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Review

Translating Biochemistry Concepts into Cartoons and Graphic Narratives: Potential and Pitfalls

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Abstract: Simple biochemical concepts can be hard to grasp by non-specialists, even when they are related to practical contexts in industry, day-to-day activities, or well-acknowledged pathological conditions. This is especially important in instances where accurate communication of biochemical aspects for different types of stakeholders may be crucial. Examples include interacting with policymakers to establish guidelines, with patients (and/or caregivers) to identify key concepts in promoting awareness and adherence to therapeutic regimens, or with teachers and students for novel approaches in critical thinking. Focusing on our own work in developing communication tools for different purposes, in this review we will focus on some examples of how biochemical concepts can be effectively translated into illustrations and graphical narratives. For this purpose, engagement with target audiences in developing the materials themselves is key. We also discuss how specific projects can be tailored for different purposes, as well as evidence that comic-book strategies are effective in conveying biochemical and biomedical knowledge.

Keywords: metabolism; comics; biomedical knowledge; health communication; science communication

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1. Introduction

Scientific concepts in Biochemistry, and the life sciences in general, can be hard to understand, and the use of images to better convey information is common at all levels, from very basic leaflets tailored to a lay audience to schoolbooks and the most advanced scientific papers [1–6]. In fact, no Biochemistry or Molecular Biology textbook is devoid of images (photos, graphs, diagrams, and schematics) to help guide the reader [7,8].

In many cases, sequential images are used to display a sequence of events, for example relating to enzyme-mediated catalysis, the binding of ligands to receptors, signaling cascades, or steps in embryo development. One of the challenges in both education and outreach towards different types of audiences is translating biochemical concepts to a target audience that may need assistance in grasping the most basic information. While classical textbook images are effective at more professional levels, they may not be the ideal choice to communicate with all audiences.

It is therefore unsurprising to note that science communication aiming at different target audiences often uses illustrations, sketch notes, cartoons, and comics, with or without an accompanying narrative [9–15]. In this review, we will discuss examples of how biochemical concepts can be effectively translated into graphical narratives, providing tools for both formal and informal education, as well as for more effective stakeholder engagement. Importantly, we will also discuss the appropriate methodology needed to

create effective comics-based materials. The considerations to take into account include content selection, graphic considerations regarding style and representation, preparatory interactions with a putative target audience to tailor the content to specific needs, and the monitoring of impact to ensure that key messages are indeed transmitted. To the best of our knowledge, this is the first review to simultaneously focus on all these aspects of comics-based science communication.

2. Using Sequential Images and Comics in Science Communication

By combining words and images, comics, in particular, embody a reliable format to effectively communicate biomedical knowledge [16] as well as for introducing scientific information in the classroom [12,17]. Moreover, using narrative techniques and well-designed characters and narratives can also potentiate effectiveness in terms of scientific or health-related beliefs, attitudes, intentions, and behaviors [18–22]. Although some understanding of the specificities and conventions of the language is needed, comics seem to be approachable and able to reach and engage new audiences, also showing that entertainment and education are not mutually exclusive [23]. On the other hand, the narrative dimension contextualizes the scientific or health-related knowledge, both through verbal and visual cues, and engages the reader at a personal level [14,16,23]. Importantly comics have been clearly shown to be a successful tool in science communication, in some cases outperforming other forms of communication dealing with the same content (text, animations, etc.) [17,23–27].

In a biomedical context, examples include efforts dedicated to human immunodeficiency virus (HIV)/AIDS prevention programs [28,29], but later also sexual health education [30–32], rheumatoid disease [33,34], cancer [35–37], mental health [38–43] and metabolic disorders [44–47]. More recently, and concomitant with a gradual transition from hard copies to digital media, several comics designed to promote healthier diets, increased physical activity, and weight loss as preventive and therapeutic practices for obesity, diabetes, and cardiovascular diseases have been produced [48–53].

