

Article

Development, Uptake, and Wider Applicability of the Yo-yo Strategy in Biology Education Research: A Reappraisal

Marie-Christine P.J. Knippels * and Arend Jan Waarlo

Freudenthal Institute, Utrecht University, 3584 CC Utrecht, The Netherlands; a.j.waarlo@uu.nl

* Correspondence: m.c.p.j.knippels@uu.nl; Tel.: +31-302-532-213

Received: 16 July 2018; Accepted: 21 August 2018; Published: 24 August 2018



Abstract: Heredity is a biological phenomenon that manifests itself on different levels of biological organization. The yo-yo learning and teaching strategy, which draws on the hierarchy of life, has been developed to tackle the macro-micro problem and to foster coherent understanding of genetic phenomena. Its wider applicability was suggested and since then yo-yo learning seems to be noticed in the biology education research community. The aim of this paper is to reappraise yo-yo thinking in biology education research based on its uptake and any well-considered adaptations by other researchers in the past fifteen years. Based on a literature search we identified research that explicitly and substantially build on the characteristics of yo-yo thinking. Seven questions guided the analysis of chosen cases focussing on how key concepts are matched to levels of biological organization, interrelated, and embedded in a pattern of explanatory reasoning. The analysis revealed that yo-yo thinking as a heuristic of systems thinking has been an inspiring idea to promote coherent conceptual understanding of various biological phenomena. Although, selective use has been made of the yo-yo strategy, the strategy was also further elaborated to include the molecular level. Its functioning as a meta-cognitive tool requires more specification, and teachers' perceptions and experiences regarding yo-yo thinking should be addressed in future studies.

Keywords: systems thinking; levels of biological organization; genetics; conceptual coherence; explanatory reasoning; yo-yo learning; metacognition

1. Introduction

Biology covers a broad range of subjects and concepts from ecology and evolution to cell biology and genetics. The life sciences, biology included, are rapidly developing and new insights, such as from synthetic biology, molecular genetics, and epigenetics constantly inform the updating of the school biology curriculum. The 'hierarchy of life' is a fundamental concept in biology, and biologists are used to thinking within and between levels of biological organizations. Developing coherent conceptual understanding of the diverse biological phenomena and processes, and integrating knowledge across different levels of biological organization is challenging for school students (e.g., [1–4]). To support students' learning from a systems perspective, the different levels of biological organization should be explicitly taught and the conceptual relations within and between these levels should be elaborated [5,6]. An example of the way biological phenomena and processes on different levels of biological organization (e.g., molecule, cell, organ, organism, and population) can be linked, explained, and embedded in a reasoning pattern is sickle cell anaemia. Symptoms of this disease at the *organism* level can be explained by deviating red blood *cells*, which cause problems with the blood flow (*organ* level). The sickle shape of the red blood cells is connected with a change in the three-dimensional structure of the protein haemoglobin (*molecular* level) caused by a point mutation in the DNA that leads

to a different amino acid (*molecular level*). On the *population level*, sickle cell anaemia heterozygosity is related with protection against malaria. So in order to fully understand this genetic disorder one should be able to interconnect phenomena and concepts on the different levels of biological organization and use different corresponding vocabulary per level of biological organization. Thinking to-and-fro between the levels of biological organization is part of systems thinking in biology and of biological reasoning [5,7,8]. Building on this idea, the so-called yo-yo learning and teaching strategy was developed to cope with the abstract and complex nature of genetics in schools [5]. Explicitly asking questions about hereditary phenomena on different levels of biological organization is an important characteristic. The questioning should start on the concrete level of the organism that students are familiar with (e.g., their family: what makes you look like your parents, without being identical to them?) and gradually descending to the cellular level, or ascending to the population level. After every change of level students monitor the progress of their conceptual understanding of genetic processes by returning to the overarching starting question, reflecting on the answer so far and by formulating a new partial question that needs to be answered next in order to come to a full understanding of the studied phenomenon. The levels of biological organization are characterised by different key concepts and terminology related to the biological process under study. Actually yo-yo thinking means reframing biological phenomena and processes over and over again on different levels of organization, using and integrating different key concepts and terminology per level, and constructing a cross-cutting narrative.

The studied yo-yo learning and teaching strategy for genetics resulted in a formal proposal for yo-yo learning to be applied to other biological subjects. All of this has been published as a PhD study available through the Utrecht University Repository [5] and referred to in biology education research and teacher education, as well as in biology teaching methodology books (e.g., [9–12]).

The aim of this paper is to reappraise yo-yo thinking in biology education research based on its uptake and any well-considered adaptations in the research community. So the research question is: How fruitful has yo-yo learning been in biology education research over the past 15 years? We will first describe in what educational problem context yo-yo thinking was developed, tested, and justified originally. Then we will analyse how yo-yo thinking has been interpreted, applied, criticised and/or adapted by others, by studying selected cases. We conclude with an overview of its strong and weak points and suggestions for exploiting its potential in (research on) teaching and learning biology.

2. Context in Which Yo-yo Thinking was Developed, Justified, and Tested Originally

Yo-yo thinking was developed originally in the domain of Mendelian genetics. Multiple studies reported on learning difficulties students encountered with this specific biology school topic [7]. In the context of a PhD study these difficulties were explored further and a possible way to handle these problems was developed and studied through an educational design research [5].

2.1. Learning Difficulties in Classical Genetics

First, the main educational difficulties with classical genetics were identified by means of a literature study, focus group interviews with Dutch biology teachers, content analysis of school genetics, and a case study of a traditional series of 13 genetics lessons in school. The domain-specific key difficulties in genetics education revealed to be the complex and abstract nature of (school) genetics [7]. The complex nature of genetics refers to the manifestation of heredity phenomena on different levels of biological organization, and to the use of different corresponding vocabularies. Neglecting to interrelate the molecular, cellular, organism, and population aspects causes learning difficulties, because relevant structures and processes differ per level. Biologists, including biology teachers and schoolbook authors, often implicitly change levels of biological organization when explaining a biological topic. Dealing with the curriculum topics heredity, reproduction, and meiosis in an isolated way and at different times seems to be responsible for the abstract nature of the subject.

Students have poor understanding of the genetic relationships due to misunderstandings about the process of meiosis and the underlying chromosome behaviour [13–15].

The identified abstract and complex nature of school genetics indicated that genetics teaching should focus on interconnecting heredity, sexual reproduction, and meiosis from a systems perspective, and on interrelating the key concepts associated with the involved levels of biological organization. To specify this four educational design criteria were formulated:

1. To adequately sequence the subject matter, genetics education should start on the phenomenal level of the organism that students are familiar with, i.e., their family, and should gradually descend to the cellular level. However, consistent references between the different levels of biological organization should be included;
2. The relationship between meiosis and heredity should be dealt with explicitly;
3. Two main cell lines, the somatic line (mitosis) and the germ line (meiosis) should be distinguished in the setting of the life cycle;
4. Students should actively explore the relationships between the levels of biological organization themselves, guided by the structure of the learning activities and/or by the teacher [5] (p. 61) and [7] (pp. 111–112).

2.2. Designing and Studying a Learning and Teaching Strategy for Genetics

Based on the four educational design criteria a learning and teaching strategy targeted at 15–18 years old upper secondary students in three Dutch schools was developed, studied, and improved [5] (for more details about the educational design research approach we refer to previous papers [16,17]). The resulting so-called *yo-yo strategy* focuses on explicitly distinguishing the hierarchical levels of biological organization, on interrelating hereditary phenomena and genetics concepts on these levels and on thinking to-and-fro between the successive levels. The latter is metaphorically called *yo-yo thinking* based on the yo-yo toy.

In the learning and teaching strategy yo-yo thinking was fostered by: (a) the genetics content structure cross-cutting the levels of biological organization, and (b) the use of a problem posing approach to structure the teaching and learning process and to promote meaningful learning. The genetics content structure in the yo-yo learning and teaching strategy aimed at exploring an explanation for heredity is outlined in Table 1. The outline comprises the genetics key concepts classified by the levels of biological organization and presented as a sequence of relevant biological questions and answers: the conceptual thread.

The problem posing approach [18] to teaching and learning aims to provide students with both local and global content specific motives for learning. It is based on the idea that students should be aware of what they are doing and of why they are doing that at any time during their learning process. A global motive is necessary to give students a sense of direction as to where the whole learning and teaching process will take them. The local motive should be evoked by learning activities that have been designed in such a way that they raise questions students cannot fully solve yet, but that can be answered by carrying out the subsequent learning activity. The solution to a partial problem gives rise to the next partial problem in the sequence that will be answered or solved in the next learning activity. The learning activities should be chosen in such a manner that working on these partial problems will help students to solve the main problem, and to acquire the desired scientific knowledge.

