known, has also played a great role in philosophy. It is due to the Greek philosopher Plotinus (around 200 A.D.). He formulated the statement "The thinking thinks the thinking". You may say: "Of course, what else?". But try to program this statement in a computer! As far as I know, this statement cannot be formulated in any known computer language but if it could, a horribly destructive infinite loop would follow. We know the reason: a computer can work at one level only, whereas Plotinus' sentence comprises no less than three logical levels: one for the subject "The thinking", a lower level for the verb "thinks" and a still lower level for the object "the thinking".

By the way, Plotinus' theorem was very influential in philosophy: from providing the basis of St. Augustinus' theory of the Christian trinity to the dialectic triad of Fichte, Hegel and followers.

3.6 Artificial intelligence

Artificial intelligence (Weizenbaum 1976) is considered to comprise activities which are performed by computer–type systems and which previously were thought to be performable only by human beings, such as *language recognition* (a speaker dictates a letter and the computer prints out the letter automatically in an almost perfect form), *computer vision* (image processing similar to the activity of the eye), *expert systems*, *robotics* and similar operations.

They have reached a high state of perfection and are very useful indeed. An advanced medical *expert system*, in addition to performing "logical reasoning", is also able to acquire data from measuring systems (possibly including language and image processing) and to incorporate knowledge from the enormous body of previous experience of the most prominent medical experts. If expert systems are "intelligent", the incorporated intelligence is provided by the physicians, programmers and by other *human* experts.

Robots no longer belong to science fiction. They largely have replaced human workers at the assembly line for automobiles etc., relieving man of monotonously recurring simple operations. There are, however, also "intelligent robots" capable of performing surgery in cases where high precision is needed, such as replacement of hip joints or even brain surgery. The robot not only performs surgery, but also measures, processes his measuring data, and performs automatic image processing to assure that he is working at the right place within the patient. Naturally, everthing must be done under the supervision of an experienced surgeon, who can also direct or stop the robot if necessary.

This is certainly an impressive feat of "artificial intelligence".

Is it possible that robots get more and more and more intelligent, behave more and more like human persons, and finally are tired of their subordinate role so that they make a revolution, enslaving or finally eliminating humankind?

Goedel's theorem tells us not to fear this. Robots can only think along an algorithm, however complex it may be. They have no self–consciousness: they do not know what they are doing, and cannot be made responsible for it. Thus strikes, frustration and fights of robots against mankind belong to science fiction.

Finally, a few words on the relation between "natural" and "artificial" intelligence. We "naturally" use our legs to walk from one place to another. If the two places are far apart, such as Berlin and Graz, it is better to take an automobile (if possible). The car, so to speak, is an "artificial" extension of our legs, increasing their power to cover distances. An automobile certainly is not a *replacement* for our legs, which we need even to operate the car. In the same way, *artificial intelligence is not a competitor, but an extension of our mind*, greatly increasing its power and opening new fascinating possibilities.

Nevertheless, the language of artificial intelligence is useful to describe natural phenomena: Our brain obtains and stores, by means of the eyes, geometrical colored patterns, by means of the ears, acoustical patterns, by means of nose and mouth, chemical patterns, etc. Thus we get an enormous amount of various interacting patterns, which our brain seems to handle without great difficulty. The medical doctor thus first makes a classical anamnesis, on the basis of which he will decide which measuring technology he will then apply. Pattern analysis with or without technology is essential also, e.g., for language and for economical sciences.

3.7 How accurate are laws of nature?

Laws of nature are never *absolutely* exact. The reasons partly are based on the various uncertainties discussed in previous sections, and partly they are considered in (Moritz 1995, sec. 6.5). For most practical purposes — engineering, medicine etc. — they can be considered *practically* exact.

Classical physics is usually sufficient. Quantum physics may be necessary in the study of brain processes. It should be understood, however, that *tomography* (magnetic resonance, positron emission etc.) involves quantum phenomena and the usual books explaining this theory to physicians, for instance the excellent booklet (Horowitz 1989) must be regarded with a grain of salt.

On the crude materialism of "neural philosophers" we have already talked in sec. 3.2. Generally, we have the curious phenomenon that biologists have a naive trust in physics (more exactly, in the kind of physics they had learned at their university studies); chemists take physics, especially quantum theory, for granted (justly); physicists have a naive belief in mathematics, and the most rigorous mathematician usually does not like to hear about the uncertainties of set theory, and hardly knows much about Goedel.

Reductionism, reducing thinking to neuronal activity, biology to chemistry and physics, etc. has been a highly important and incredibly successful working hypothesis. To accept it at full face value is difficult because quantum theory, in some way, seems to be related to mental activity, so that there is a strange loop of reductionism (Fig. 1). Again it is curious that biologists are usually the most fervent partisans of reductionism, whereas most great physicists of this century, such as Schroedinger and Wigner, have expressed their doubts in this regard.

But nevertheless, in medicine the trust in science and technology is practically justified, if measuring errors are duly taken into account and if inverse problem structures are handled appropriately.

In fact, the greatest enemy to exactness in the application of technology etc. does not come from science, but from mathematics. It is the *instability of inverse problems*, which applies to NMR tomography as well as to long–time weather forecast, in spite of the high development of both medical technology and meteorology.

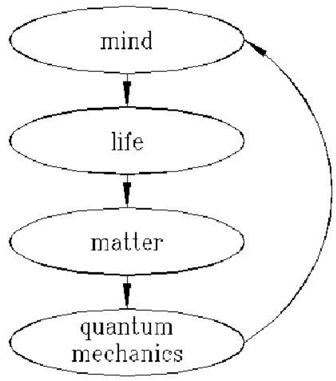

Figure 1: The self–reference loop of reductionism according to E. Wigner

3.8 Uncertainties in inverse problems

The theory of inverse problems is very difficult even for mathematicians. Therefore we shall relegate the mathematical theory to the Appendix. In this place we shall only try to outline some of the most fundamental aspects in a very simple and informal way. Fortunately, this can be done.

