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Convenience experimentation

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ABSTRACT

Systems biology aims at explaining life processes by means of detailed models of molecular networks, mainly on the whole-cell scale. The whole cell perspective distinguishes the new field of systems biology from earlier approaches within molecular cell biology. The shift was made possible by the high throughput methods that were developed for gathering 'omic' (genomic, proteomic, etc.) data. These new techniques are made commercially available as semi-automatic analytic equipment, ready-made analytic kits and probe arrays. There is a whole industry of supplies for what may be called *convenience experimentation*.

My paper inquires some epistemic consequences of strong reliance on convenience experimentation in systems biology. In times when experimentation was automated to a lesser degree, modeling and in part even experimentation could be understood fairly well as either being driven by hypotheses, and thus proceed by the testing of hypothesis, or as being performed in an exploratory mode, intended to sharpen concepts or initially vague phenomena. In systems biology, the situation is dramatically different. Data collection became so easy (though not cheap) that experimentation is, to a high degree, driven by convenience equipment, and model building is driven by the vast amount of data that is produced by convenience experimentation. This results in a shift in the mode of science. The paper shows that convenience driven science is not primarily hypothesis-testing, nor is it in an exploratory mode. It rather proceeds in a gathering mode. This shift demands another shift in the mode of evaluation, which now becomes an exploratory endeavor, in response to the superabundance of gathered data.

1. Introduction: Convenience experimentation

In the beginning of systems biological experimentation there was genomics. The projects of sequencing the human genome[1] were based on the hypothesis that detailed and complete knowledge of the genetic material could be related to knowledge about diseases of different classes, and would therefore allow for designing drugs against these diseases ("from genes to drugs"). The falsification of this hypothesis required the most expensive research program biology had ever seen. An alternative would have been to ask more independent biologists and perhaps even philosophers of biology[2] whether the hypothesis is worth testing—but the decision for the human genome project was a political one. And indeed, prevention of the Large Data Collection project of genomics would have prevented other results that were achieved along its way, since the project had important consequences besides genomic sequences and insights into their uselessness. Those were mainly on the methodological side. The project led to the development of high throughput data-acquisition methods and sophisticated data mining techniques. Once developed and since then continuously refined, these methods did not only enable large scale sequencing, but also made stock-taking of all kinds of cellular components and their interactions into almost fully automated and highly convenient procedures.

High throughput methods were further developed into some of the most valuable tools for systems biology. One branch of systems biology, namely the top-down approach, relies heavily on these methods (Krohs & Callebaut, 2007). While many groups apply high throughput methods for doing wonderful and sophisticated cutting

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[1] International Human Genome Sequencing Consortium (2001), Venter et al. (2001).

[2] Philosophers of biology by then, however, were mainly focussing on evolutionary theory, hardly acknowledging that physiology and experimental biology are not only reputable fields of biology, but also important for an adequate philosophical understanding of biology. An early insightful philosophical account of the genome project was given by Ankeny (2001).

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edge research, it is also possible—and obviously tempting—to buy the equipment and ready-made analysis kits, including microarray probes (so called 'gene chips'), in order to produce lots of publishable data without much effort. Equipment and money replace experimental skills and invested time. However, the obtained data are indeed valuable, and without this equipment it would not be possible to obtain them at all. This does not disavow those prerecorded data sets. Quantity sometimes results in a qualitative leap, so omic data often become extremely useful in some later context of evaluation by data mining techniques. I simply want to stress that many experiments are done, or at least: done in the way they are actually done, because they are so extraordinarily convenient to perform. This characteristic is not completely new with systems biological experimentation. High throughput experimentation is only the latest development of the "kittification" of biochemistry. Many experimental procedures are standardized and based on kits that are supplied by the industry. There are PCR kits, mutagenesis kits, gene knockout kits, expression kits—not even to speak about analytic and diagnostic kits in biomedicine.[3] Running experiments along the preconditioned lines of standardized kits became an important methodology, which I call *convenience experimentation*.[4] Convenience experimentation in omic disciplines banks on equipment for high throughput automated target preparation as well as on automated high throughput data acquisition.[5]

On the one hand, convenience experimentation is extremely helpful in many fields of research and opens up experimental opportunities that would otherwise not be available. It is thus an important driving force of modern bio-scientific research, essential for many cutting edge projects. On the other hand, it strongly channels research. The sorts of experimental results which are at all achievable are determined to a large extent by the sort of available convenient equipment. Even more formidable, convenience experimentation also drives dramatic changes in biological theorizing. While many changes in experimentation are by and large intended, the changes in theorizing follow in a clandestine manner.

