Genome Editing Public Engagement Synergy (GEPES)

Guide to analogies and metaphors

13th August 2019
Introduction

Analogies and metaphors can be really useful in helping people understand genomics and genome editing. This guide will help you decide which could work best for your engagement activity. The guide covers:

i) The science the analogy/metaphor is seeking to explain
ii) The pros and limitations of using this analogy/metaphor; and
iii) Helpful tips to put it into practice

This guide has been created in consultation with researchers, engagement experts and others interested in the use of analogies and metaphors in engaging publics with genome editing.

Key considerations

• It is important to consider your audience. How is the analogy or metaphor relevant to them? Are there any ethical or religious considerations?
• Whilst we have not offered any recommendations about which analogies and metaphors are best to use, the Progress Educational Trust and Genetic Alliance UK’s ‘Basic Understanding of Genome Editing’ report singles out ‘final and replace’, ‘copy and paste’ and ‘cut and paste’ as particularly good (if still imperfect) analogies/metaphors for genome editing.
• The use of analogies or metaphors is not always helpful. Referencing something familiar to the publics being engaged can help build understanding, but they are imperfect. So use with care.

Please note that any terms highlighted in bold are explained at the end of the document in the ‘some key terms’ section.
Introduction

Further information

The Wellcome Genome Campus and National Coordinating Centre for Public Engagement have developed a short training workshop on the use of analogies and metaphors in public engagement. To find out more contact: nccpe.enquiries@uwe.ac.uk
A DNA sequence can be written as a series of letters, but each of these letters represents one of the four possible nucleobases that exist in the units that make up a DNA molecule. A genome is all of these letters together so is like 'a book of life'.

The 'genome as text/book' was an especially popular metaphor during and after the Human Genome Project of 1990-2003.

This analogy is commonly used to explain: Genomics
‘cookery book’ or ‘recipe book’

Our genes are like recipes that guide our development / body function. The genome is the book full of these recipes.

If there is a mistake in a recipe then the ingredients we use to make a dish may not come together to create the dish we expected. Genome editing enables us to change the recipe (e.g. 1 tsp salt instead of 1 tbsp) which helps to create the dish we want.

Pros

- The analogy/metaphor is very flexible and can be used to generate a very sophisticated understanding. For example, many different recipes can be used to make the same dish.

- Conversely, the same recipe can result in quite different dishes, depending on the chef’s decisions and the ingredients available. Also not all mistakes in a recipe lead to a problem with the dish. Similarly, with genome editing, not all off-target effects have adverse (or even discernible) consequences.

Cons

- Requires extra context to explain

- It is quite a complex analogy/metaphor and this may hinder or cloud understanding of the basic genomics that sits behind editing

- Not obvious how it can be used to explain the methodology of genomics

- It loses the concept of ‘difference’ and that we are individuals

This analogy is commonly used to explain: Genomics
A blueprint is a reproduction of a technical drawing, an architectural plan, or an engineering design, using a contact print process on light-sensitive sheets. The original blueprints allowed for rapid and accurate copying, such that everyone involved in the build would be working from the same drawing. The process is now largely obsolete but continues to be used informally to refer to various types of plans.

It is commonly used as an analogy/metaphor to describe the genome. It’s use emphasises that the genome contains the complete set of instructions used for making a particular person, animal or plant. ‘Blueprint of life’ is commonly used analogy/metaphor to describe DNA.

Genome editing is like altering that blueprint.

**Pros**

- It conveys the idea of a plan which can then be used to develop multiple copies from an original set of instructions.

**Cons**

- Blueprints have been used since the 1800’s, however with digital reproduction they have become redundant and therefore the term may not be familiar to some audiences.
- ‘Blueprint’ may imply design and this may be divisive when it comes to the different religious beliefs that shape understanding of evolution.
- Very little of our genome codes for anything. Most of it contains no instructions whatsoever.
- Over simplistic – the analogy/metaphor makes people think of a very deterministic code, in which instructions are simply read off a plan, but biology is not like this.
- Ideas of gene expression control, signalling etc. are not incorporated. Genetic instructions in the form of DNA are not really good for anything unless the gene is expressed, and the analogy/metaphor doesn’t really convey this idea – if the blueprint was really a blueprint then all cells would be identical.
- It is hard to convey the consequences of ‘altering’ the blueprint in terms of genome editing.