Instability. In sec. 1 we have seen the fundamental importance of inverse problems in medicine etc. Now inverse problems are frequently instable. Instability can be succintly formulated: *Stability* means that small causes have small effects. *Instability* means that small causes may have large effects. (Only for mathematicians: A reason of such an instability is often the fact that only smoothed properties, averaged over molecular structures, are accessible to measurements. They represent, so to speak, compact operators, the inverses of which are frequently highly unstable: e.g. integration is stable but differentiation is unstable.)

A typical example of instability occurs in meteorological weather prediction. A small inaccuracy in the meteorological data may change the predicted results completely. This is the reason why weather prediction over more than a few days is extremely unreliable.

The American mathematician and meteorologist Edward Lorenz made a detailed mathematical investigation of this phenomenon. His work made popular what today is known as *chaos theory* (see sec. 3.9). It has the advantage that it can be easily programmed and produces beautiful pictures, so it is popular with computer fans. Applications to biology and medicine are discussed in (Glass and Mackey 1988).

Discretization. This is a main reason why methods such as NMR tomography may have difficulties (Anger 1990, 1997). Fortunately it can be understood very easily.

For simplicity, consider the onedimensional analogue of a twodimensional computer picture. This is a *curve* representing a certain *function*, for instance a diagram of body temperature which plots temperature against time. What is measured is body temperature (say) at 7 a.m., 12, and 5 p.m. every day. The curve is interpolated by hand to get the full curve.

Usually this poses no problem except if the body temperature changes very rapidly and irregularly. Of course, in this case temperature will be measured more often, and this will cause no problem.

Assume now, however, that the patient (unrealistically) always has a constant temperature of 36.0 degrees Celsius, say. The temperature is again measured, or "sampled" at constant intervals (Fig. 2) The "true" curve will coincide with the horizontal straight line.

Let us assume that we know the function only at the discrete sample points. The function between the sample points is not known. The reconstruction of the entire function is done by *interpolation*. Thus:

$$\begin{array}{rcl} \text{direct problem} & \longrightarrow & \text{sampling} \\ \text{inverse problem} & \longrightarrow & \text{interpolation} \end{array}$$

Sampling is also *discretization*, because samples are taken at discrete points only.

Now you will say, for interpolation take the simplest interpolation function, and you will exactly get the true initial straight line.

This is true, but from a mathematical point of view, *all* interpolated functions are equally possible, as long as they are zero (or rather 36.0) at the sample points. Thus from a mathematical point of view, also the "crazy" interpolation curve of Fig. 2 is perfectly legal.

Again you will say: just program the computer such that it gives you a straight line. If the real curve is not straight, however, this will not work. You will then say: tell the computer to find an interpolation curve that is as smooth as possible. This will work in most cases, but assume that for other reasons (e.g. to be applicable to realistic non–straight curves) the computer is programmed so (intentionally or accidentally) that it does give the interpolated curve of Fig. 2, which is less unrealistic than it looks.

The patient will be scared to have such a wild temperature curve and may think he or she is seriously ill. It may help if the doctor patiently explains that the computer has solved his inverse problem poorly, and that the picture is not reality but rather a "*ghost*" (Louis 1981, Anger 1981, Vlaadingerbroek and de Boer 1966). Hopefully he can convince the patient, but the patient may also consider this as an unconvincing evasion.

Now let us turn to the twodimensional images of *tomography*. Since the computer can work only with discrete data, discretization and interpolation must be done also

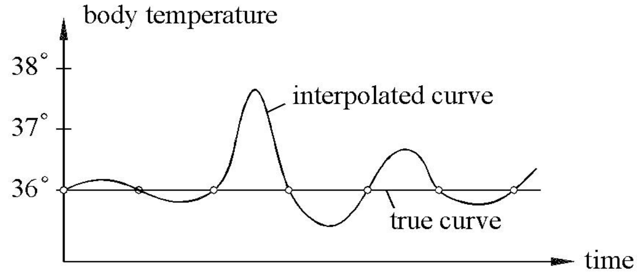

Figure 2: A fictitious temperature curve

here. Let us now again assume that all sample values are zero (no tumor). For some reasons, the computer nevertheless produces a nonzero "ghost image", which is the twodimensional analogue of Fig. 2. The patient may be scared to death, thinking he has a tumor which in reality he does not have ... This is not science fiction but "*ghosts in tomography*" may really occur.

We may also repeat: *Measuring errors and discretization errors are blown up in inverse problem* because of instability.

These conclusions are independent of a detailed mathematical understanding. The mathematically interested reader will find the details in the Appendix.

We have, however, seen very clearly that the inverse problem structure may be the most dangerous aspect in medical problems, from expert systems to various methods of tomography. In spite of (or because of) advanced medical technology, the experience and wisdom of the medical doctor are as necessary, and even more necessary, now than they were ever before.

3.9 Complexity and reductionism

Simplicity. It is said that all great physical theories (from classical mechanics to quantum theory) are simple. This is generally true, and great theories are selected with a view to beauty and simplicity (Section 2).

Chaos theory. For this reason, it was very surprising that even "simple" nonlinear classical mechanics applied to planetary motion has solutions which exhibit a very chaotic and "complex" behavior, although some order is usually present (Fig. 3), as first shown by Poincaré around 1890. Nowadays *nonlinear dynamics* has become very

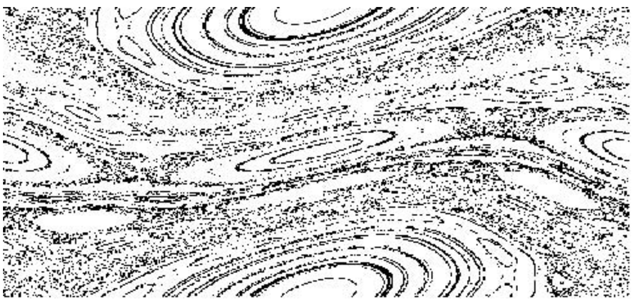

Figure 3: Chaotic behavior in classical mechanics according to Poincare

fashionable by the name of *chaos theory*. It describes phenomena as different as perturbed planetary motion in astronomy (H. Poincaré), the essentially irregular behavior of weather in meteorology (E.N. Lorenz); a turbulent mountain stream as well as human heartbeats. *Fractals* with their strange "complex" beauty, arising solutions of very "simple" equations, are closely related (Briggs 1992). The fascinating interplay between complexity and simplicity is described in the very readable book (Cohen and Stewart 1994).