Such clandestine effects of convenience experimentation on model building in systems biology are the subject of this paper. I shall argue for the thesis that convenience experimentation does not only reflect a shift in the mode of experimentation, but also on model building in top-down systems biology.

I am first characterizing the roles of hypotheses and data in classical metabolic pathway analysis and in top-down systems biology, both in experimentation and in modeling (section 2). Then, I am inquiring how convenience experimentation shifts the mode of science, both on the experimental side and on the side of model building (section 3). Then I follow some considerations about convenience experimentation and research politics (section 4), and present a short conclusion (section 5).

2. Hypotheses and data now and then

Hypotheses play various roles in scientific practice and theorizing. The relevance of each of those roles, however, may on the one hand change, and, on the other hand, be judged differently from different philosophical perspectives. This is well known from their role in experimentation. The classical picture of scientific experimentation, from Bacon (Novum Organon) to Popper (1935) and even to Lakatos (1978), was that its basic role in the research process was to test hypotheses. Meanwhile, the status of hypotheses was relativized. We have learned that experimentation is itself theory laden (Kuhn, 1963). Experimentation is now regarded as an epistemic process in its own right and with its own dynamics (Hacking, 1983).[6] Experimentation is multiply entangled with theorizing and instrument making (Galison, 1997) and able to reshape central concepts of a field (Shapin & Schaffer, 1985; Chang, 2004). All these well-justified relativizations need not result in a denial of some relevance of hypotheses in experimentation. They do result, however, in a denial of the claim that science is necessarily hypothesis driven. Consequently, we are ready to investigate other modes of experimentation and regard the searching mode of exploratory experimentation (Burian, 1997; Steinle, 1997) and data driven research (Leonelli, this volume) as serious epistemic strategies, besides, and in combination with, hypothesis driven research.

As just shown with regard to experimentation, hypotheses also play a role in model building. Here as well, a change in the validation of hypothesis-drivenness may be stated, though this is made explicit less often than in the case of experimentation. That the driving forces of modeling are similar to, but somehow independent from, the driving factors of experimentation may become clear in the case of data driven research. Data-drivenness holds for modeling on the basis of superabundant data independent of the data drivenness of experimentation itself. So, besides the mode of experimentation, I am interested in the consequences of a substitution of hypotheses by data sets as the driving agents in model building, where models are understood as theory- and data-related theoretical epistemic tools that help in explaining phenomena by conceptual and formal—typically mathematical—means (Morgan & Morrison, 1999).

Let me compare the role of hypotheses and of data sets in two different research programs that aim at explaining metabolic networks. The first is the classical case of Metabolic Pathway Analysis (MPA), the second is top-down Systems Biology (tSB). Hypotheses and data sets play crucial, but considerably different roles in both cases.

2.1. The classical case: Metabolic Pathway Analysis

MPA regards metabolic networks as being made up from more or less isolable pathways. Those may be classified as anabolic and catabolic pathways, redox pathways, signaling pathways etc. Pathways are characterized by their characteristic metabolites, rate-limiting steps, type of regulation (e.g., feed-back and feed-forward control), by being linear or circular, etc. Regulation and other biological functions are regarded as being localized at specific steps. Regulation of a pathway may, e.g., be modeled as being brought about by a particular regulatory enzyme. If metabolites or enzymes are shared with other pathways, this is regarded as a case of cross-talk between the pathways, which is usually taken to be more or less negligible. Alternatively, a shared metabolite may be counted as forming a pool so that the concentration remains unaffected by each single metabolic pathway in which it is engaged. (For this classical picture, c.f. any classical textbook of biochemistry, e.g., Berg et al., 2007).

Besides investigating the structure of the pathways, MPA is interested very much in their regulatory and kinetic properties. The aim is to model the dynamic of a pathway quantitatively. Only this is regarded as providing a satisfying explanation (or even an adequate understanding) of the regulation of the pathway. Building such models requires the measurement of changes of metabolite concentrations and the characterization of the enzymes involved. This means that the kinetic constants of the enzymes are to be determined (i.e., Michaelis constant and V_{max}), as are regulatory mechanisms (if any) and regulatory constants.