Table 1. Content structure of the yo-yo strategy for human genetics [5] (pp. 145–146).

| Questions | Answers |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Organismic level <i>What makes you look like your parents, but not being identical to them?</i> (central question) | Everybody is familiar with hereditary phenomena in families. Sex life links parents and offspring (sexual reproduction: SR), but this does not apply to organisms that produce identical progeny (asexual reproduction: AR). |
| What distinguishes sexual from asexual reproduction? | In AR there is one parent and in SR a fusion of egg and sperm cell, originating from mother and father respectively, takes place. |
| What structures are being passed on in AR and SR? | |
| Cellular level What happens to chromosomes during cell division? | In AR as well as in SR dividing cells , which contain nuclei with chromosomes , are the vehicle of genetic instructions. In AR the chromosomes are copied and divided equally among the daughter cells (mitosis). So the parent cell divides to form two identical cells. In SR a cell divides by two divisions into four germ cells, each containing half the original number of chromosomes (meiosis). |
| How does mitosis fit in the life cycle of multi-cellular organisms? | AR is analogous to the somatic cell line : from the zygote mitosis leads to growth and development. Any mutation in this cell line will not affect the next generation, contrary to a mutation in the germ cell line . |
| What makes chromosomes determine the different hereditary traits in an organism? | Chromosomes contain genes (and alleles) which instruct the cell to produce all kind of proteins . The latter have different structural and functional roles, which are expressed in hereditary traits. |
| How do genetic traits on the organismic level relate to chromosome structure and behaviour on the cellular level? | |
| How unique is an individual's genetic make-up? | Fusion of two gametes forms a zygote with a random recombination of homologue chromosomes (and their genes) from both parents. The forming and fusion of gametes in SR are random processes, which add to a very large genetic diversity , i.e., unique individuals. |
| Molecular level How do genes work? | The genes in the chromosomes are made of DNA , which stores and faithfully transmits information. The information-carrying capacity of DNA comes from the 4 bases; they are 'read' as if they were letters, making up words of three bases long. These words give the information needed for building proteins, and for organising the activity of the cell. |
| Meta-reflection Which levels of biological organization have been transected in succession and what is the added value of thinking backward-and-forward between these levels? | In descending from organism to cells and molecules and ascending vice versa biological structures, processes and concepts can be interrelated enabling us to build up a coherent conceptual understanding of heredity. This backward-and-forward thinking is helpful in grasping hereditary phenomena. |

Key concepts are depicted in italic bold.

The problem posing sequence that can be recognised in the successive learning activities (see [5] pp. 140–142) of the yo-yo strategy for genetics consists of the following steps and resembled the didactical phasing of Kortland [19]:

- i. Central steering question (posed at the beginning of the learning and teaching sequence; global motive);
1. Partial question (PQ) and local motive to explore and answer the PQ: creating a need for extending knowledge;
2. Information and/or investigation: extending knowledge;
3. Application: using the extended knowledge in a new situation;
4. Reflection: reflecting on the extended knowledge.

By activating students' prior knowledge and relating to real life situations in a guided learning dialogue a central question is posed that serves as a global motive (i). The sequence of partial problems (questions) should then serve as a content-related motive to explore the next steps in the learning and teaching sequence. The structure of the reflection step and its position within the problem posing sequence is outlined in Figure 1.

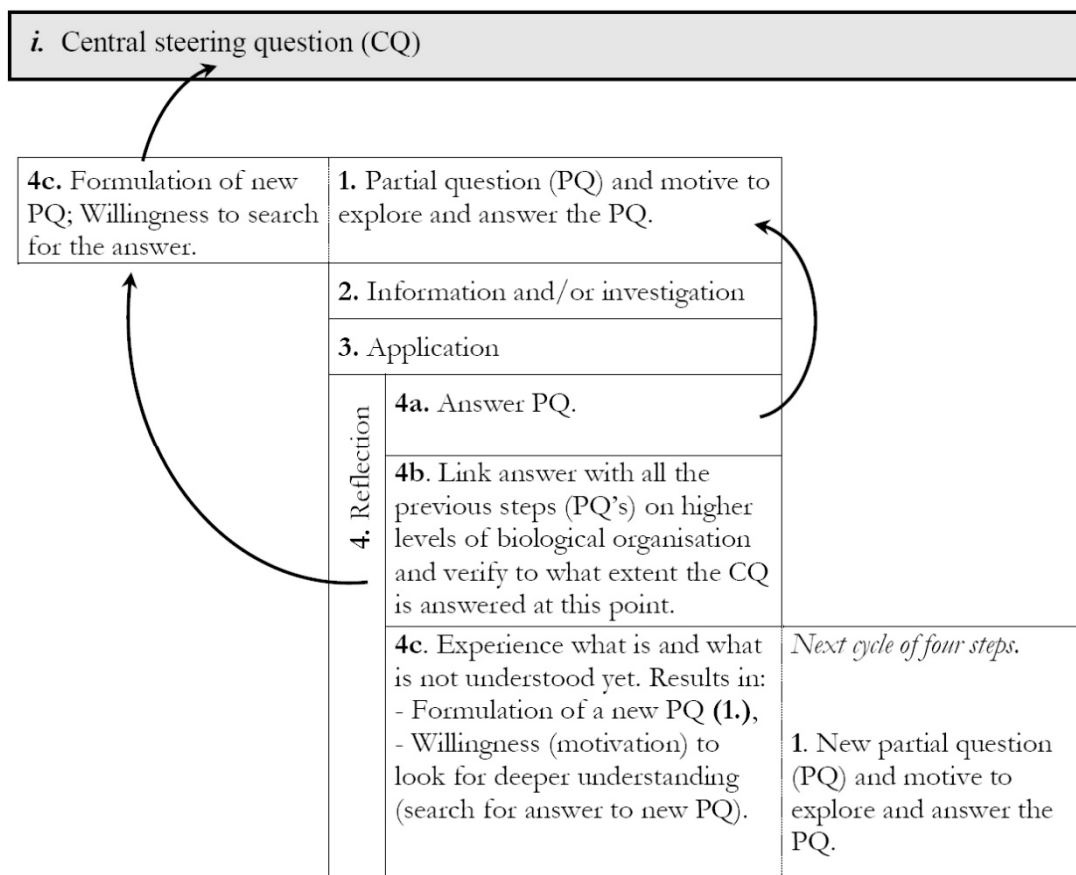


Figure 1. The structure of the reflection step and its position within the problem posing cycle. The arrows show the feedback and linking within one cycle as well as the previous partial question (concepts on the higher levels of biological organization) and the central question.

In the reflection Step 4 the partial question posed at the beginning of the learning activity will be answered, so there is feedback to Step 1 (4a, Figure 1). Subsequently, the answer to this partial question is linked with all the previous steps (partial questions) on the higher levels of biological organization, in order to verify to what extent the central question has been answered at that point and to co-guide the formulation of the next partial question (4b, Figure 1). In these reflection steps (or during the investigation and/or application step, i.e., reflection-in-action) the students experience what they do and do not understand or know yet, which should challenge them to take a next step in the learning sequence (4c, Figure 1) by formulating a new partial question with the central question in mind. With this new partial question the next sequence of four steps starts (4c, Figure 1). A number of successive sequences, cycles, on different levels of biological organization are enacted. Every new cycle starts with the formulation of a partial question to be explored and answered through the next learning activities (Figure 2).

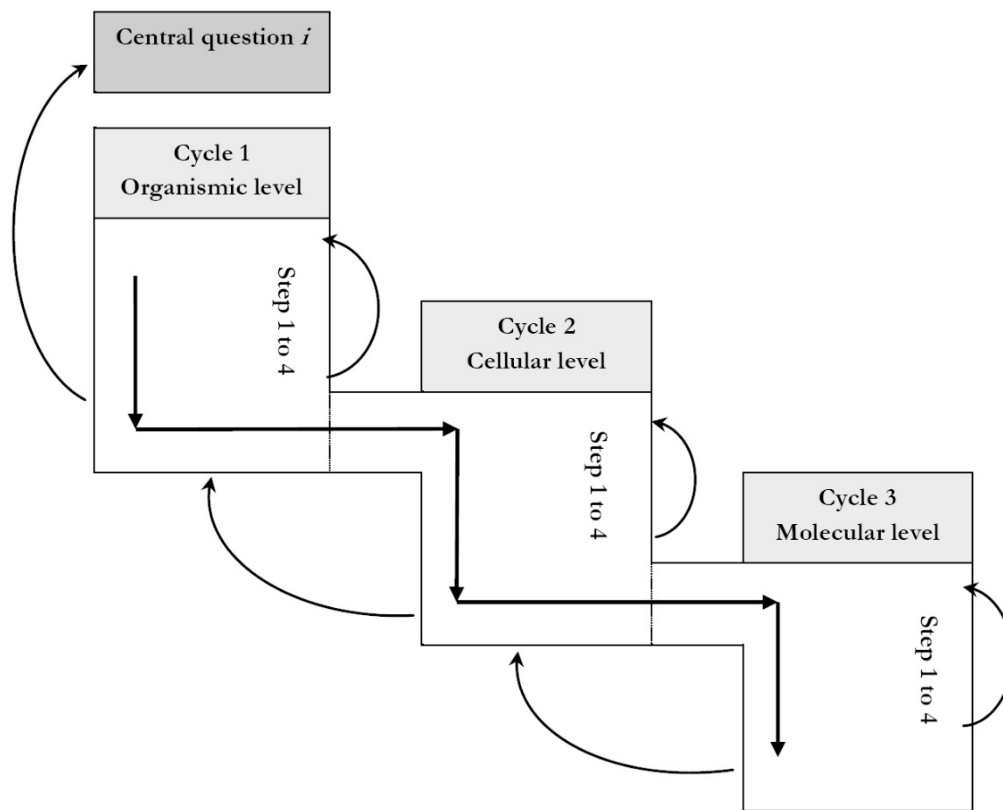


Figure 2. Schematic representation of the yo-yo strategy: descending and ascending the levels of biological organization by means of the problem posing cycles (consisting of 4 steps, see Figure 1).