3. Defining Representations, Topics, Characters, and Storylines

Several aspects can be considered when using comics or visual-related language via a series of illustrations. These must be carefully considered and tailored towards the specific goals of a given project, starting with the choices to show scientific content in a simplified (not simplistic) manner.

For example, the use of analogies or metaphors is pervasive throughout scientific discourse in general and to convey biochemical concepts in particular. As shown in Figure 1, ATP production in the mitochondria follows a well-understood process that involves electron transport through several complexes coupled with proton pumping across the inner mitochondrial membrane. The resulting electrochemical gradient (mitochondrial membrane potential) is then used by the ATP synthase to phosphorylate ADP to ATP. At the molecular level, the mechanism regarding ATP synthase activity is often represented as rotating paddles converting different forms of energy. On the other hand, to convey the basic notions of what is at stake, the mitochondrial membrane potential can be metaphorically represented as a hydroelectric dam and the organelle itself as a battery (Figure 1C). Although these metaphors or analogies can also lead to misconceptions and improper simplifications, they can nevertheless be useful, especially as a first approach or in contacting audiences with limited scientific knowledge. In another example, discussing the molecular basis of actin-myosin interactions leading to voluntary skeletal muscle contraction in sarcomeres can be done logically in the context of exercise (possibly also related to the promotion of healthy lifestyles), for example, using the similarities with rowing as a metaphor (Figure 2).

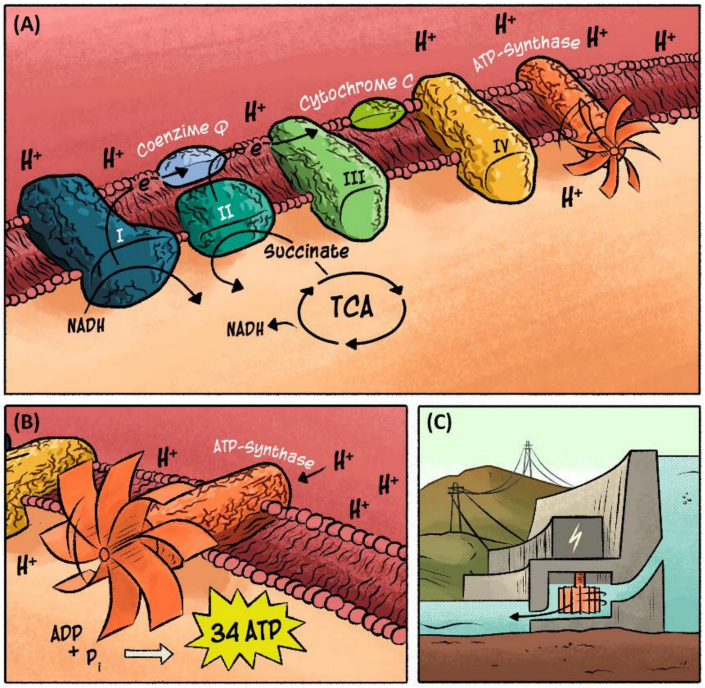

Figure 1. Typical representation of the electron transport chain in the inner mitochondrial membrane and the generation of an electrochemical gradient (**A**). The use of the gradient to synthesize ATP by the ATP synthase can be depicted as a system of rotating paddles based on structural information (**B**). More metaphorical is an analogy to show how a hydroelectric dam produced electricity (**C**).

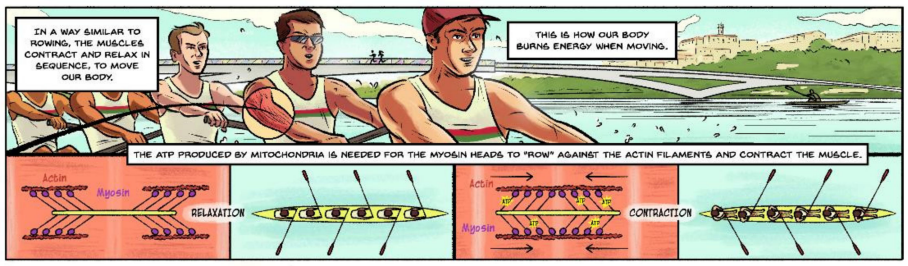

Figure 2. The introduction of a common activity (rowing) to stress the movements of myosin and actin filaments relevant in muscular contraction.