[3] Kits and equipment are often called 'systems' (cf. www.sigmaaldrich.com).
[4] The situation resembles industrial prefabrication of meals, *convenience food*, which simplifies home cooking—and standardizes its outcome.
[5] ww.w.beckmanncoulter.com; www.affymetrix.com.
[6] Besides experimental success, experimental error also plays an important epistemic role in this process (e.g., Hon et al., 2009).

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Experiments within the framework of MPA are driven by hypothesis about the sort of substrate binding, intermediate steps, co-operative effects, etc. and, with respect to regulatory mechanisms, about mechanisms of allosteric effects, about competitive, non-competitive, un-competitive inhibition etc. So data are gathered according to hypotheses about the kinetics of the steps involved. Modeling of the pathways is *a fortiori* driven—at least indirectly—by the hypotheses on which conduction and evaluation of the experiments was based.

I propose regarding those particular hypotheses which lead experimentation on and modeling of metabolic pathways as specializations of the following general one:

(EHL) The general explanatory hypothesis of localization:

Biosynthesis and breakdown of all those metabolites which do not enter and leave the organism unaltered can be explained by sequences of enzymatic steps, which may loop, branch, or combine, but where each reaction has an identifiable, more or less stable role within the pathway. Regulatory functions are localized at these steps.

While the role of the general hypothesis is to guide MPA as a field, any model within MPA is based upon particular hypotheses about the regulatory mechanisms and enzymatic parameters of the enzymes involved, and on hypotheses about the kinetic order and the sequence of the involved steps.[7] An example for the reconstruction of a metabolic pathway in terms of a linear sequence with distinct regulatory steps is the Embden-Meyerhof-Parnas-pathway of glycolysis (Voet & Voet, 2004; Berg et al., 2007). The ten step sequence of the conversion of glucose into pyruvate is modeled as being regulated at three steps, namely at the enzymes hexokinase, phosphofructokinase, and pyruvate kinase. This model is based on (EHL) in so far as the regulatory properties of each enzyme are investigated in isolation and that the particular findings are integrated in the explanatory kinetic model of the pathway as a whole. Data on the overall reaction play a minor role in modeling, though this role is important, namely in checking the adequacy of the model. Crucial to modeling, however, is (EHL), the hypothesis of localized functions. Hundreds of similar cases can be found in textbooks and research literature from MPA. Among the well known examples are the citric acid cycle, beta-oxidation of fatty acids, signaling pathways, the respiratory chain, and light reactions and dark reactions of photosynthesis.

2.2. The case of top-down Systems Biology

Let me now consider the case of top-down Systems Biology (tSB). tSB investigates the genome, proteome, interactome, metabolome etc. on a whole cell scale. In contrast to the omic disciplines, it aims not only at a static picture, but at an understanding of cellular dynamics. To achieve this, it analyzes the activation pattern of, e.g., all genes of the whole cell. Each whole cell measurement yields a snapshot of the state of the cell. Primary results, besides sequences, are maps of the presence or absence of components and metabolites from the cell at a certain state. Sometimes, rough estimates of the concentration of metabolites can be achieved (which are nevertheless disregarded in most top-down models). Interactions between components of the network may also be analyzed. Data on those are often central to the model that is built to reconstruct the cellular network. However, tSB does not aim at characterizing isolated enzymes and measuring precisely metabolite kinetics. Enzymes are just regarded as nodes of the network.

Though tSB can justifiably be classified as being data driven (Leonelli, this volume), we find—of course—also hypotheses in this field. Besides the background assumptions mentioned in footnote 7, which are by and large shared between MPA and tSB, the following general hypothesis, which is incompatible with (EHL) and thus with MPA, seems to play a crucial role in tSB:

(EHD) The general explanatory hypothesis of delocalization:

Metabolic capacities of the cell are brought about by metabolic networks. Single reactions or enzymes do not have identifiable, stable regulatory roles. Regulatory functions are delocalized dispositions of the network.

Taking (EHD) serious, it makes neither much sense within the framework of tSB to look for regulatory properties of isolated enzymes, nor to delineate "minimal" metabolic pathways, as MPA often does.