The yo-yo strategy helped students to actively explore the main inter-relationships in hereditary phenomena on different levels of biological organization. To illustrate this process a key learning and teaching activity will be discussed in more detail: a chromosome practical (including a whole class reflection on this practical). This activity aimed to visualise the relationship between meiosis and heredity in the context of the life cycle, by interrelating reproduction and hereditary traits on the organismic level and hereditary processes and concepts on the cellular level. Moreover the practical was performed in small groups of students to elicit content-related discussions in solving the practical, see also [5] (pp. 117–120) and [20].

In the chromosome practical, a box with paper strips that differed in length and colour (representing chromosomes) was available for every group of students. The activity started on the organismic level, by selecting four genetic traits of their own family. Next, students had to select three pairs of chromosomes out of the box in order to constitute a somatic cell of the father and a somatic cell of the mother. Subsequently, they had to form gametes by the process of meiosis and finally choose the correct gamete combination for the offspring, i.e., the new combination of chromosomes and alleles that corresponds with the genetic traits of the offspring established at beforehand (Figure 3).

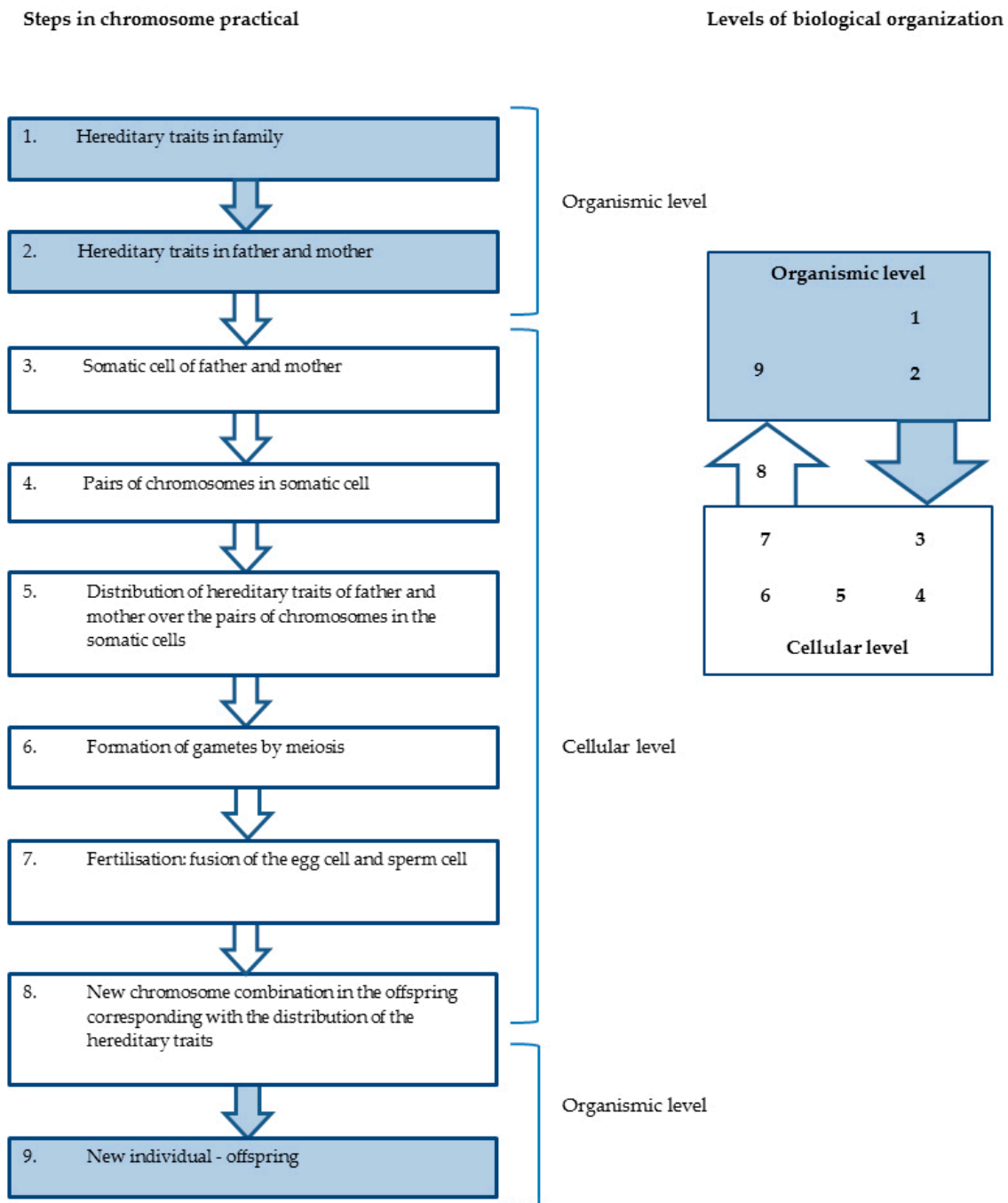


Figure 3. Successive steps in the chromosome practical representing hereditary phenomena on different levels of biological organization [5] (p. 118).

So students had to relate various concepts and processes on the organismic and cellular level. Mostly, students were well able to solve the problems they encountered in the practical by consultation of and discussion with the group members. But, when students really got stuck, the teacher guided them by asking questions that took them to the ‘higher’ level of biological organisation. For instance, a group of students disagreed on the homologue chromosome concept. The teacher asked them ‘What is a pair of chromosomes’ and ‘How did you receive those pairs of chromosomes?’, helping students to ascend to the organismic level. This made students think about the origin of the homologue chromosomes, and they indicated that one originated from mother and the other from father. So, they had to ascend to the organismic level, and rethink the reproduction process on that

level, the formation of gametes (students responded with ‘Oh yes, 23 chromosomes of father and 23 chromosomes of mother’) and rediscover the cause that resulted in nonidentical homologue pair.

When students had to equip the child with the correct combination of chromosomes according to the child’s hereditary features (established at forehand), they actively linked hereditary features of the organismic level with hereditary phenomena of the cellular level, so as to verify the underlying chromosome and gene division.

In this practical students had to relate the genetics concepts (hereditary traits, sexual reproduction, meiosis, chromosomes, genes, and alleles) dealt with in the preceding learning activities, in a new situation. Solving the problems posed in this practical required students to think to-and-fro (yo-yo) between the organismic and cellular level (see Figure 3).

The implemented lesson module concluded with a written test; students had to distinguish the different levels of biological organization in a text that dealt with the hereditary trait of albinism. Three quarters of the students were able to attribute statements in a text on albinism to the different levels of biological organization, and almost two thirds of these students could explain their answers correctly showing a quite satisfactory understanding of the levels of biological organization.

2.3. Formal Characteristics of the Yo-yo Strategy

Essential in the yo-yo strategy is to start at the concrete organismic level, students are familiar with, by posing a central steering question serving as the starting point of a conceptual story line (see Table 1) in a problem posing structure. Next, key concepts need to be identified on the different levels of organization and to be interrelated. The key concepts per level of biological organization identified in the yo-yo strategy for genetics (distracted from the conceptual structure, Table 1) are depicted in Figure 4.

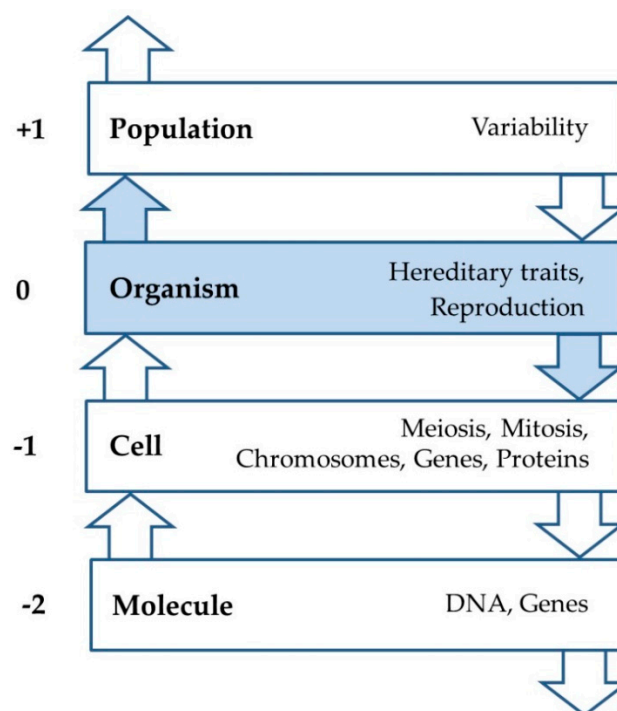


Figure 4. Arrangement of key concepts on the different levels of biological organization according to the yo-yo strategy for classical genetics: thinking to-and-fro between the levels, starting from the organismic level and interrelating the key concepts on these levels. Gene is a dynamic, transformative concept and proteins could be positioned at the molecular level as well.