Another use of images to convey biochemical concepts includes the recently established Graphic Medicine genre, which applies to comics paradigms and principles generated with Narrative Medicine. This approach aims to humanize medical care, focusing on the experiences of those involved (patients, practitioners, family members, caregivers, health care systems, community) [54–59], stemming from individual experiences [60–63]. However, while the stories may resonate with others under the same circumstances, their goal is not necessarily to convey biochemical aspects related to a specific pathology or explain a treatment regimen from a scientific/clinical standpoint. Therefore, in a more educational context, this type of strategy may not be useful, as it introduces subjectivity and can neglect paramount scientific information [55,57].

A similar discussion may be had in terms of visual style [64,65], as both realistic depictions and cartoonish representations are possible. Indeed they are often combined, for example, using human characters as patients and cartoons to anthropomorphize phenomena (such as cancer, for example), cells, or proteins, thus equipping them with a clearer sense of (metaphorical) agency [14,16,66–68]. The goal is to engage readers using different strategies, leading to very different tools. The issues at stake are evident in three comics that focus on DNA and its functions. While the subject matter is essentially the same and

accurately depicted in each case, one [69] opts for a more realistic style characteristic of classical textbooks (drawn photos of key researchers and detailed schematics of molecular events), another relies on the anthropomorphizing of important molecules (helicases, transcription factors, repair enzymes) to better represent their actions [70]. Yet another has human characters interact directly with molecular aspects [71]. These choices may be related to the different goals of each approach: a thorough historical narrative on the discovery of DNA, an accessible approach on DNA function for the general population, and a textbook in Japanese comic (mangá) format to engage young readers, respectively. Regardless of the choices made, the images should not distract the reader from the main message. This can be the case with more expressionist styles drawings featuring unclear or unnecessary details, a confusing color palette, over-complex visual analogies, or even page layouts with an unintuitive reading experience.

On the other hand, the choices of what to communicate and how should actively involve the potential end-users, in other words, adopt a participatory approach in co-producing the content [72]. One has to start by identifying the main topics to communicate and the target audience, and then try to work with said audience (in focus groups or short interviews, preferably with some open questions) to establish a realistic knowledge baseline [73–76]. A few questions may need to be answered, for example: what is the background knowledge? In material focused on a specific medical issue, what do patients know about their own condition? What do learners know about the topic? What are the gaps in knowledge? What are audiences curious about knowing? Could it make a difference in how they interact with a given technology, adherence to treatment, or lifestyle changes? What do practitioners think would be useful information for patients (and caregivers) to have in order to elicit behavioral changes? What do teachers and professors think would be useful for the students' perception and cognition?

Patients and other learners, even those with limited literacy, have their own experiences and may have more developed and detailed knowledge than should be assumed, although misconceptions are also common [14,16]. These mutual interactions may also be useful if the goal is to create characters and narratives. If, for example, characters in an educational comic, as well as their biographies/behaviors, are based on a composite of different members of a target audience, there might be a better chance of other readers from the same population identifying with the fictional characters. One example is shown in Figure 3 and discussed in detail below [77].

It is important to note that this should be as open and as collaborative a process as possible, although financial, organizational, and time constraints will likely play a role. Ideally, an initial effort should lead to a first draft that can then be shared for possible feedback and eventually result in the refining of both visual and verbal narratives [75,76,78–80]. Did the audience understand the key concepts and message accurately? Did they appreciate the comic or think the story, characters, and script were convincing? Did they find something off-putting, and why? Finally, distribution of the final product should not be considered as the ending, but rather an evaluation of impact should be performed, if possible. Again, the goal, in this case, is to determine how effective the comic (or whatever other tool) was in a wider context, or if, for instance, its effectiveness varied with different segments of the population (age, gender, culture, literacy levels). These two aspects can be carried out using appropriately structured questionnaires (or interviews), which must nevertheless be validated using appropriate methodologies and expertise [26,77].