The well–known condensed–matter physicist Philip Anderson believes that complexity is getting increasingly important also in physics; a whole issue of *Physics Today* (February 1994) is devoted to the topic "Physics and Biology" where complexity comes natural.

Static complexity. Most *crystals* have a simple structure. *Snowflakes*, etc. have more complex structures, combining symmetry and randomness. The *genome* of any living organism is known to consist of DNA which is an extremely complex arrangement (Schrödinger's "aperiodic crystal") of 4 very simple amino acids (A, G, C, T). These 4 amino acids are the same for any organism, from bacteria and algae to man! DNA, so to speak, supplies the genetic *information*. Information is related to a complex order, whereas negative information (*entropy*) is characteristic for disorder.

Dynamic complexity. It is difficult, if not impossible, to define complexity, especially if it is not static but dynamic, such as in a living organism. Nevertheless, we shall try to list some features of complex systems.

– A *great number of elements* seems to be necessary but by no means sufficient. A heap of sand contains many grains, but this does not yet make it a complex system. A biological organism consists of many cells and is a prototype of a complex system because:

– A complex system possesses a rich *structure* at each level (from the macroscopic to the microscopic level), an order which is intrinsic rather than imposed from the outside, e.g., an animal versus an automobile.

– The intrinsic order of a complex system is *dynamic* rather than static: it must always defend itself against *chaos.* Think of a warm–blooded animal: it must permanently strive to keep its bodily temperature constant, in spite of the usually colder environment with all its random temperature changes. Another example is a person who must constantly strive to maintain mental equilibrium in spite of many disturbing impressions and experiences.

– A picturesque description of this situation is to say that complexity *lies at the edge of order and chaos* (Waldrop 1992).

  A typical complex system encompassing order and randomness is also the terrestrial environment consisting of atmosphere and hydrosphere, which is governed by "orderly" laws but is subject to chaotic fluctuations going as far as hurricanes.

– The element of *chaos* is by no means only negative: frequently it provides spontaneous novelty and creativity. Natural selection in Darwinian evolution is based on random mutations that occur spontaneously. (The "survival of the fittest" then restores order, possibly on a higher level.)

– The antithesis to Darwin's "struggle for survival" is "*cooperation for survival*", e.g. between algae and fungi to form lichens. Similar to cooperation is *adaptation* to the environment. An important example of self–organization, struggle, cooperation and adaptation is the *market economy* which is, however, beyond the scope of the present paper. An exemplary case of cooperation between natural scientists and socio–economists is the *Santa Fe Institute*, cf. (Waldrop 1992; general) and (Lewin 1992; emphasis on biology).

Complexity and reductionism. Let us now consider the problem of complexity from a different angle.

In biology there have been essentially two opposite opinions:

(A) *Vitalism*: A living organism is not determined by the laws of physics only; there exist special "vital forces" which cause the purposeful behavior of living organisms, their special structure, their ability to heal wounds and even to regenerate lost organs (this is in particular conspicuous in lower animals such as polyps or starfish), etc.

(B) *Reductionism*: a living organism is nothing else than a very complex and well–structured system, which is completely governed by the ordinary laws of physics and chemistry. Since chemistry, through the laws of quantum mechanics, is thought to be reducible to physics, also the laws governing the apparently so special behavior of living organisms are reducible to the laws of physics. This is reductionism or physicalism.

The main empirical data are clear:

(1) The behavior of animals and plants is completely different from any mechanisms or similar man–made automata.

(2) All physical experiments performed with living organisms or with living tissue have never indicated any measurable deviations from the ordinarily known laws of physics and chemistry.

(3) There seems to be no sharply defined boundary between highly–organized macromolecules and the most elementary organisms, between chemistry and biology.

It is safest and least controversial to consider living organisms as very elaborate and highly organized complex systems (Shorter 1994, Ulrich 1997, Ulrich and Treder 1998, Wilson 1998)

Thus complexity is a "complex" collection of interesting ideas and mathematical models rather than a unified scientific theory such as, for instance, quantum mechanics. It is a field that contains many fascinating open problems.

Nowadays, reductionism is fashionable in biology, and vitalism is considered obsolete or even nonscientific. The famous biochemist and Nobel laureate A. Szent–Györgyi once wrote: "When a molecular biologist calls you a vitalist it is worse than when an FBI man calls you a Communist" (quoted after W.M. Elsasser's autobiography).

This topic is thus very emotional. An objective approach may be to compare a living being to a highly complex computer. Is a computer governed by the laws of physics? Undoubtedly, *yes*. Is it *fully* governed by the laws of physics? *No*. Let me explain.

For the work of a computer, not only the *hardware* (which is fully governed by physical laws), but also the programs (called *software*) are essential. The programs are written by humans and are not fully determined by physics, but also by the intelligence of the programmer, who provides essential non–physical *information*.

With no input, the computer will not work in the sense of producing a useful output. As soon as the software is introduced, the computer starts to work and produces a useful output.

The input may consist of a complicated program *which in itself may contain a law*: for instance a sequence of highly complex mathematics. Or the program for computing income tax may contain a mathematical–logical form of the income tax law (Davies 1988, p. 144). Hence we may well speak of *software laws*.

Thus, the operation of a computer is governed by the physical hardware laws and the non–physical software laws! (Nobody would claim that the income tax law is derivable from the laws of physics . . .)

Using our simplified model of an animal as a computer, we may say

$$\text{life} = \text{matter} + \text{information}$$

(Küppers 1988, p. 17).

Thus, in addition to the physical "hardware laws", there are "software laws" based on information. Both kinds of laws are, so to speak, complementary, that is, they complement each other.