In the yo-yo strategy students are invited to take a systems perspective on the biological phenomenon under study by conceptually (a) distinguishing and relating the involved levels of biological organization. These levels are usually defined by part whole relationships, with emerging phenomena at higher levels being linked with structures and processes at the next lower level. Relating levels of biological organization includes (b) matching of key concepts with the involved levels of biological organization and (c) interrelating concepts. Doing this with concepts belonging to one level is specified as making horizontal coherence [6], whereas making vertical coherence refers to linking concepts of successive levels. (d) Looking for causal explanations means moving down (reductionist framing); moving up aims at providing functional explanations (holistic framing). To (e) acquire yo-yo thinking as a *metacognitive tool* in learning biology a concluding crucial step entails naming, articulating, and reflecting on the (outcomes of the) passed through activities, including how and when to apply yo-yo thinking in studying other biological phenomena. The above mentioned characteristics might emerge in different order during teaching and learning.

So in teaching topic-related yo-yo thinking five questions should be addressed:

- a. Which levels of biological organization are involved in thinking upwards and downwards?
- b. Which conceptual understanding has been gained per level (horizontal coherence)?
- c. How are the concepts on the different levels interrelated (vertical coherence)?
- d. How are the conceptual understandings per level integrated and embedded in a pattern of explanatory reasoning about a biological phenomenon (pictorial representation, narrative storyline)?
- e. How did the yo-yo approach of this topic contribute to grasping the subject matter and when, why, and how could yo-yo thinking be applied in studying other biological topics? To acquire yo-yo thinking the student has to internalize this approach as a metacognition, i.e., asking himself and answering the questions a–d and thus regulating his/her own learning for coherent understanding of new biological topics. (metacognition: self-monitoring and self-controlling learning biological topics by addressing the above points a–d).

3. Analysis of Yo-yo Thinking in Selected Biology Education Research Cases

3.1. Searching, Selecting and Analysing Cases

In order to reappraise yo-yo thinking in biology education research, based on its uptake and any well-considered adaptations in the research community, a literature search was conducted. In Google Scholar, we searched for publications that cited the Ph.D. thesis on yo-yo thinking [5]. This yielded 123 hits (18 April 2018). By close reading the abstracts and doing a quick scan of the main texts we selected research articles that actually build on the idea of yo-yo thinking in their empirical study. We excluded studies that merely referred to our source publication for underpinning learning difficulties in genetics in their theoretical framework, or mentioned it in the context of the method section (e.g., the yo-yo study as an example of educational design research). This screening step revealed two main categories of biology education studies: (a) studies that apply (characteristics of) yo-yo thinking to another biological subject, e.g., evolution, cell biology, carbon cycle, and metabolism, and (b) studies that draw on yo-yo thinking in genetics and further elaborated the molecular level. We ultimately chose substantial studies related to German, Dutch, and American research groups.

Based on this screening three specific cases were selected, which were analysed based on the following questions:

1. Which problem is being addressed in the study?
2. How is yo-yo thinking interpreted in the study?
3. How are students getting involved in yo-yo thinking?
4. How are key concepts matched to levels of biological organization and how are the key concepts interrelated and embedded in a pattern of explanatory reasoning?

5. What has been the added value of applying yo-yo thinking?
6. What difficulties were encountered in implementing yo-yo thinking?
7. Which recommendations for further research have been proposed so as to realise the full potential of yo-yo thinking?

3.2. Applying Yo-yo Thinking to Other Biological Subjects: The German Case

A number of studies have mentioned (characteristics of) yo-yo thinking in studying a diverse range of biological topics mostly for lower and upper secondary education. For instance, the human body [21,22], cell division (e.g., [23]) and specifically the topic of evolution is broadly studied (e.g., [24–27]). However, many articles interpret learning difficulties students encounter in understanding these biological topics among other things in terms of confusion of levels, and do not build intrinsically on yo-yo thinking in the empirical section. Rocksén and Olander [26] also refer to the levels of biological organization, but the focus of their study is on the textual and verbal ‘link-making’ process in the classroom. Two doctoral theses use the core idea of yo-yo thinking in the context of systems thinking in cell biology [6] and ecology [28], but these studies are about modelling in particular.

Yo-yo thinking is well-known in Germany. Hammann and Asschof [29] (p. 298) refer in their comprehensive book on biology-related student conceptions to the yo-yo strategy as a means to cope with the macro-micro problem in biology teaching. Kattmann [9] describes in his biology teaching methodology book respiration-related concepts on the different levels of biological organization and suggests to connect the organismic and cellular level through downward and upward thinking without skipping intermediate levels. The latter should start at the organismic level. However, he does not mention a central steering question and the aligning of follow-up questions and educational activities according to the problem-posing approach. At the Center for Biology Education in Münster the idea of yo-yo learning is incorporated in various research projects. In a diagnostic study aimed at probing lower secondary students’ understanding of the carbon cycle, Düsing, Asshoff, and Hammann [30] determined which components students indicated to be relevant in the carbon cycle, how they interrelate these components, and how students trace carbon atoms over the different levels of biological organization. Students identified few components of the carbon cycle and the majority traced carbon atoms only on the level of the organism without any reference to other levels of biological organization. Core characteristics of yo-yo thinking were used as an analytic framework in probing students’ understanding of biological phenomena, but this study is not about a learning and teaching strategy. Another empirical study of this research group that explicitly builds on the core characteristics of yo-yo thinking is the work of Jördens et al. [27,31]. This German case will be analysed and described in more detail based on the seven questions.

(1) Which Problem Is Being Addressed in the Study?

Jördens et al. [27,31] conclude in their literature review that students’ explanations of biological phenomena are often characterised as incoherent and fragmented since they are less able to think across levels of biological organization, in particular concerning the topic of evolutionary change. That is why their studied teaching method for secondary students focuses on vertical coherence and on reasoning across levels in evolutionary biology by means of a hands-on lab activity.

(2) How Is Yo-yo Learning Interpreted in the Study?

Jördens et al. [27,31] explicitly refer to five components identified in learning and teaching strategies aimed at fostering thinking across levels in genetics [5,7] and cell biology [32]: “(1) distinguishing different levels of organization; (2) interrelating concepts at the same level of organization (horizontal coherence); (3) interrelating concepts at different levels of organization (vertical coherence); (4) thinking back and forth between levels (also called yo-yo learning); and (5) meta-reflection about the question which levels have been transected” [27] (p. 961). They

explicate that their focus is not on horizontal coherence (component 2) but on addressing persistent macro-micro problems that students encounter when thinking across levels in a diverse range of biological topics including evolutionary biology. These problems entail confusion of levels (also referred to as ‘slippage between levels’ [33]) and disconnects between levels (also associated with fragmented and compartmentalized knowledge [34]) [27] (p. 961). So in interpreting yo-yo learning they focus on components 1, 3 and 4.

(3) How Are Students Getting Involved in Yo-yo Thinking?

Jördens et al. [27,31] adopted a pre-post-test comparison group design study. Starting from the question ‘Why are Atlantic cod shrinking?’ the experimental group engaged in a lab activity designed to demonstrate how artificial selection affects both phenotype and genotype so as to interrelate concepts from genetics and evolution. The comparison group engaged in a lab activity that focused on phenotype alone (see Jördens et al. [27,31]).

The simulation activity addresses an authentic macrolevel problem, introduced by watching a video or reading a text informing students about the effects of size-selective harvesting of this fish. Next the students enacted the simulation in small groups.

The introduction resembles the start of a problem posing approach by formulating a central steering question albeit on the population level. Although, Jördens et al. [27] (p. 983) indicated they did not use the problem posing structure, which they interpreted as teacher-led. They claim that “the structure of the lab activity itself—rather than a series of teacher questions—guided the students’ thinking across levels” Jördens et al. [27] (p. 983).

(4) How Are Key Concepts Matched to Levels of Biological Organization and How Are the Key Concepts Interrelated and Embedded in a Pattern of Explanatory Reasoning?

After the introductory text the students were presented 10 drawings of fish (phenotype) that contained six circles representing two gene loci of three genes (genotype) that contribute to body size. Alleles were represented by coloured chips. The simulation represents concepts at different levels of organization as different entities [31]; coloured chips for the genotype, and drawings of Atlantic cod for the phenotype. Alleles (molecular level) were randomly drawn from the gene pool (population level) at the start of the activity and allele frequencies (population level) and body sizes determined (phenotype, organism level). Next, the five largest fish were removed by removing their alleles from the gene pool (simulating artificial selection) and the remaining fish reproduced, after which the five largest were removed again and so on.