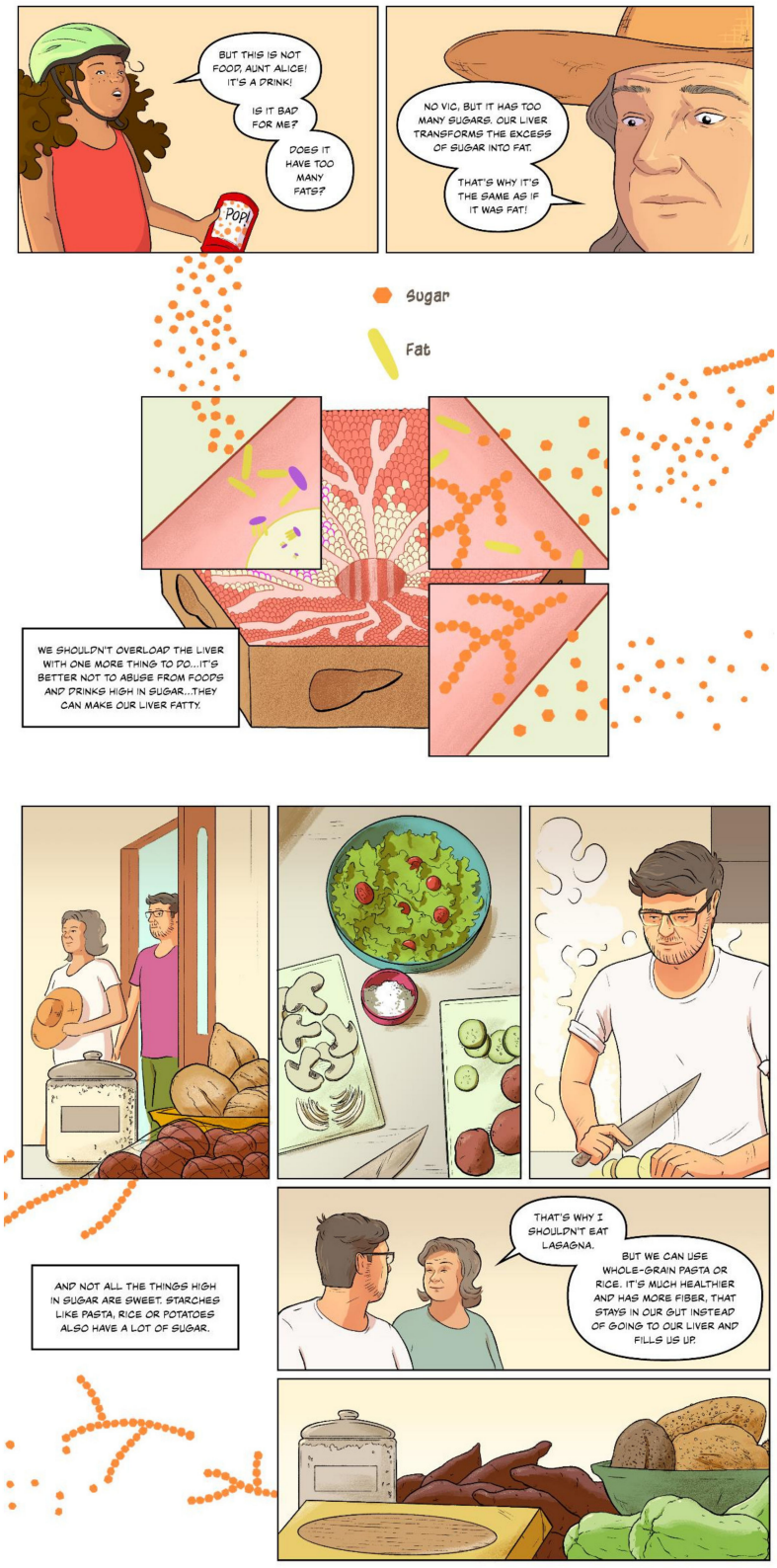

Figure 3. The use of characters with specific biographies and storylines to help convey both biochemical information (the synthesis of fat from sugars) and to help convey information relative to nutrition and healthier lifestyles (see text for discussion).