This has been drastically formulated as follows ("*Bohr's paradox*"): in order to determine whether a cat is fully governed by physical laws, it is not sufficient to determine its weight or its bodily temperature. One must use an X–ray equipment, which has to be very powerful to determine the cat's exact internal structure, so powerful that it may well kill the cat or damage it irreversibly. This is not sufficient, however: to get other physical parameters, we must implant physical equipment in the cat's body, and finally we must dissect it. By then, the cat is surely dead. Thus, life and a "full" physical examination are incompatible with each other!

A living organism is an individual "whole". This is what the concept "*holism*" means: *the whole is more than the sum of its parts*.

Reductionism may be defined as the opposite of holism (Hofstadter 1979, p. 312): it is the view that "a whole can be understood completely if you understand its parts, and the nature of their 'sum' ". This concept is more general than the usual reducibility to the laws of physics. We shall call it "*H–reductionism*" (H because it is the opposite of *H*olism or because it is due to *H*ofstadter).

Holism versus reductionism. Most scientists are reductionists: they believe that biology can be reduced to chemistry and physics. This approach is very useful as a working hypothesis. It is, however, not the whole truth because the "software laws" are neglected. Cf. (Hofstadter 1979, pp. 310–336; Popper 1982, pp. 131–132; Davies 1988, p. 142).

Strictly speaking, the universe must be considered as *one* complex system. This is what "strong holism" asserts. In practice, however, some part of the universe: the

Earth, a tree, or a patient are considered without regard to its environment. This is a typical case of H–reductionism as defined above. This approach, common in science and medicine, is necessary because we can study a finite system only. It also works frequently, but not always, as we shall see in the next section.

4 Conclusion: the relation between man and nature

4.1 General remarks

The Earth, where the basic forces of physics act, is a tiny part of the Universe. We know four basic forces: gravitation, electromagnetism, and the strong and weak interactions of atomic physics.

We are able to test the fundamental laws of physics basically only on the Earth's surface and, recently, in interplanetary space. If these laws hold at all, we are rigorously permitted to apply them only to this limited space and to our limited time.

It is believed that the laws of physics hold throughout the universe from its very beginning, the famous "big bang" of creation, to its end. Is this extrapolation to the infinite realms of space and time justified? The only answer we can give is that this assumption is the simplest one and has not so far been obviously contradicted by astronomy, astrophysics, paleontology etc. The assumption thus certainly serves as a working hypothesis, but we shall probably never be able to confirm it exactly.

Even our Earth is a very complex system. As we have seen in sec. 3.9, the laws of biology cannot be completely reduced to the laws of physics and chemistry, although this "reductionism" serves as an excellent working hypothesis.

The *biosphere*, that is, the environment in which life exists, must be treated as a whole. This is *holism* (sec. 3.9).

It is *theoretically* impossible to exactly consider only a *part* of the whole, neglecting the rest. Every *partial system* is only an *open* system, exchanging energy, information etc. with the whole system. Only the whole system is *closed*; any partial system is open to the environment.

In practical science and medicine we *must* consider incomplete partial systems which nevertheless are regarded as *closed*. For instance, if a scientist performs an experiment, the experimental system must be considered closed. E.g., the laboratory in which the experiment is performed, is considered closed (not only by putting a sign "Do not enter" at the door). Activities performed in Nigeria are practically neglected in an experiment performed in Berlin, but the experiment is shielded, as well a possible, even from activities going on in other rooms of the same building. Physics and chemistry are based on the assumption that this "reduction" of the whole to a laboratory subsystem is possible. This is "H–reductionism" as defined in sec. 3.9.

Purposely exaggerating, we may say: In medical technology, such as MR tomography, the patient is "reduced" to a limited physical object, only the factors relevant for tomography being of relevance. In surgery, what is relevant is only the part of the patient from which something is to be removed (apart from considering the patient's behavior with respect to anesthesia). This does not mean that, for the supervising doctor, the patient as a whole person is of no importance, but there are some tendencies along this direction (Ulrich 1997).

Generally an adequate scientific treatment of a problem requires a careful synthesis of H–reductionism (the experiment) and holism (influence of the environment). Similarly in medicine: the data furnished by technology, must be subordinated to the "holistic" view of the supervising physician. This distinguishes true medicine from "health engineering" (Ulrich 1997, p. 26).

In many cases a simple H–reductionism is not applicable because the partial system under consideration is too complex to "reduce" it to simple physical laws. The partial system is principally open and cannot be considered closed. This is true for the study of the Earth's interior by (only) seismic tomography, the study of the patient by (only) MR tomography, prediction of earthquakes, even prediction of weather, and medical diagnosis in general.

An exact error analysis in the sense of sec. 3.1 is highly desirable but frequently not possible.

These facts do not diminish the importance of highly sophisticated mathematical, physical, chemical and technological methods. It is only intended to put these methods into a proper perspective, which by its very nature must incorporate a good amount of holism.

This is particularly important in biology and medicine. As we have seen in sec. 3.3, observation of animals and humans frequently changes the result of observation in a rather unpredictable way (Heisenberg–type uncertainty, placebo effect).

The application of electrocardiography and electroencephalography are based on Maxwell's equations, fundamental for all electromagnetic phenomena. This application requires the knowledge of certain physical parameters within the human body, which are only imperfectly known, although practical assumptions frequently provide quite useful results.

Modern cosmology, based on Einstein's general theory of relativity, quantum theory etc., has provided very interesting models of our universe, from the 'big bang" to our present time and even to the future possible end of the universe. Interesting as they are, they are limited by the (to many scientists questionable) universal validity of the physical laws throughout space and time and by the imperfect knowledge of essential parameters such as the amount of invisible "dark matter" in the universe. Depending on the value of these parameters, we get a *set of possible models* for our universe rather than one single model. (This concept of *set of solutions* is very important for inverse problems, as we have seen in sec. 1.)