This analogy is commonly used to explain: **Genomics**
Genome editing allows us to 'cut and paste' using methods such as CRISPR/Cas9 to actually 'cut' DNA at a chosen site. The DNA is replicated on a provided new matrix (of our choice), and is 'pasted' into the genome.

**Pros**
- Widely used
- Commonly used in the media
- Easy to visualise
- Most people have experience of word processing
- Useful starting point before adding the nuance
- Reflects the actual biological process involved

This analogy/metaphor works well as part of an example e.g. changing a single sentence in a novel, use like this it can help give an indication of the complexity and scale of genome editing. Choose an appropriate book for your audience and point out that genome editing is the biological equivalent of replacing sentence three on page 112. (see also find and replace)

**Cons**
- Oversimplification of the technology
- Doesn't capture things like off-target effects
- Makes it sound really easy to do and used in isolation may not give a sense of the scale or complexity.
- May not apply for all versions of genome editing used in the laboratory. Therefore, when using it, you need to understand when it truly applies.

This analogy is commonly used to explain: Genome editing
Genome editing allows us to 'find' the area of DNA to be changed, and we can then 'replace' it with other DNA.

**Pros**

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- Commonly used in the media
- Easy to visualise
- Reflects the actual biological process involved
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This analogy is commonly used to explain: **Genomic editing**
Genome editing technology (e.g. CRISPR) acts like a pair of scissors, cutting or snipping out sections of DNA. The scissors in this context represent a nuclease that is a 'cutting' molecule that breaks DNA during genome editing.

This analogy is commonly used to explain: Genomic editing

**Pros**
- Easy to understand how scissors work
- This analogy/metaphor is used frequently in the press

**Cons**
- Over simplifies
- By itself doesn't cover the repair/change or insertion aspects of genome editing
- Some audiences might take this too literally, and think that real scissors are used. Scale is especially important here as real scissors are several orders of magnitude larger than nucleases.
- Audiences may have different perceptions of scissors e.g. some may perceive as scary and some may perceive as precise.
- Nucleases do not resemble scissors. It's important to convey that the analogy/metaphor relates to function, not appearance.
‘satnav’ (sometimes molecular scissors)

This analogy/metaphor helps represent the **guide** molecule that takes the **nuclease** (or scissors) to the **target** site in a **genome**.

The 'scissors' and 'satnav' analogy/metaphors are often used in combination in relation to **genome editing** (the former conveying the **guide**, the latter conveying the **nuclease**).

One disadvantage of this is that satnavs and scissors are a counterintuitive combination, because these two things are not used together in real life.

### Pros
- Describes the process of the **guide** RNA well
- Can help to discuss **off-target effects** (as sat navs aren't always right)
- Flexibility with desired editing location e.g. change postcode

### Cons
- It doesn't tell the full story. Doesn't deal with editing.
- Hard to embrace the analogy/metaphor fully. What represents the car? How does the **guide** molecule work?
- Hard to extend beyond the sat nav and **guide** RNA
- Not flexible
- Implies that there is outside support (e.g. satellites.) This then naturally begs the question about the role of the scientist.
- Not universally used in English speaking countries

This analogy is commonly used to explain: **Genomic editing**
‘book and editor’

Our DNA is made up of a series of letters, all of these letters together is the genome, like a book. Sometimes books might have mistakes such as typos, genome editing corrects mistakes in DNA the same way a book editor will correct typos.

**Pros**

- Relatable
- Conveys the concept of improvement or repairing 'damage' and the precision by changing a single letter
- Genomes are often described as a series of nucleic acids symbolised by four different letters that form the genetic code which relates to letters in a book

**Cons**

- It evokes the 'book of life' analogy/metaphor, which may not be an accurate
- Books once published cannot be edited.
- Hard to get across the idea of off-target effects
- May suggest that the genome needs to be edited on a normal basis
- Places the role of the editor in a very powerful position
- An editor is usually involved in all aspects of a book, genome editing is usually about very small changes to a genome and this might exaggerate what scientists can do.