4. Comics and the Communicating Biochemical Concepts in a Context of Metabolic Disorders

Biochemical aspects related to metabolic disorders are a good place to start, as they can be important in many relevant biomedical and educational contexts [38,81]. Previously we faced the tensions of discussing accuracy versus aesthetics in our work on metabolic disorders focusing on mitochondrial biology [47]. Is there a realistic limit for depicting cellular mechanisms in a graphic narrative? What were the best strategies to bring mitochondria to 'real-life', convey the fundamental research, and engage in healthier habits? The narrative is about a young woman diagnosed with a metabolic disorder, and transports the reader to a realistic view of mitochondrial biology blended with the changing daily routines of the character. The intent was to target different types of lay audiences, not only patients but also children or at-risk segments, and students at different levels of education. This is relevant both in conditions that are relatively well-known, such as diabetes, as well as conditions where that is not at all the case, such as Nonalcoholic Fatty Liver Disease (NAFLD). NAFLD has been the target of a few campaigns exactly because it is not only underdiagnosed but a burden predicted to increase, especially in the developed world [77].

But, besides the obvious healthy lifestyle aspects related to both prevention and management of metabolic disorders (proper nutrition, regular physical activity, and exercise) as well as regular monitoring (blood sugar and cholesterol levels, liver enzyme activity etc.), what biochemical aspects can be conveyed to strengthen the message? In our work focusing on type 2 diabetes patients at high risk for NAFLD [82], a few issues arose out of conversations with researchers, practitioners, and patients who were interviewed for the project, albeit at different levels [83]. Two of these issues can be cited because they involve clear mechanistic biochemical insights: Why do people who avoid fatty foods (but not sweets) have fat accumulation and obesity-related problems (de novo lipogenesis)? Why does insulin sometimes "stop working" (insulin resistance)?

The advantage of excess sugars being converted to fat is clear from the standpoint of efficient energy storage, but conveying even a simple version of the biochemical reactions involved would likely confuse more than enlighten a lay audience [84]. One possible solution (Figure 3) is using a well-known nutritional choice (the ingestion of a sugary beverage) in parallel with a simple schematic showing that the liver can convert sugar to fat. The narrative, in this case, involves an older relative explaining to a child why drinking that particular beverage is, in a biochemical sense, equivalent to eating fatty foods [85,86]. The older character functions both as an explainer and a positive role model [20], and it should be noted that this particular character is aware of these issues because she suffers from type 2 diabetes. She is, in fact, a composite character based on the biographies and experiences of some of the patients interviewed at the start of the project [83]. This is an example of how more abstract notions may be interspersed with real-life situations different readers can relate to.

On the other hand, the concept of insulin resistance is crucial to explain when interacting with a lay audience [87,88]. First of all, the normal situation regarding the function of pancreas-produced insulin to ensure proper blood sugar management must be explained before its deregulation can be addressed. In this case, a possible solution is using cartoons that embody cells and molecules with anthropomorphic characteristics, as well as with an omnipotent narrator solution [82]. After explaining how the process usually works, insulin resistance is then represented as a systems overload that, by burdening biochemical circuits with an excess activity it can no longer cope with, causes a "rebellion" or a "strike", leading to several important health-related consequences (Figure 4).