Such a set of possible models may be considered a limitation of science, but as well it may be regarded a victory of science: a tribute to intellectual honesty which does not pretend to know more than it really does. (Everyone can then select one's favorite model, just as from the set of literary authors one may select one's favorite author(s).)

Another contribution to intellectual honesty, was Goedel's theorem (sec. 3.5) and related undecidability theorems (e.g., on Cantor's continuum hyptheses which are known only to a small number of specialists). Why pretend that mathematics is "absolutely exact" if it shares the fate of all our knownledge, namely to be imperfect?

4.2 Methods for the study of problems of science and medicine

Only one or two centuries ago, the study of nature was based on the data furnished by our senses. The eyes use visible light (electromagnetic waves of frequency 3.75×10^{14} to 8.4×10^{14} Hertz), the ears analyze acoustic waves (20 to 20.000 Hertz) etc. What is given is a "projection" of the real world on our senses, rather than the real world directly (Kant's "thing–in–itself"). Theories, experiments, and technologies permit to know practically the whole spectrum of electromagnetic waves (from X–rays to radio waves), and it is frequently believed that no radically new phenomena, beyond the reach of our contemporary physical theories, exist. The present authors do not share this view.

To return to sense data, bats are able to orient themselves in space by "acoustic radar" (82.500 Hertz), produced by their mouth. Thus the concept of sense data and their use is variable for different animals.

The informations of our senses are analyzed by our brain, which is much more complex than any imaginable computer (see also Goedel's theorem, sec. 3.5). Computer vision has explained many features of human vision (pattern recognition etc.) but an unexplained rest will remain.

It is in fact possible and highly important that some features of our senses, and even some features which are not directly accessible to our senses, such as invisible electromagnetic waves or magnetic fields, are at present precisely measurable. The use of these data frequently requires "hard inverse function problems" which are mathematically very difficult and complex (sec. 1 and Appendix). (An example is the "geodetic boundary–value" problem which was solved (partially) only by the famous Swedish mathematician Lars Hörmander.) Inverse problems have recently become fashionable, but they are extremely difficult. Their introduction into the regular curriculum of applied mathematics is nevertheless urgently recommended.

In view of this complexity and lack of information, a complete mathematical system theory, particularly for biological systems, does not exist. Solutions are usually non–unique, so the concept of the *set of all possible solutions* comes into focus again. If a physician gets this set of solutions, he can (by experience, intuition, etc.) select one or several realistic solutions, thus narrowing down the possibilities.

Already some 2.400 years ago, Hippocrates and his students (Ginsburg 1983), based on experiences of Egyptian, Babylonian and Indian medicine, asserted that it is only possible *to elaborate the "history" of the various illnesses by observing the symptoms carefully and tracing them down with great accuracy: the illness itself is unattainable.* For the reasons mentioned above, this is valid even today. In a world determined by "exact" sciences and engineering, Hippocrates' assertion is largely forgotten. Exceptions are traditional "holistic" systems such as Chinese medicine (Unschuld 1995). Such and other "alternative" systems should not be condemned *a priori*, but their possible use should be studied, with due mistrust of charlatanry.

4.3 Further thoughts about complex systems

Every real system of nature consists of very many atoms and thus has a very complex structure. A cubic centimeter of a solid body contains about 10^{23} atoms, and about 10^{22} atoms in the case of a liquid. A human person consists of about 10^{27} atoms in about 10^{13} cells. For these cells and atoms it can be assumed that they obey physical and biological laws. No computer can deal with such an atomic system directly; simplifications based on practical experience and experiments are needed: *praxis cum theoria*.

A crude measurement of complexity of a living system is the amount of information necessary to encode its genetic information; see also sec. 3.9: life = matter + information. The smallest autonomous living beings are the bacteria. However, even *their* genetic information comprises four million nucleotides (Küppers 1988). The human genetic code consists even of several billion nucleotides. If N is the number of possible alternative sequences contained in a macro–molecule, if n is the number of nucleotides of a chain molecule, and if $\lambda = 4$ is the number of elements of the genetic 'alphabet' (A, G, C, T) (sec. 3.9), then there are

$$N = \lambda^{4n} = 4^{4 \text{ million}} \doteq 10^{2.4 \text{ million}}$$

alternatives, a number beyond all our comprehension. N obviously is a measure of the structural and functional richness of a biological system at the molecular level. We see how complex life and its evolution must have been.

4.4 Principal differences between the approaches of engineering and medicine

As we have seen already in sec. 1, the problems of engineering and medicine are, roughly speaking, direct and inverse problems, respectively.

In the constructive engineering sciences partial physical systems are combined to form efficient machines or instruments. Space technology and microelectronics are obvious examples. These systems frequently have a hierarchical structure which can be more or less fully understood by logical deduction (sec. 2). The materials used are usually well known by long–time experience, both concerning their properties and their change of material parameters with time and stress ("ageing"). This is not completely true as accidents of airplanes because of material faults show. Fortunately, they are rare. If we go to the limits of physics and technology, such as with space rockets, our knowledge is less and accidents are more frequent.

Electronics is getting more and more miniaturized and computers are getting bigger and more complex. The number of atoms needed to represent 1 bit (unit of information) are decreasing dramatically: 1970 we needed about 10^{15} atoms/bit, 1990 about 10^{8}

atoms/bit. The extrapolation to the year 2010 gives about 1000 atoms/bit, and to 2020 a few atoms/bit, which reaches the size of quantum systems and introduces quantum computation (Williams and Clearwater 1997, p. 8). Systems are getting more and more complex but remain (hopefully) under the control of science and advanced technology.

On the other hand, biological systems are much less under our control. The reduction of biological systems to physics and chemistry is possible only to a certain degree. So far, a complete mathematical systems theory for biological systems is not available at present and may well never be possible even in the future. Only a partial description, e.g. by expert systems (sec. 3.6) seems to be possible.

Here we must work with *induction* rather than *deduction* (sec. 2), and a "holistic" *practical experience* plays a decisive role: *praxis cum theoria*. Dissipative, dynamic, and open (sec. 3.9) thermodynamical systems in biology are the counterparts of the largely conservative, static, and closed systems of engineering.