Jördens et al. [27,31] indicate that the hands-on activity stimulates students to think back and forth between levels and interrelate concepts at levels, in particular, track changes in phenotype to changes in genotype over several generations [31] (p. 136). However, from the perspective of yo-yo thinking (not skipping any level in ascending or descending) the cellular level is not explicated in this learning strategy (e.g., somatic and germ cell line). Phenotypes of the fish (body size of the cod; organism level) are related to genes/genotype of the fish (molecular level) and allele frequencies in the population. The conceptual story line (pattern of explanatory reasoning) is not explicitly formulated, e.g., key concepts depicted per level of organization and conceptual questions per level that shows the need for ascending or descending a level of biological organization. Jördens et al. [27,31] claim the activity addresses different levels, interrelates them, and helps students to distinguish them. However, the learning materials provided in these articles do not seem to explicate the levels of biological organization to the students, e.g., provide visual representations of the levels and linking the story line to of the activity to the levels.

In retrospect, we try to reconstruct which key concepts are addressed in this activity on which level of biological organization (Table 2).

Table 2. Arrangement of key concepts on the different levels of biological organization based on the description of the ‘Why is the cod shrinking?’ simulation activity of Jördens et al. [27,31].

| | Levels of Biological Organization | Key Concepts |
|---------|-----------------------------------|------------------------------------------------|
| ↓ Start | Population | Variability, gene pool, allele frequencies |
| ↓ ↗ | Organism | Hereditary traits, phenotype (size of the cod) |
| ⋮ | Cell | – |
| ↓ ↗ | Molecule | Alleles, genes |

Jördens et al. [27] (p. 971) explicate that “students were encouraged to move among the levels of the population, the organism and the genes”, indicating ‘genes’ as a level of organization.

(5) What Has Been the Added Value of Applying Yo-yo Thinking?

Inspired by yo-yo thinking, Jördens et al. [27,31] designed a learning and teaching activity that emphasised the interrelation between the biological concepts of phenotype and genotype in the context of evolution (process). They indicate that the hands-on activity stimulates students to think back and forth between levels and interrelate concepts at levels, in particular, track changes in phenotype to changes in genotype over several generations [31] (p. 136). Moreover, they specify that they build on the crucial role of thinking across levels, and that this study offers quantitative support that vertical coherence (thinking across levels) is difficult for students and should be supported with learning activities [27] (p. 983).

(6) What Difficulties Did They Encounter in Implementing Yo-yo Thinking?

The authors did not discuss any difficulty in implementing the hands-on lab activity that aimed to foster vertical coherence and thinking across levels of biological organization. Yet, they did not build in a meta-reflection phase, and the “the lab activity did not explicitly address the issue of inheritance of genes vs. inheritance of traits” [27] (p. 973). They indicate that in a next step (suggestion for further research) lab activities should include a meta-reflection, encouraging students to reflect on which levels have been transected, since this meta-cognition ‘might be beneficial to thinking across levels’ [27] (p. 984).

(7) Which Recommendations for Further Research Have Been Proposed so as to Realise the Full Potential of Yo-yo Thinking?

Jördens et al. [27] formulated three practical implications of the study for fostering thinking across levels: (1) Concepts at different levels of biological organization must be represented as separate conceptual entities to student; (2) activities must be involved that encourage students to think back and forth between the levels of biological organization; (3) meta-reflection about the question of which levels were transected should be incorporated. So they argue that in further research activities aimed at fostering thinking across levels should include and focus on the impact of meta-cognition.

3.3. Molecular Level: The American and Dutch Case

Studies on learning and teaching molecular genetics also address the macro-micro problem. The original yo-yo strategy was developed in the context of classical (Mendelian) genetics and only touched upon the molecular level. American (‘Duncan’) and Dutch (‘Van Mil’) research specifically elaborated yo-yo thinking for molecular genetics. Duncan and Tseng [35] and Van Mil et al. [36,37] refer to one another and both focus on the molecular level in interrelating gene-protein-trait in an educational design study. These cases will be analysed together.

(1) Which Problem Is Being Addressed in the Studies?

Learning about DNA, RNA, and proteins is part of the upper secondary biology curriculum in most countries. Many studies report that students fail to connect molecular knowledge to phenomena at the higher level of cells, organs, and organisms. Duncan and Reiser [38] (p. 939) state that grasping ‘genetic phenomena entails understanding how mechanisms and interactions at the molecular (genes, and proteins) and micro-levels (cells) bring about effects at the macrolevel (organism, and population)’, but students struggle to provide mechanistic explanations of genetic phenomena that explain how genetic information brings about physical traits [39]. Students’ knowledge of proteins and their role in genetic phenomena is limited. Van Mil et al. [36,37], tapping into Craver [40] and Craver & Bechtel [41], diagnose that students lack the competence of molecular mechanistic reasoning required for bridging the gap between the molecular and cellular level. Molecular mechanistic reasoning entails interpreting cellular phenomena as the overall result of the interactions between underlying physical entities. Duncan & Tseng [35] and Van Mil et al. [37] focus on developing and studying teaching units to foster students understanding of genetic information and the mechanisms that link genes to traits (link phenotype and genotype within an individual).

(2) How Is Yo-yo Thinking Interpreted in the Studies?

Duncan and Tseng [35] state that understanding genetic phenomena as a system of interrelated organization levels that affect one another is an important aspect of attaining a coherent and meaningful understanding in this domain. One of the four learning goals concerns reasoning across levels to generate explanations of genetic phenomena. Van Mil [36] agrees that students should constantly be aware of the levels of biological organization that are relevant to the concepts discussed. However, in his view it will not always be possible to unequivocally relate biological concepts to levels of biological organization, e.g., the gene concept. He criticizes the idea of yo-yo thinking for not discussing relationships between levels in the context of providing explanations. After all, understanding of how the discussed phenomenon at one level comes to be from underlying structures and processes and therefore can be accounted for by describing the phenomenon in terms that belong to lower organizational levels is crucial. Therefore, based on the philosophy of molecular systems biology, a framework for molecular explanations of cellular processes was developed, including heuristics used to construct these explanations. This approach is related to the work of Duncan and Tseng [35] aimed at helping students to understand that the observed phenotype emerges from interactions at lower organization levels and in particular the interactions of proteins.

(3) How Are Students Getting Involved in Yo-yo Thinking?

The American and Dutch teaching unit both start with exploring a phenomenon at subsequent organization levels and explaining patterns at one level through the interactions of entities at a lower organization level. It mirrors the reasoning the authors want students to engage in. Duncan & Tseng [35] start at the organismic level with an authentic problem that allows students to explore and discuss it in ways that are relevant to them: Why do some people continue to have high cholesterol? Can these people be helped? Students explore the symptoms of heart disease and determine that high cholesterol is connected with unhealthy lifestyle or genetic predisposition. In the next five lessons they descend via organ/tissue, cells, proteins, genes to the genetic system. Driving questions and various activities structure the learning trajectory. Question–investigation cycles were used to structure students’ exploration of multiple organization levels. For example, a question at the level of genes is: What determines the number and sequence of amino acids in a protein? The students explore the role of genes in specifying the amino sequence.

The Dutch design [36,37] draws explicitly on the problem-posing approach and also starts with diseases. The guiding question was ‘I expect that scientists studying cancer/diabetes/HIV are interested in how cells ...’ aimed at letting students reason between cells and bodily phenomena by clarifying the role of cell activities in the human body. The chosen two-step top-down approach

entails: (1) Identifying cell activities in phenomena in the body and (2) subdividing cell activities and hypothesizing underlying mechanisms. Next the bottom level was explored including understanding the cause and effects of molecular interactions and chaining molecular interactions into activities of proteins and protein-based modules. The third (bottom-up) phase aimed at explaining cell activities of increasing complexity (Figure 5).

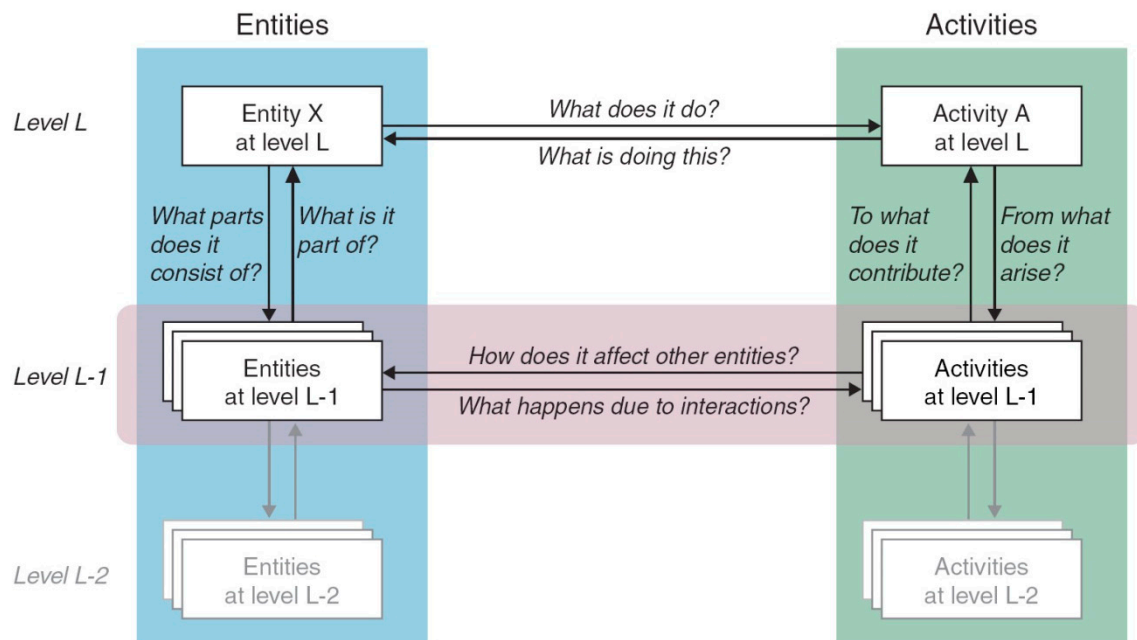


Figure 5. Schematic representation of the general mechanistic reasoning structure, as depicted in van Mil et al. [37] (p. 524).