(EHD) is not usually subjected to experimental testing and the contrary would not be a very plausible project. As I have shown elsewhere, the kind of data sets used in tSB has lead to this change in modeling strategies as compared with MPA and consequently to a change in the epistemic goals that can be followed (Krohs, 2010). Specifically, within the framework of MPA, researchers aim at kinetic models that explain the dynamic properties of metabolism. Such models allow for mechanistic explanation of cell physiology, i.e., they explain how biological functions on the cellular and subcellular level are physically brought about—realized—by molecular processes (Machamer et al., 2000; Darden & Craver, 2002; Krohs, 2004; Bechtel & Abrahamsen, 2005). tSB, on the other hand, aims at discrete models, like Boolean networks. Those models do not predict cellular dynamics, but rather cellular statics, namely metastable states. A network model enables gaining knowledge about the principle possibilities of the modeled network: it may be used to answer questions for the maximum number of stable states or sta-

[7] In addition, a set of background hypotheses is invested in metabolic pathway analysis, which may at some point be challenged but which are not usually put to test. Prominent are the following:

–The 'Central Dogma' of molecular biology.

–ATP is the convertible source of chemical energy.

–pH and other ion gradients serve as chemi-osmotic energy sources.

–Exchange of redox-equivalents proceeds via the $NADP^+$/NADPH + H^+ and NAD^+/NADH+ H^+ -Systems.

–Transfer of acetyl-groups is performed via pooled CoA.

–Other coenzymes fulfill also specific roles (e.g., transfer of Methyl-Groups by cobalamin).I will not deal here with these background hypotheses, but merely want to point out that they may also be found (perhaps with the exception of the Central Dogma) in systems biology.

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ble cycles of states of the respective network (Chavez, 2005; Albert, 2005). This is important, e.g., for explaining cell differentiation and also for understanding switching between different metabolic states. It is, however, much less adequate than results from kinetic models in explaining "smooth" transition between stable states or accounting for fine tuning of metabolic flows.

In tSB, regulatory properties cannot turn out other that delocalized. A single node in a Boolean network can, for structural reasons, not be a locus of regulation. Regulation in Boolean networks requires a motif of a certain complexity, i.e., the interaction of several nodes. Therefore, no experimental setting and no particular model within tSB can ever challenge (EHD). At best, one could say that (EHD) is put to test by top-down SB as a field of research: if the field failed in general to meet expectations in its explanatory power, the hypothesis would probably be given up. The hypothesis instructs modeling insofar as it demands modeling networks rather than pathways. However, particular hypotheses derived from (EHD) would be testable, provided they are put to test in an adequate way. Such hypotheses would claim the non-locality of some regulatory property—which could only fail when tested by experiments and models that allow addressing (i) kinetic constants of enzymes, (ii) the particular mode of inhibition/activation or (iii) co-operative effects. In other words: in order to test particular hypotheses about the delocalization of functions, models are needed that include those parameters on which pathway models are based. But these parameters cannot be extracted from the data gathered by the high-throughput methods of tSB. Their resolution is far too low for in principle reasons: the arrays used in convenient experimentation yield yes/no-results only. No fast kinetic can be extracted from the data and there is no possibility to systematically change concentrations of single metabolites. In other words: MPA models, but not tSB models may challenge (EHD).

The data sets produced by tSB represent the state of the cell as a collection of interacting components that are in either or two states: on or off, present or absent, active or inactive. So the data demand a model that reduces the state of the cell to a network with nodes that can assume exactly two states. This reductive demand is independent of (EHD), though necessarily compatible with it. It excludes (EHD) and (EHL) as well as any hypothesis derived from one of these hypotheses from being affected by empirical data gathered with the convenience methods of tSB. Consequently, experimenting and modeling in tSB is not driven by particular hypotheses. It might or might not be exploratory, an issue which is taken up in the next section.

3. Convenience, the gathering mode of experimentation, and exploration

So far we have seen which role some general explanatory hypotheses (EHL) and (EHD) may play in experimentation and model building within MPA and tSB. We have also seen that experimentation, though partly hypothesis based, is not always hypothesis testing. To a large amount it is exploratory; it is not obvious in advance how results might be conceptualized or which of the particular hypotheses might afterwards be regarded as being tested by an experiment (or by a series of experiments) (Kell & Oliver, 2004; Kelder et al., 2010). Superficially regarded, the exploratory character seems to be most obvious in tSB. In this field, enormous amounts of data are collected, made available to the community, and analyzed independent from experimentation by means of data mining techniques (Leonelli, this volume). However, while modeling in tSB is certainly data-driven, this does not necessarily mean that experimentation is in general exploratory. This was certainly the case during the times when theoretical treatment of omic data was limited to mere depiction (e.g., Kitano, 2002). But is it still mere depiction, even after sophisticated data mining and evaluation techniques are regularly applied? Given the extremely high and exponentially growing number of publications in the field of systems biology, nobody will be able to answer the quantitative question.[8] What I undertake instead is looking for possible effects of the ubiquitous application of convenience experimentation on the supposedly exploratory character of experimentation and model building in tSB.