Medicine is able to solve an "engineering" problem only if the problem is uniquely defined and admits only one solution, for instance treating a well–defined infectional disease or performing a precisely prescribed surgical operation, such as the removal of a tumor. In medical diagnostics, the doctor has to determine the illness on the basis of limited information, which usually is an ill–defined "inverse" problem. The surgeon, however, usually deals with well–defined "direct" partial problems for which, in the course of time, standard solutions (operational techniques) have been developed.

In general, complex problems of nature pose the following task: *all decisions must be made on the basis of incomplete information* (Anger 1990). This fact underlines the great importance of practical experience, which cannot be replaced by the best possible mathematics. On the other hand, very sophisticated mathematics may be needed in order to make best use of the experimental data. The question is not: theory or practice, but practice with theory (*praxis cum theoria*).

Besides a theory of measuring errors (sec. 3.1), we would urgently need a *theory of measurement* itself: For a complex system, which quantities must be measured *outside* of it, in order to determined certain *inner* parameters, which cannot be directly measured, in a unique and stable manner (Anger 1985, 1990)

4.5 Remarks on the further evolution of mankind

Concerning evolution of man, we do have a problem which never arose before. In former times, man has lived from plants, seeds, and animals which are themselves complex systems which had enough time to undergo a slow and relatively stable evolution. Water was available and was usually relatively clean. At present, man is faced with a rapidly changing environment, and also plants and animals from which he lives are rapidly changed by breeding and, recently, genetic engineering, not to speak of very recently developed chemicals (e.g., pharmaceutical substances). Will mankind be able to evolve so fast as to keep pace with this rapid development?

Modern civilization also provides other disturbances of our environment: chemical pollution of water and air, and, recently, electromagnetic "smog" from electrical transmission lines, radio stations, computers, mobile telephones etc. These disturbances are not made harmless by the very fact that they are invisible. Of course, it is astonishing what amount of new chemicals, pharmaceuticals and electromagnetic and other noise the human organism can take.

So far, the average life time of women and men is constantly increasing, to a great measure by more hygiene, better food, not to forget incomparably better medical treatment and the new pharmaceutical products, e.g., antibiotics. It is only to be hoped that this trend will continue. For this, a certain beneficial equilibrium in the biosphere, an equilibrium between man and his environment, seems to be necessary. Fortunately, this problem is now being extensively studied, e.g., by the Geosphere–Biosphere–Project of the International Council for Science (ICSU).

For the continued survival of humankind, all efforts of natural, medical, and social sciences must be combined in a good synthesis which contains reductionistic as well as holistic aspects. Cooperation is required, according to the statement of Hans Urs von Balthasar:

Truth is symphonic.

Appendix: The mathematics of inverse problems

As we have already mentioned in the introduction, mathematics is the language of physics. Most physical problems are inaccessible to direct observation by our senses, especially on an atomic or molecular scale or in medicine. In order to characterize particular physical processes one needs a mathematical model, frequently involving sophisticated mathematics, in addition to experiments to determine their range of application.

Denoting by f the inner (physical) material parameter, by $g = Af$ measurable quantities expressed in terms of the parameters f, then the relation between f and the measurements g may be formally written as an equation of first kind:

$$Af = g \quad . \tag{1}$$

Here f is an element of a set X, and g is an element of a set Y. In both sets we define metrics which are necessary for defining convergence and for determining the numerical stability of numerical procedures. The determination of $g = Af$ if A and f are known is called *a direct problem*, and the determination of f from given g and A is called an *inverse problem of first kind*, symbolically written as

$$f = A^{-1}g \quad . \tag{2}$$

The determination of A by measurements f and g, as for instance in impedance tomography to be treated below, is called an *inverse problem of second kind*, following the terminology of (Moritz 1993).

Definition 1: Let X and Y be two metric spaces. Further let $A : X \to Y$ be a mapping from X into Y. Following J. Hadamard, the equation $Af = g$ describing the corresponding problem is called *well–posed*, if

1. for every $g \in Y$ there exists at least one f satisfying $Af = g$ (*existence*),
2. the element f satisfying $Af = g$ is uniquely determined (*uniqueness*),
3. the solution f depends continuously on g (*stability*).

If one or more of these three conditions is not fulfilled, the problem is called *not well–posed, ill–posed or improperly posed.*

Most mathematical problems in science, technology and medicine are inverse problems (Anger 1990, Anger et al. 1993). Studying such problems is the only complete way of completely analyzing experimental results. Often, these problems concern the determination of properties of some inaccessible regions from observations on the boundary or outside the boundary of that region, as in geophysics, astrophysics and medicine. Further, the automatization of physical processes leads necessarily to inverse problems, which absolutely must be solved. The practical importance of inverse and ill–posed problems is such that they must be considered among the pressing problems of mathematical research.

A main problem in mathematical physics is to study the *information content* of an inverse problem, i.e., to find out which internal parameters of a system inaccessible to measurement can be determined in a stable and unique manner. In order to solve an inverse problem, the following points have to be studied:

- mastery of the special process both experimentally and theoretically,
- possibility of mathematical modelling of the process,
- mastery of the direct problem both theoretically and numerically,
- studying of the information content of the inverse problem,
- development of algorithms for the numerical solution of the inverse problem.

Since almost every mathematical model is a (weak) projection of the real world, every such model has solutions which are not necessarily real–world solutions. The problem whether a given solution is a "real–world solution" can only be decided by experiment (praxis cum theoria). Real–world systems have such a great information content that the system cannot be characterized completely by measuring data. A consequence are essential difficulties of measuring physics (Anger 1990) and particularly of medical diagnostics (Anger 1997, Ulrich 1997).