The Dutch strategy taps into the intuitive notion of parts and wholes and causality; that is what people do when they reason about the working of a machine, a car engine, or other daily-life mechanisms. Students are more or less familiar with the functioning of a whole as a linking and nesting of the actions and interactions of components and subcomponents [37] (p. 225). Every activity, process, or event can be analysed in two directions: (1) the downward question ‘How does it arise from the underlying parts and their activities?’ and (2) the upward question ‘What is its role or function, or how does it contribute to the larger whole?’ Asking both upward and downward questions with respect to one level requires the consideration of (at least) one higher and (at least) one lower level. Cartoon-like graphics and more realistic molecular animations are brought into action to foster students’ reasoning about (sub)cellular events as the result of concrete activities and entities.

The American and Dutch series of lessons both use strategies to provide scaffolding.

(4) How Are Key Concepts Matched to Levels of Biological Organization and How Are the Key Concepts Interrelated and Embedded in a Pattern of Explanatory Reasoning?

Both studies seem to relate concepts and levels in passing, i.e., embedded in various activities. In the overview of the teaching unit driving questions and activities [35] (p. 28) are linked with levels. The questions and activities contain relevant concepts. For example, at the level of proteins the question is ‘How does cholesterol get into the cells and what is the role of the receptor protein?’ The activity: ‘Students read and discuss about the receptor protein in transporting cholesterol into the cell.’ Next to writing a letter, students were invited to make a concept map of given genetic and biological terms. Or to put a story together using provided statements that explain the biological cause of a genetic disease, and to explain the story in their own words. The Dutch study, which focuses on explanatory reasoning (by posing downward mechanistic ‘how’ questions and upward functional

‘what’ questions), is critical about matching key concepts with levels of organization (as mentioned above). By inserting intermediate levels with different entities and activities the Dutch even complicate the endeavour of matching concepts with levels.

(5) What Has Been the Added Value of Applying Yo-yo Thinking?

Duncan and Tseng [35] state that traditional instructional approaches often focus solely on the structure of DNA and the details of how the genetic code is translated into proteins, with little discussion of how proteins then mediate genetic traits. Furthermore, the study clarifies that the genetic system is a hybrid of ontologically distinct layers: an information layer (genes) and a biophysical layer (proteins, cells, tissues, etc.). The biophysical layer is organised hierarchically. The American study focuses on the link between genes and traits within individuals, whereas the original yo-yo strategy addressed genotypes and phenotypes across individuals and generations. The focus on the mechanistic and systems-oriented understanding of genetic phenomena included a general understanding of proteins as key entities in genetic phenomena, and more specific understandings about the types of functions of proteins. Duncan and Tseng [35] claim to have shown that adding a molecular level cycle to the curriculum is easily implemented, and that students are capable of engaging with concepts at the molecular level. The structuring of the unit as cycles of inquiry that begin at the organismic level and then delve down to lower organization levels ending with the gene level, seemed to have been successful in motivating the need for genetic information only to explain the structure of proteins.

Yo-yo thinking has been critically accepted by Van Mil [36] and subsequently further detailed for the cellular and molecular level by introducing and elaborating molecular mechanistic reasoning. It explicitly framed yo-yo thinking as explanatory reasoning, i.e., emphasizing the downward ‘how?’ instead of focusing mainly on the upward ‘why’ of (sub)cellular activities. The educational design study of van Mil [37] delivered a proof of principle.

(6) What Difficulties Did They Encounter in Implementing Yo-yo Thinking?

Duncan and Tseng’s study [35] did not point to serious implementation problems. The design resembles the original yo-yo strategy in terms of starting at the organismic level and using question-investigation cycles (not indicated as problem-posing approach) to structure students’ exploration of multiple organization levels. The explicit matching of key concepts with the levels remains unclear.

Although Van Mil et al. [37] delivered a proof of principle of teaching and learning molecular mechanistic reasoning (pre-university students, aged 17–18), he developed, enacted, and studied the series of lessons himself. His unusual approach puts high demands on fellow biology teachers who are challenged to start genetics education with the introduction of genes and proteins and to rethink the use of graphics and animations in molecular mechanistic reasoning.

(7) Which Recommendations for Further Research Have Been Proposed so as to Realise the Full Potential of Yo-yo Thinking?

The American design-based study [35] is about instruction to foster generative and mechanistic understandings in genetics by inquiry learning. As the biggest shortcoming of the design the authors mention that the examples provided might not have been enough to support the construction of robust understandings of protein functions that would be sufficiently generative.

Van Mil et al. [36,37] focuses the attention to the role of yo-yo thinking in inquiry learning. Students are encouraged and empowered to explanatory reasoning comparable to how scientists proceed.

Both studies suggest to start genetics education with the fundamental role of proteins instead of positioning classical genetics in the context of the somatic and germ cell line. The elaboration of the molecular and cellular level seems to complete the original yo-yo strategy. However, from the research reports on molecular genetics education it cannot be readily deduced how the studies contributed to articulating yo-yo thinking as a meta-cognitive tool.

4. Discussions

This study sought to further articulate yo-yo thinking by analysing and discussing selected cases so as to answer the research question: How fruitful has yo-yo learning been in biology education research over the past 15 years?

4.1. *Selective Use and Further Completion*

Although the number of citations suggests that yo-yo thinking has been widely noticed by the biology education (research) community, the extent of research-informed further elaboration and testing has been quite modest. Biology education researchers seem to endorse systems thinking and agree to explicitly address the connection between levels of biological organization in teaching and learning about an array of biological phenomena. Yo-yo thinking is best learned through explicit, reflective content instruction, but what teaching materials and activities could support that? Up to now it seems that selective use had been made of the yo-yo strategy for genetics, i.e., not fully applied as intended. The German case focused specifically on vertical coherence and contributed to yo-yo learning by stressing that concepts at different levels of biological organization must be represented as separate conceptual entities to students. However, the researchers seem to skip the cellular level in exploring the relation between phenotype and genotype nor do they explicate the conceptual storyline in their study. The American and Dutch case contributed to the further development of the yo-yo strategy by firstly, highlighting upward thinking as functional reasoning (cf. [42]) and downward thinking as causal reasoning (based on the work of Craver [40]). Secondly, by articulating and bridging the gap between the molecular and cellular level for understanding heredity in greater detail. In research papers detailed guidance in organizing instruction about other topics is rare. So topic-specific yo-yo thinking as a general idea needs more research-informed elaboration so as to transform adoption of this metacognitive tool into its implementation.

4.2. *Nature of 'Levels of Biological Organization'*

Yo-yo thinking invites students to take a systems perspective, which is theoretical in nature. This leads to a paradoxical situation: the simultaneous use of yo-yo thinking as a means to acquire topical biological understanding and the development of yo-yo thinking as an end (metacognitive tool). However, the systems perspective in yo-yo thinking is limited to the general systems theory and students may accept the concept of levels of biological organization intuitively by referring to empirical nested part-whole units before it is articulated in the concluding meta-reflection. But confusing empirical and theoretical concepts could be easily overlooked [8]. The analysed cases do not report specifically on problems students might have encountered with the theoretical nature of the systems perspective. The Dutch case indicates it builds on the intuitive notion of parts and wholes and causality, and the German case emphasises the importance of meta-reflection about the levels that have been transected, recommending that further research should focus on the impact of meta-cognition.

Thinking about causes and effects at multiple levels entails to establish the relevant structures, processes, and concepts per level. New properties or behaviour at an above level that arise from multiple simple interactions at the underlying level cannot be reduced to the sum of its parts. Yo-yo thinking may be adopted intuitively. However, it will be confronted with counter-intuitive distributive causality and emergence [43]. Strictly speaking, a correlation does not mean an explanation of emergent properties in causal terms.

Eronen & Brooks [44] comment: 'Yet, in spite of the ubiquity of the notion, levels of organization have received little explicit attention in biology or its philosophy. Usually they appear in the background as an implicit conceptual framework that is associated with vague intuitions. Attempts at providing general and broadly applicable definitions of levels of organization have not met wide acceptance.' This makes the task of biology educators even more challenging. The question remains to what extent the systems perspective should be elaborated at the beginning, during, and/or at the end

of a teaching unit. In all cases the teacher should be familiar with the idea of systems thinking and think about appropriate teaching and learning activities. Biology education research should provide further input on these issues and inform teacher education.