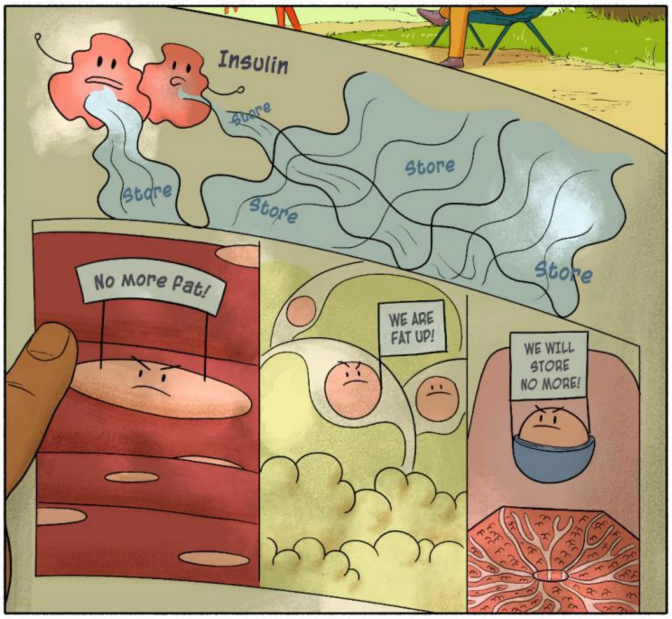

Figure 4. Anthropomorphizing biochemical elements such as molecules (Insulin) or cells/tissues (from left to right: muscle fat, liver) as a communication tool, in this case to convey the concept of insulin resistance using a "cells on strike" metaphor. See text for discussion.

5. Planning a Project: Monitoring Impact and Tailoring Strategies in Graphic Narrative-Based Science Communication

Although comics-based science communication is not new, what is novel is the increasing interest in scholarly research in this field, involving different types of analyses [89–92]. In addition, an important issue is whether concepts are in fact learned by a target audience. Importantly, comics have been shown to be effective in this regard in different contexts, notably in the classroom [12,42]. In our work, we previously showed that comics were particularly effective compared to other methods in terms of conveying meaning and complex biomedical concepts to diverse audiences. Specifically, readers with little previous knowledge of the basic characteristics and biomedical applications of stem cells could grasp complex notions (pluripotency, multipotency, differentiation, reprogramming) by interacting with a tailored comic [26]. The methodology to assess this knowledge increase used structured questionnaires given to participants before and after interacting with different science communication materials on the same topics (texts, interviews, and animations, besides the comic). However, this initial effort had two clear limitations. On the one hand, the materials had been produced by basic researchers without any interaction with target audiences to pre-validate the different approaches or introduce any clarifying changes. On the other hand, impact monitoring was planned after the materials were produced, not as an integral part of the project. It is extremely important that besides the issues already discussed (choosing a type of narrative and graphic style), both issues should be considered when planning a project.

In our current work on metabolic disorders, and as previously stated, we interacted with patients [83] to better tailor the comic book produced [82]. Additionally, we also planned to assess impact using two structured questionnaires before and after interaction with the comic. While the data obtained suggest that the comic was indeed effective in both increasing awareness related to NAFLD, explaining the biochemistry behind the pathology, and transmitting key concepts such as insulin resistance (Alemany-Pagès et al., submitted), it is worth noting that the COVID-19 pandemic greatly limited contact with users of an online platform, thus selecting a specific segment of the possible target audience.

Additionally, although the biochemical aspects may be the same regardless of context, the context does matter when communicating effectively. Besides an understandable and approachable scientific content, if a message is to be received and acted upon, the

audience must be able to fully identify with the situations depicted. These should not seem "foreign" to them [14,16,20,74]. For example, when fictional elements are depicted related to everyday life situations involving human characters, the types of people represented, landscape, housing, clothing, social dynamics, eating habits, environment, etc., must be considered [74,89]. In this case, one size might not fit all, and the same materials might have to be changed to reach different audiences in different contexts (social backgrounds, countries, local environment) effectively [77].

In conclusion, although more structured and planned projects meeting the criteria noted above are certainly needed, comics-based narratives seem to be a valid tool in the field of science communication, specifically in transmitting biochemical and biomedical concepts.

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