A basic concept for modelling physical systems is the concept of distribution of mass or of density. The mathematical concept of a measure describes this fact quite adequately (Anger 1990). In the 19th century, the general concept of measure was not yet known; one worked with the concept of density ρ, or of mass element ρdy, where dy is the volume element. In this form, the equations of mathematical physics may be found in textbooks. However, not all models relevant for application can be obtained using this restriction. Also, density distributions may be heterogeneous which is evident in the case of the Earth. Since the Earth does not have a smooth density structure, the use of ρdy is an idealization. In electrostatics, we have charges which are concentrated on the surface of the body.

The present concept of measure was introduced by the Austrian mathematician J. Radon in 1914, and G.C. Evans (1920–1936), H. Cartan in 1946 and G. Anger in 1958 used it for studying the gravitational and the electrostatic fields, applying the methods of modern mathematics. Without this general concept of measure a systematic study of inverse problems is impossible. The mathematical methods must fit the physical problems in a natural way (Anger 1990, Anger et al. 1993). Let us mention here that already in 1917, J. Radon has solved the problem of computed tomography as a geometric problem (Anger 1990, v. Wolfersdorf 1996). Both problems, the physical and the geometric, are mathematically equivalent.

As examples of (noninvasive) inverse problems we mention:

1. Determination of the mass density $\rho(y)$ of the Earth by measurements on the Earths surface (gravimetry, seismics).

2. Determination of the mass density $\rho(y)$ of the human body using absorption of (very many) X–rays (computed tomography). For technical reasons, this method can only be used in the laboratory.

3. Determination of electrical conductivity $\gamma(y)$ of the Earth or of the human body by measurements outside the body (impedance tomography, cf. Anger et al. 1993, Isakov 1998).

4. Determination of electrical parameters of the heart (ECG) or of the brain (EEG) by measurements outside the body (see Ulrich 1994).

5. Determination of the density of water (protons) in the human body using nuclear magnetic resonance tomography (cf. Anger 1997, Schempp 1998, Vlaadingerbroek and den Boer 1996).

Further examples of inverse problems may be found in (Anger 1990, Isakov 1998, Kirsch 1996, Lavrent'ev and Savel'ev 1995, Prilepko et al. 1999, Romanov and Kabanikhin 1994, Tanana 1997, Tikhonov et al. 1995 and 1998, Vasin and Ageev 1995).

A simple example for (1) is the linear equation system in the plane $\mathbf{R}^2$ with the coordinates f_1 and f_2:

$$\begin{aligned} a_{11}f_1 + a_{21}f_2 &= g_1 \\ a_{21}f_1 + a_{22}f_2 &= g_2 \end{aligned} \tag{3}$$

with the matrix A and $f = (f_1, f_2)$, $g = (g_1, g_2)$. If A and f are known, then $g = Af$ can always be computed from (3) in a unique way.

The determination of f if A and g are known is essentially different and more difficult. Each of the two equations of (3) defines a straight line in the plane. There are three possible types of solutions:

- The two straight lines of (3), given $g = (g_1, g_2)$, intersect at precisely one point $f = (f_1, f_2)$. Then (1) has exactly *one* solution.

- The second equation of (3) is identical to the first equation, i.e. $a_{11}f_1 + a_{12}f_2 = a_{21}f_1 + a_{22}f_2$, $g_1 = g_2$; then, because of underdetermination, (3) has *infinitely many* solutions (all points of the straight line).

- The equation system consists of two parallel straight lines, i.e., $a_{11}f_1 + a_{12}f_2 = a_{21}f_1 + a_{22}f_2$ and $g_1 \neq g_2$. In this case there is *no* solution of (3).

Similar considerations can be made in n–dimensional space $\mathbf{R}^n$ concerning linear or nonlinear systems of equations. In such relatively simple inverse problems, a certain plausible geometrical intuition is possible (algebraic surfaces of degree n, the structure of which is relatively well known). Regarding inverse problems for gravitational or electrodynamic fields, which require infinitely–dimensional function spaces, such plausibility considerations are hardly possible. The scientist must rely here completely on the formal mathematical apparatus and on the experiment. This may explain the relative unpopularity of inverse problems even with mathematicians and other scientists. An additional difficulty with inverse problems in mathematical physics is furthermore the fact that we must frequently rely on rather unprecise measurements. This occurs, for instance, in medical diagnostics, where the practical knowledge, experience and intuition of the medical doctor gives indispensable basic and additional information (praxis cum theoria).

The simplest example of a differential equation which must be studied in an infinitely–dimensional function space, is the ordinary differential equation

$$u' = f\,, \quad u(a) = 0\,, \quad f \quad \text{continuous}\,. \tag{4}$$

The solution of (4) is

$$u(x) = Af(x) = \int_a^x f(y)dy = \int \Theta(x-y)f(y)dy \tag{5}$$

where $\Theta(z) =$ for $z > 1$ and $\Theta(z) = 0$ for $z \leq 0$. For the study of problems of mathematical physics certain functional spaces are required, for instance the space $C(K)$, $K = [a, b]$ of functions continuous on K, with the norm

$$||f||_C = \max\{|f(x)|,\, x \in K\} \tag{6}$$

by which a concept of convergence is defined. Another example is the space $L^2(K)$ of functions square integrable on K, with the norm

$$||f||_{L^2} = \left(\int_K |f(x)|^2 dx\right)^{1/2} \quad . \tag{7}$$

This again defines a metric $d(f, g) = ||f - g||$ and hence a convergence concept.

The inverse $f = A^{-1}u$ of (5) has the form

$$A^{-1}u = u' \quad . \tag{8}$$

The assignment $u \to A^{-1} = u'$ is a discontinuous operation in the spaces $C(K)$ or $L^2(K)$, an *ill–posed problem*, which makes the numerical treatment rather more difficult (Anger 1990). In order to demonstrate the discontinuity of $u \to u'$ one uses the following counterexample:

$$u_k(x) = \frac{1}{\sqrt{k}} \sin kx \to A^{-1}u_k = u_k^{'}(x) = \sqrt{k} \cos kx \tag{9}$$

which tends to infinity as $k \to \infty$.