In order to do so, I need to characterize exploratory experimentation in a new way. I regard exploratory experimentation within(!) an existing research program as an experimental attempt to find results that satisfy the general explanatory hypothesis of the program, and at the same time further specify the particular hypotheses that depend on it. This can be spelled out as research being based on methodological hypothesis in the following way. While a research program can be characterized by general *explanatory* hypotheses, as in section 2, exploratory experimentation *within* the research program can be characterized by *methodological* hypotheses.

As an example, we may look at MPA. MPA in its exploratory mode, which clearly exists besides its hypothesis testing mode, can be characterized by the following methodological hypothesis:

(MHL) The general methodological hypothesis of localization:

Any case of pathway regulation either matches the known kinds of enzymatic regulation (e.g., competitive, uncompetitive, non-competitive inhibition), or can eventually be explained by formulating a new kind of localized regulation.

(MHL) sets the reference for the interpretation of any exploratory experiment performed within the framework of MPA. It can thus be said to characterize the exploratory mode of MPA.

The methodological hypothesis leaves room for playing with its status. Elevating (MHL) into the rank of a principle of research would immunize MPA against challenges by, e.g., tSB, demanding to look in any case for localized regulation until it is found. Nevertheless, (MHL) as it stands might be challenged by data that resist explanation in terms of localized regulation.

But notice that something different results from a parallel methodological hypothesis for tSB:

(MHD) The general methodological hypothesis of delocalization:

Any case of metabolic regulation either matches the known motifs of delocalized regulation or can eventually be explained by the dynamics of yet unknown motifs of a discrete network.

Though (MHD) is construed analogously to (MHL), it is not merely a methodological principle that might be frustrated in application to data generated within the field of tSB, and that could be strengthened further by elevating it into the rank of a methodological principle. Insofar as tSB depends on convenient experimentation, (MHD) already has the status of a principle: It can neither be challenged by any data gathered with the methods of the field because convenience methodology as it is de facto available cannot produce any other data than what satisfies the preconception of delocalized functionality. A set of binary data on presence/absence or activity/inactivity of the nodes of a Boolean

[8] During the phase of exponential growth of publication number, a serious answer could only be based on a system of tagging the papers routinely during the process of publication—which is not present practice.

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network does not allow for any modeling of regulation other than by motifs within the network, i.e., by subnetworks. Regulation thus is necessarily delocalized in any model based on the data sets gathered by the methods of convenience experimentation presently available for research in tSB. The data are simply not of a sort that would allow for any deviating outcome. Consequently, (MHD) could not be strengthened in order to further immunize the field. As long as tSB is committed to the available methods of convenience experimentation, (MHD) has already the status of a principle of research. There is no room left for exploring whether and how data match the hypothesis. Thus, convenient experimentation in tSB hardly leaves room for exploratory experimentation. It channels experiments in a way that the gathered data necessarily satisfy the methodological hypothesis. Convenience equipment in its standard use is kind of a materialized commitment to delocalization. It only allows for gathering data that match the demands of the program.

Despite this diagnosis, I am not at all claiming that convenience experimentation *might* not perfectly well be used in hypothesis driven and in exploratory research. Moreover, I am not denying that different modes of experimentation will often be entangled. My point in this regard is merely that de facto, convenience experimentation in tSB is most often used to design and run experiments that avoid epistemic risk and that are, for methodological reasons, not appropriate to challenge or refine the general methodological hypothesis of the field. Convenience experimentation has significant seductive power to switch experimentation to its gathering mode. Where data rather than, e.g., models are the result a project aims at, experimentation may help in exploring the range of possible applications of the method. It hardly helps in exploring conceptual fields or unexpected phenomena. Exploration is a matter of allowing for the unknown, learning from error, and being ready to change perspective. Convenience experimentation in tSB fosters none of these epistemic attitudes.