4.3. Pedagogical Approach

Yo-yo thinking requires pedagogic content knowledge. The yo-yo teaching and learning strategy for genetics is based on the content structure of genetics and on the pedagogic of the problem-posing approach. The latter transforms the content into a well-considered sequence of questions and explorations or investigations to promote meaningful learning [45]. This approach may be demanding in itself if an educator is not familiar with it. The German case decided not to use it [27,31]. However, in our view this is for the wrong reasons: they misinterpreted it as teacher-led. In the classroom the questions should not be imposed by the teacher. Although he/she acts upon a carefully thought-out plan, the (sequence of) questions should be the outcome of a guided learning dialogue with students ('reinvented' in the classroom) as well as initiated by well-rigged designed learning and teaching activities. In the American and Dutch case the pedagogic of inquiry-based learning was used, which requires adequate scaffolding (learning activities and/or the teacher guidance). Van Mil [36,37] also used the problem-posing approach (together with the cognitive apprenticeship approach) and Duncan states that a cyclical process of discussion and questioning drives the progression through this learning sequence [35]. The problem-posing approach might be replaced by another pedagogic, but in that respect the studied cases were not very informative.

4.4. Explanatory Context and Reasoning

In Section 2.3, on characteristics of yo-yo thinking we wrote that relating levels of biological organization includes matching of key concepts with the involved levels of biological organization and interrelating concepts. Key concepts were not always explicitly matched with the involved levels, whereas inserting intermediate levels (e.g., subcellular level) and reasoning in explanatory contexts got more attention. Matching and interrelating concepts is necessary but not sufficient. Explicating the explanatory context and fostering biological reasoning is of vital importance for deepening understanding. Concept maps, visualisations, pictorial representations, and narrative storytelling are helpful in promoting coherent understanding.

In the original genetics-related yo-yo study we deliberately addressed the complex nature of genetics, i.e., cross-cutting multiple levels of biological organization. We only touched upon the molecular level and did not problematize the particular connection between the cellular (biology) and the molecular (physics and chemistry) level. Duncan and Van Mil suggested and elaborated molecular-mechanistic reasoning to bridge this gap, starting from the molecular level. In addition, genetics is also complex because its body of knowledge entails three interrelated models; the genetic, meiotic, and molecular model [46]. These models reflect the history of genetics and conflating them may result in misunderstandings if no attention is being paid to Nature of Science [47].

Duncan [35,48] also distinguishes a physical and informational level (the use of 'level' in various word combinations is complicating in itself). Physical refers to cells, organelles, protein complexes, DNA, and other molecules. Genes contain the information needed to make functional molecules called proteins. Both levels intersect in proteins. In sum, the multiperspective content structure of genetics likely interferes with the acquisition of yo-yo thinking as a metacognitive tool. Other subjects may be more appropriate to initiate students into yo-yo learning.

4.5. Conceptual Transformation in Genetics and the Use of Mental Models

Starting genetics education from molecular genetics as suggested in the learning progression [49], and thus turning the curriculum upside down, might unintentionally contribute to a deterministic view of the gene. From epigenetics we know that environmental factors can interact with our

genetic information and that gene-expression might be influenced by higher levels of biological organization [50,51]. This may complicate causal reasoning within yo-yo learning.

When moving downward, at the cellular level we are confronted with a transition from observable (sub)microscopic phenomena and structures like cell division and organelles to mental representations of biochemical processes like molecular graphics and animations. The latter make the abstract molecular world more concrete. However, students should be made aware of the difference between realistic displays and mental models.

Concluding, yo-yo thinking as a heuristic of systems thinking has been an inspiring idea to promote coherent conceptual understanding of biological phenomena across different levels of biological organization (cf. [52]). To exploit its full potential more topic-specific educational design research is needed, that should take the five aspects of teaching yo-yo thinking (described in Section 2.3) into account. Especially, its functioning as a metacognitive tool in self-regulated biology learning requires more specification. Knowing when, why and how yo-yo thinking could be applied in studying other biological topics, asks for explicitly reflecting with students on distinguishing and conceptually interrelating levels of biological organization when constructing explanatory stories. Elaborating this theoretical systems perspective remains challenging. For *initiating* students into yo-yo thinking the topic of genetics seems too complicated due to its multiperspective content structure. Last but not least it is time to study teachers' perceptions and experiences regarding yo-yo thinking so as to inform teacher education and to facilitate its implementation (e.g., [53]).

Author Contributions: Both authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Acknowledgments: We thank M.H., U.K. and D.J.B. who were willing to share their perceptions on the challenges and opportunities they identified in implementing yo-yo thinking in biology education research.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Marbach-Ad, G.; Stavy, R. Students' cellular and molecular explanations of genetic phenomena. *J. Biol. Educ.* **2000**, *34*, 200–205. [[CrossRef](#)]
2. Ferrari, M.; Chi, T.H. The nature of naïve explanations of natural selection. *Int. J. Sci. Educ.* **1998**, *20*, 1231–1256. [[CrossRef](#)]
3. Ummels, M.H.; Kamp, M.J.; Kroon, H.; Boersma, K.T. Promoting conceptual coherence within context-based biology education. *Sci. Educ.* **2015**, *99*, 958–985. [[CrossRef](#)]
4. Šorgo, A.; Šiling, R. Fragmented knowledge and missing connections between knowledge from different hierarchical organisational levels of reproduction among adolescents and young adults. *CEPS J.* **2017**, *7*, 69–91.
5. Knippels, M.C.P.J. Coping with the Abstract and Complex Nature of Genetics in Biology Education: The Yo-Yo Learning and Teaching Strategy. Ph.D. Thesis, Utrecht University, Utrecht, The Netherlands, 19 September 2002.
6. Verhoeff, R.P. Towards Systems Thinking in Cell Biology Education. Ph.D. Thesis, Utrecht University, Utrecht, The Netherlands, 5 November 2003.
7. Knippels, M.-C.P.J.; Waarlo, A.J.; Boersma, K.T. Design criteria for learning and teaching genetics. *J. Biol. Educ.* **2005**, *39*, 108–112. [[CrossRef](#)]
8. Verhoeff, R.P.; Knippels, M.C.P.J.; Gilissen, M.G.R.; Boersma, K.T. The Theoretical nature of systems thinking. Perspectives on systems thinking in biology education. *Front. Educ.* **2018**, *3*, 1–11. [[CrossRef](#)]
9. Kattmann, U. *Schüler Besser Verstehen. Alltagsvorstellungen im Biologieunterricht [A Better Understanding of Students. Everyday Notions in Biology Education]*; Aulis Verlag: Hallbergmoos, Germany, 2015; pp. 206–208, 330–331. ISBN 978-3-7614-2941-9.
10. Wilhelm, M. *Wirksamer Biologieunterricht [Effective Biology Education]*; Schneider Verlag Hohengehren: Baltmannweiler, Germany, 2018; ISBN 978-3-8340-1900-4.