This analogy is commonly used to explain: Genomic editing
Our DNA contains instructions to build us in the same way that you could follow instructions to build a house out of Lego.

All the instructions together is called a 'genome', which is like the instruction manual for the Lego house.

Genome editing allows us to make small changes to DNA, similar to if you changed a brick for one which is a different colour or shape.

Pros

• Easy to visualise
• Fun and can be used in conjunction with ‘hands on’ exercises
• Can be adapted easily for engagement activities
• Relates to the idea of building blocks for life
• Could be used broadly to explain genomics

Cons

• When used for genome editing, important to show how this relates to ‘fixing’ or ‘changing’ something. Therefore to demonstrate the process of genome editing whether you are focussing on changing the colour of the brick or changing the shape of the brick, may like to link this to improvements (e.g. a more uniform colour, or a new shape that brings about new functions or form.)

This analogy is commonly used to explain: Genomics and Genomic editing
A 'tool' can help us achieve a goal. The term is used here to refer to the suite of tools that might be available to someone to help us solve a problem. For example, a molecular biologist might employ a specific 'tool' to answer a biological question – just as a builder or electrician might have a box of tools suitable for different jobs.

In the context of genome editing the use of this term need not be limited to a scientific researcher, but could also refer to a doctor treating someone, or even a citizen using genome editing for their own purposes (for example with a DIY CRISPR kit). Needless to say, different jobs will require different tools – hence the idea of a toolbox is useful to convey the wide range of methods and approaches, but also the fact that although many tools are available only one might be suitable in a given application.

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### Pros

- Relatable and can be tailored to all ages
- Can be translated into a visual prop
- Helps convey that there's a range of approaches that can be used in the process of genome editing

### Cons

- Quite vague
- Not a good visual for what the 'tools' are in the toolbox
- Could cause confusion between toolbox as an analogy/metaphor and real 'scientific tools' e.g. pipettes and therefore required lots of context.
- It has been used with different meanings e.g. some people think genome editing is a toolbox in and of itself, rather than part of a set of tools or 'approaches' for understanding gene function. 'Base editing', 'CRISPR', 'TALENs' and 'ZFNs' are generally referred to as approaches rather than tools.
- Doesn't provide a mechanistic explanation of the technology

This analogy is commonly used to explain: Genomic editing
Genome editing allows us to perform a form of chemical 'surgery' on our DNA to fix problems using 'surgeon’s' tools such as CRISPR-Cas9 and TALENs. This happens by accurately excising a precise segment of DNA, which may be replaced with another piece.

The term is generally associated with genome editing, namely 'base editing' though it can be used with other approaches.

This analogy is commonly used to explain: **Genomic editing**

**Pros**
- Conveys the concept of precision in how segments of DNA can be removed (excised) and replaced (swapped). Gives a sense of mechanism (excision – like in surgery) and also accuracy (surgery has to be extremely accurate)
- Conveys a sense of application and helping improve people’s lives.

**Cons**
- Surgery (particularly ‘chemical surgery’) could be seen as scary and daunting and painful
- Might over-sell the likelihood of this being a widely applicable viable therapeutic strategy: most diseases won’t be curable by genome editing, although many conditions are treatable with surgery.
- Doesn’t convey how you would do the surgery in a patient – e.g. which cells? How do you get the DNA into the cell?
- Context needs to be clear e.g. genome editing is really small scale changes
- Oversimplifies the process, raises more questions than it answers (which, in some circumstances may be beneficial.)
‘invisible mending’

'We cut your DNA, open it up, insert a gene and stitch it back up. Invisible mending...It becomes part of your DNA and is there for the rest of your life'

The analogy/metaphor is part of a wider family that relate to textiles and tailoring. Currently these are not widely used, especially in the UK where such industries are in decline.