Elliott (2007), to the contrary, counts "collecting and analyzing large swaths of data using new experimental strategies" among exploratory experimentation. Rightly so, but only in one of the conjuncts he addresses. The criterion of new strategies is not per se fulfilled by convenience experimentation. Though the techniques are historically recent, the very idea of convenience experimentation is to transform research technology from a novelty into a standard method as quick as possible. Data collection by these methods consequently is all but exploratory. Relevant with regard to exploration, in contrast, seems Elliott's reference to data analysis. I agree that, when data mining is taken into consideration, convenience experimentation-*based* research becomes exploratory. But, in fact, data mining in tSB is disjunct from data collection, and data gathering is independent from data mining. Convenience experimentation keeps science in the gathering mode. Blended modes, however, are occurring, where the exploratory character is owed to data mining projects operating on the convenience-generated data. One might thus say that the exploratory character is brought into gathering mode experiments retrospectively, when bioinformaticians are looking in the data for phenomena that the data might be taken to explore.

We might see this in parallel to the case of bringing hypotheses into exploratory research retrospectively during the phase in which researchers try to make sense of the results of an exploratory experiment (Kelder et al., 2010). But notice, introducing post hoc a hypothesis does not transform exploratory experimentation into a hypothesis driven procedure. Neither does post hoc exploration of data transform the process of data collection into an exploratory endeavor. Though data collection and analysis are, even in tSB, often entangled, such a view blurs a useful conceptual difference. Convenience experimentation in tSB does not foster exploratory experimentation. It keeps the field in the gathering mode.[9]

4. Convenience experimentation and research politics

As I have stated in the introduction, in convenience experimentation many experiments are done in the way they are actually done for the reason that they are so extraordinarily convenient to perform. Since convenience equipment and supply is all but cheap, we may well regard this as a replacement of experimental skills—in the sense of manual skills—by money. One might be tempted to regard it also as the replacement of brain power by money. This, however, would be an unfair way of looking at it. Current research politics demands that brain power is invested mainly in pre-experimental stages of a project. Though the rhetoric of funding agencies stresses hypothesis testing as the silver bullet of scientific—or of grant proposal—success (O'Malley et al., 2009), the scientific community often interprets the agencies as looking for hypothesis confirmation rather than for open research questions. Already at the stage of fundraising the tentative results are described in great detail. One viable approach to match the felt demands is running projects with in principle predictable outcome, where only steps with low epistemic risk are left over for the implementation phase of a project. Convenience experimentation provides low risk epistemic procedures. If, now, experimentation is run at low epistemic risk, it exemplifies neither the hypothesis testing nor the exploratory mode—granted there are some exceptions. (i) It can not usually be in the hypothesis testing mode because uncertainty about the outcome is minimized rather than the very reason for performing the research. (ii) It can also not usually be in the exploratory mode because this would require openness of the result on an even more fundamental level, namely uncertainty about the conceptual framing of the experiment, its relevance, or even about the very phenomenon to be investigated (Elliott, 2007). On my account as given in the last section, it would require tSB to refrain from (MCD), i.e., running different kinds of experiments. This may of course be done and is certainly done within systems biology, but it requires taking epistemic risks and using custom-made experimental equipment. Convenience experimentation does not easily allow for any of those. Consequently, convenience experimentation as well as present funding policy does not usually foster experimentation in an exploratory mode.

5. Conclusion

Convenience experimentation in tSB results in a restriction to particular kinds of data and demands for novel modeling strategies. The resulting models differ in kind and epistemic role from models known from MPA. Data and new strategies favor discrete models over continuous kinetic models. At the same time, convenience methods shift the mode of scientific practice from hypothesis-testing or exploratory experimentation into a data gathering mode. Convenience experimentation shifts the epistemic endeavor into the lab-mediated description of the molecular makeup of biological systems. This development is indirectly supported by present research policies. The exploratory mode returns secondarily, via projects that try to make physiological sense out of the data by data mining techniques. It is an open question whether and

[9] The gathering mode of experimentation is closely related to descriptive science (c.f. Müller-Wille & Charmantier, this volume): Gathering mode experiments themselves yield basically descriptions of biological entities on the molecular level. The descriptions are based on observations that are indirect to a high degree. We may call them "experimental descriptions", where "experimental" has a wider meaning than in exploratory experimentation or in hypothesis-driven experimentation: it does no longer mean that something is tried out, but simply means "equipment-mediated" or "laboratory mediated".

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how far experimentation itself can regain its modes of exploration and hypothesis testing.

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