Many problems (1) have the implicit form

$$Af(x) = \int_a^b G(x, y) f(y) dy \tag{10}$$

with known kernel $G(x, y)$; this is an inverse problem of the first kind. The integral (10) may be considered as a kind of "averaging over atomic structures". This frequently gives good mathematical properties of A. However, what we really need is $f = A^{-1}g$, the inverse problem. We can measure values of g at finitely many points $x_1, x_2, \ldots, x_N$ only. The discretization of (10) has the form

$$A_n f(x_k) = \sum_{j=1}^{n} G(x_k, y_j) f(y_j) = g_k \,, \quad k = 1, \ldots, N \quad . \tag{11}$$

It is very simple to show by 19th century mathematics that the system (11) at best determines f only at the points x_k. Hence there follow so–called "ghost–images" (phantom images, artifacts). In fact, let ϕ be a continuous function defined on K for which

$$\phi(y_1) = \phi(y_2) = \ldots = \phi(y_n) = 0 \quad . \tag{12}$$

Then in (11) we have

$$A_n(f + \phi) = A_n(f) \quad , \tag{13}$$

which means that the function $f + \phi$ is also a solution of the discretized equation (11). Hence infinitely many functions $f + \phi$ satisfy the system (11). A finite set of points has the dimension zero. Thus, in inverse problems of form (11) we wish to draw conclusions regarding a continuous function (on the space $\mathbf{R}^n$) from a set of dimension 0, which is impossible without essential additional conditions. Such a condition might have the form $|f^{''}(x)| \leq H$.

Since inverse problems are frequently underdetermined in a mathematical sense, such additional conditions play an essential role (Anger 1990, Hofmann 1999, Vasin and

Ageev 1995). Phantom images exist in all inverse problems in which an equation of form (10) is to be solved for f. These simple fact should be familiar to students already at the very first university year.

One of the first inverse problems of mathematical physics was solved by N. H. Abel in 1823. It consists in determining the shape of a hill from travel time (Anger 1990) and is reduced to an (Abel) integral equation of the first kind ($\alpha = 1/2$)

$$\int_a^\eta (\eta - \xi)^{\alpha-1} f(\xi)\, d\xi = g(\eta),\ (\xi, \eta) \in [a, b],\ 0 < \alpha < 1. \tag{14}$$

Its solution is given by

$$f(\xi) = \frac{\sin\pi\alpha}{\pi} \frac{\mathrm{d}}{\mathrm{d}\xi} \int_a^\xi (\xi - \eta)^{-\alpha} g(\eta)\, d\eta. \tag{15}$$

From this relation it follows that, if a and $g(a)$ are finite and g' exists,

$$f(\xi) = \frac{\sin\pi\alpha}{\pi} [g(a)(\xi - a)^{-\alpha} + \int_a^\xi (\xi - \eta)^{-\alpha} g'(\eta)\, d\eta]. \tag{16}$$

Since the right-hand side contains a derivative, the solution $f = A^{-1}g$ depends discontinuously on g relative to the norm of $L^1([a, b])$.

If the kernel G in (10) is quadratically integrable, i.e., $G \in L^2([a, b] \times [a, b])$, then the mapping A has very good mathematcial properties. It maps any bounded set $\{f : \|f\|_{L^2} \leq M\}$ into a relatively compact set. This means that any sequence $\{Af_j\}$ contains a subsequence $\{Af_{j_k}\}$ converging to a solution $Af_{j_k} \to g$. Such a mapping $A : X \to Y$ is called a compact mapping. This is the basis for the well known Fredholm-Riesz-Schauder theory (1900 - 1930) relative to equations of the second kind

$$Af + \lambda f = g. \tag{17}$$

For such equations a complete theory exists (Lavrent'ev and Savel'ev 1995). Most results of mathematical physics are results relative to equations of the second kind. But equations of the first kind were not studied extensively, since the inverse $f = A^{-1}g$ of an equation of the first kind $Af = g$, A a compact one-to-one mapping on infinite dimensional spaces, is discontiuous (F. Riesz 1918).

In the case of a discontiuous operator A^{-1} one has to replace A by a family of operators B_α for which the inverses B_α^{-1} are continuous (Anger 1990, Hofmann 1999, Isakov 1998, Kirsch 1997, Lavrent'ev and Savel'ev 1995, Tanana 1997, Tikhonov et al. 1995 and 1998). Then one has to consider the limit of $f_\alpha = B_\alpha^{-1}u$ for $\alpha \to 0$ and to determine a solution which is of interest in applications. This method is called *regularization*, well known for linear equations on $\boldsymbol{R^n}$. Following A. G. Yagola (lecture held at the Weierstrass Institute for Applied Analysis and Stochastics in Berlin in 1999) there exist equations of the first kind for which a regularization is not possible.

One possibilty to regularize an equation of the first kind $Af = g$ is to replace this equation by an equation of the second kind $Af + \alpha f = u$, A a compact operator (Lavrent'ev and Savel'ev 1995). The simplest differential equation on the real line is equation (4) with its solution (5). The inverse $f = A^{-1}u = u'$ is a discontinuous mapping. Let

$$B_\alpha f_\alpha = Af_\alpha + \alpha f_\alpha = (A + \alpha I)f_\alpha = u. \tag{18}$$

Differentiating (18) we get $f_\alpha + \alpha f_\alpha^{'} = u'$. Its solution is

$$f_\alpha = c_o \exp(-\frac{x}{\alpha}) + \int_a^x \frac{u'(y)}{\alpha} \exp(-\frac{x-y}{\alpha})\, dy, \tag{19}$$

which tends to $u'(x)$ for $x > 0$ and $\alpha \to 0$. If $c_o = 0$ the right-hand side of (19) is equal to

$$\frac{u(y)}{\alpha} \exp(-\frac{x-y}{\alpha})\Big|_a^x - \int_a^x \frac{u(y)}{\alpha^2} \exp(-\frac{x-y}{\alpha})\, dy, \tag{20}$$

i.e., the solution of the regularized equation depends continuously on the norm of $C(K)$ and tends to $u'(x)$ for $\alpha \to 0$.

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