11. Domis-Hoos, M.; Kapteijn, M.; Boerwinkel, D.J. *Genetica in Beweging. De Moeite Waard om te Leren [Genetics in a State of Flux. Rewarding Learning]*; NVON: Utrecht, The Netherlands, 2012; ISBN 978-90-8797-008-6.
12. Kapteijn, M.; Kamp, M.; Hullu, E. *Ecologie Leren & Onderwijzen [Learning and Teaching Ecology]*; NVON: Utrecht, The Netherlands, 2018; ISBN 978-90-8797-015-4.
13. Lewis, J.; Wood-Robinson, C. Genes, chromosomes, cell division and inheritance—Do students see any relationship? *Int. J. Sci. Educ.* **2000**, *22*, 177–195. [[CrossRef](#)]
14. Lewis, J.; Leach, J.; Wood-Robinson, C. What's in a cell?—Young people's understanding of the genetic relationship between cells, within an individual. *J. Biol. Educ.* **2000**, *34*, 129–132. [[CrossRef](#)]
15. Lewis, J.; Leach, J.; Wood-Robinson, C. Chromosomes: The missing link—People's understanding of mitosis, meiosis, and fertilisation. *J. Biol. Educ.* **2000**, *34*, 189–199. [[CrossRef](#)]
16. Boersma, K.T.; Knippels, M.C.P.J.; Waarlo, A.J. Developmental research: The improvement of learning and teaching of science topics. In *Making a Difference: Evaluation as a Tool for Improving Science Education*; Benett, J., Holman, J., Millar, R., Waddington, D., Eds.; Waxmann Verlag: New York, NY, USA; Münster, Germany, 2005; pp. 85–98. ISBN 3-8309-1508-X.
17. Boersma, K.T.; Waarlo, A.J. On the theoretical input and output of 'design research' in biology education. In *The Nature of Research in Biological Education: Old and New Perspectives on Theoretical and Methodological Issues*; Hammann, M., Waarlo, A.J., Boersma, K., Eds.; CD-β Press: Utrecht, The Netherlands, 2009; pp. 463–479. ISBN 978-90-73346-66-6.
18. Klaassen, C.W.J.M. A Problem-Posing Approach to Teaching the Topic of Radioactivity. Ph.D. Thesis, Utrecht University, Utrecht, The Netherlands, 6 December 1995.
19. Kortland, J. A Problem Posing Approach to Teaching Decision Making about the Waste Issue. Ph.D. Thesis, Utrecht University, Utrecht, The Netherlands, 15 February 2001.
20. Knippels, M.C.P.J.; Waarlo, A.J.; Boersma, K.T. Betekenisvol geneticaonderwijs: Een chromosomenpracticum. [Meaningful genetics education. A chromosome practical]. *Niche* **2001**, *5*, 14–17.
21. Ben-Zvi Assaraf, O.; Dodick, J.; Tripto, J. High school students' understanding of the human body system. *Res. Sci. Educ.* **2013**, *43*, 33–56. [[CrossRef](#)]
22. Olander, C.; Per-Olof Wickman, P.O.; Tytler, R.; Ingerman, Å. Representations as mediation between purposes as junior secondary science students learn about the human body. *Int. J. Sci. Educ.* **2018**, *40*, 204–226. [[CrossRef](#)]
23. Riemeier, T.; Gropengießer, H. On the roots of difficulties in learning about cell division: Process-based analysis of students' conceptual development in teaching experiments. *Int. J. Sci. Educ.* **2008**, *30*, 923–939. [[CrossRef](#)]
24. Andersson, B.; Wallin, A. On developing content-oriented theories taking biological evolution as an example. *Int. J. Sci. Educ.* **2006**, *28*, 673–695. [[CrossRef](#)]
25. Tibell, L.A.E.; Harms, U. Biological principles and threshold concepts for understanding natural selection. Implications for developing visualizations as a pedagogic tool. *Sci. Educ.* **2017**, *26*, 953–973. [[CrossRef](#)]
26. Rocksén, M.; Olander, C. A topical trajectory on survival: An analysis of link-making in a sequence of lessons on evolution. *Res. Sci. Educ.* **2017**, *47*, 451–472. [[CrossRef](#)]
27. Jördens, J.; Asshoff, R.; Kullmann, H.; Hammann, M. Providing vertical coherence in explanations and promoting reasoning across levels of biological organization when teaching evolution. *Int. J. Sci. Educ.* **2016**, *38*, 960–992. [[CrossRef](#)]
28. Westra, R. Learning and Teaching Ecosystem Behavior in Secondary Education: Systems Thinking and Modelling in Authentic Practices. Ph.D. Thesis, Utrecht University, Utrecht, The Netherlands, 18 February 2008.
29. Hammann, M.; Asschof, R. *Schülervorstellungen im Biologieunterricht. Ursachen für Lernschwierigkeiten [Students' Conceptions in Biology Education. Causes of Learning Difficulties]*, 1st ed.; Klett Kallmeyer: Seelze, Germany, 2014; ISBN 976-3-7800-4908-7.
30. Düsing, K.; Asshoff, R.; Hammann, M. Students' conceptions of the carbon cycle: Identifying and interrelating components of the carbon cycle and tracing carbon atoms across the levels of biological organisation. *J. Biol. Educ.* **2018**. [[CrossRef](#)]
31. Jördens, J.; Asshoff, R.; Kullmann, H.; Hammann, M. Interrelating concepts from genetics and evolution: Why are cod shrinking? *Am. Biol. Teach.* **2018**, *80*, 132–138. [[CrossRef](#)]
32. Verhoeff, R.P.; Waarlo, A.J.; Boersma, K.T. Systems modelling and the development coherent understanding of cell biology. *Int. J. Sci. Educ.* **2008**, *30*, 543–568. [[CrossRef](#)]

33. Wilensky, U.; Resnick, M. Thinking in levels: A dynamic systems approach to making sense of the world. *J. Sci. Educ. Technol.* **1999**, *8*, 3–19. [CrossRef]
34. Brown, M.H.; Schwartz, R.S. Connecting photosynthesis and cellular respiration: Preservice teachers' conceptions. *J. Res. Sci. Teach.* **2009**, *46*, 791–812. [CrossRef]
35. Duncan, R.G.; Tseng, K.A. Designing project-based instruction to foster generative and mechanistic understandings in genetics. *Sci. Educ.* **2011**, *95*, 21–56. [CrossRef]
36. Van Mil, M.H.W.; Boerwinkel, D.J.; Waarlo, A.J. Modelling molecular mechanisms: A framework of scientific reasoning to construct molecular-level explanations for cellular behaviour. *Sci. Educ.* **2013**, *22*, 93–118. [CrossRef]
37. Van Mil, M.H.W.; Postma, P.A.; Boerwinkel, D.J.; Klaassen, K.; Waarlo, A.J. Molecular mechanistic reasoning: Toward bridging the gap between the molecular and cellular levels in life science education. *Sci. Educ.* **2016**, *100*, 517–585. [CrossRef]
38. Duncan, R.G.; Reiser, B.J. Reasoning across ontologically distinct levels: Students' understandings of molecular genetics. *J. Res. Sci. Teach.* **2007**, *44*, 938–959. [CrossRef]
39. Duncan, R.G.; Choi, J.; Castro-Faix, M.; Cavera, V.L. A study of two instructional sequences informed by alternative learning progressions in genetics. *Sci. Educ.* **2017**, *26*, 1115–1141. [CrossRef]
40. Craver, C.F. Role functions, mechanisms, and hierarchy. *Philos. Sci.* **2001**, *68*, 53–74. [CrossRef]
41. Craver, C.F.; Bechtel, W. Top-down causation without top-down causes. *Biol. Philos.* **2007**, *22*, 547–563. [CrossRef]
42. Boerwinkel, D.J.; Waarlo, A.J.; Boersma, K. A designer's view: The perspective of form and function. *J. Biol. Educ.* **2009**, *44*, 12–18. [CrossRef]
43. Grotzer, T.A. *Learning Causality in a Complex World: Understandings of Consequence*; Rowman & Littlefield Education: Plymouth, UK, 2012; ISBN 978-1-61048-864-8.
44. Eronen, M.I.; Brooks, D.S. Levels of Organization in Biology. In *The Stanford Encyclopedia of Philosophy*. Available online: <https://plato.stanford.edu/archives/spr2018/entries/levels-org-biology/> (accessed on 22 August 2018).
45. Lijnse, P.L.; Klaassen, C.W.J.M. Didactical structures as an outcome of research on teaching-learning sequences. *Int. J. Sci. Educ.* **2004**, *26*, 537–554. [CrossRef]
46. Freidenreich, H.B.; Duncan, R.G.; Shea, N. Exploring middle school students' understanding of three conceptual models in genetics. *Int. J. Sci. Educ.* **2011**, *33*, 2323–2349. [CrossRef]
47. Gericke, N.; El-Hani, C.N. Genetics. In *Teaching Biology in Schools. Global Research, Issues, and Trends*, 1st ed.; Kampourakis, K., Reiss, M.J., Eds.; Routledge: New York, NY, USA; London, UK, 2018; pp. 35–47. ISBN 978-1-138-08798-9.
48. Duncan, R.G.; Boerwinkel, D.J. Molecular biology. In *Teaching Biology in Schools: Global Research, Issues, and Trends*, 1st ed.; Kampourakis, K., Reiss, M.J., Eds.; Routledge: New York, NY, USA; London, UK, 2018; pp. 111–123. ISBN 978-1-138-08798-9.
49. Duncan, R.G.; Rogat, A.; Yarden, A. A learning progression for deepening students' understanding of modern genetics across the 5th–12th grades. *J. Res. Sci. Teach.* **2009**, *46*, 644–674. [CrossRef]
50. Rheinberger, H.-J.; Müller-Wille, S. *The Gene: From Genetics to Postgenomics*, 1st ed.; The University of Chicago Press: Chicago, IL, USA; London, UK, 2017; ISBN 987-0-226-51000-2.
51. Boerwinkel, D.J.; Yarden, A.; Waarlo, A.J. Reaching a consensus on the definition of genetic literacy that is required from a twenty-first-century citizen. *Sci. Educ.* **2017**, *26*, 1087–1114. [CrossRef]
52. Hammann, M. Organisationsebenen biologischer Systeme unterscheiden und vernetzen: Empirische Befunde und Empfehlungen für die Praxis [Distinguishing and interrelating levels of biological organization: Empirical findings and practical implications]. In *Biologiedidaktische Forschung: Perspektiven für die Praxis [Biology Education Research: Practice Oriented Perspectives]*; Groß, J., Hammann, M., Schmiemann, P., Zabel, J., Eds.; Springer: Heidelberg, Germany; New York, NY, USA, 2018; in press.
53. Olander, C.; Holmqvist-Olander, M. Professional development through the use of learning study: Contributions to pedagogical content knowledge in biology. *Procedia Soc. Behav. Sci.* **2013**, *89*, 205–212. [CrossRef]