**Pros**
- Conveys that genome editing is precise and can play a role in helping people
- Conveys that it's to do with repairing/improving something

**Cons**
- Could be hard to visualise
- Mending implies something is broken – which is not a helpful framing for those with conditions that may be affected by this approach.
- May work better in the context of 'tailoring' to help with the visualisation
- Maybe doesn't get across the concept that an existing fault might be taken out before the 'mending' happens
- The analogy/metaphor works well with an image, as you need to convey that it is a weaving method
- Many people will not know what invincible mending is meaning you may have to take time to explain, thereby negating its usefulness as an explanatory shortcut

This analogy is commonly used to explain: **Genomic editing**
martial analogies/metaphors (such as ‘war’ ‘fight’ ‘battle’ ‘soldier’)

Genome editing is a powerful soldier in the fight/battle against disease.

‘War’, ‘fight,’ ‘battle’ are not particularly focused on DNA/genomes/genome editing and are used more in the context of disease.

Pros

• Gets across a sense of being active, empowered – there's things we can do against disease
• Could be used to convey off-target effects through related analogies/metaphors like 'friendly fire'
• Martial analogies/metaphors are common in discussion of certain diseases and their treatment (especially cancer), and genome editing can be characterised as being used (or 'enlisted') in the fight against such diseases.

Cons

• It is violent/scary
• Negative connotations about winning/losing the fight
• Conveys little of genome editing specifically
• Portrays genome editing genome as a destructive process, whereas it is also constructive. Martial analogies/metaphors as a rule risk missing this
• Non-specific for DNA/genome editing
• Generally 'fight' and 'battle' in the context of disease is discouraged. It creates pressure to fight the disease, or implies that those not getting better are not fighting hard enough – when this is not the case.

This analogy is commonly used to explain: Genomic editing
Some key terms
Base editing – An approach to genome editing which does not involve making any breaks to DNA, but instead changes the chemistry of a very small portion of DNA. This can be achieved with a special version of Cas9.

Cas9 (CRISPR-associated protein 9) – The nuclease most commonly used in the CRISPR approach to genome editing.

CRISPR (clustered regularly interspaced short palindromic repeats) – A phenomenon originally discovered in the genomes of bacteria, which protects bacteria against invading viruses. CRISPR was then successfully adapted into an approach to genome editing, and can be used to edit the genomes of most organisms (including humans).

DNA (deoxyribonucleic acid) – A substance via which humans, and most other organisms, inherit characteristics. DNA is present in most of the cells of an organism’s body, and it contains instructions that are vital to the functioning, development and reproduction of the organism.

Genome – The complete set of a biological entity’s DNA, for the life of that entity to be maintained. Entities that have a genome include a cell, an individual organism (for example a human person) and a species (for example the human species).

Genome editing – The deliberate alteration of selected DNA sequences in living cells.

Guide – A molecule that takes a nuclease to the target site in a genome.

Nuclease – A ‘cutting’ molecule that breaks DNA during genome editing.

Off-target effects – Unintended changes to a genome, away from the target, that occur as a result of genome editing.

TALENs (transcription activator-like effector nucleases) – An approach to genome editing that was developed prior to the CRISPR approach, and that continues to be used today (although CRISPR has become more prominent).

Target – A specific part of a genome that is intended to be changed by genome editing.

ZFNs (zinc-finger nucleases) – An approach to genome editing that was developed prior to the CRISPR approach, and that continues to be used today (although CRISPR has become more prominent).
The guide has been developed by the National Coordinating Centre Public Engagement (NCCPE) GEPES team working in conjunction with the Wellcome Genome Campus, the Genome Editing Public Engagement Synergy (GEPES) network and the Progress Educational Trust. We are grateful to the many contributors for their insights, support and expertise in developing this guide as well as the 'Basic Understanding of Genome Editing' report by the Progress Educational Trust and Genetic Alliance UK (supported by the Wellcome Trust).

The NCCPE and the Wellcome Genome Campus were responsible for the GEPES programme which aimed to develop innovation and collective impact in public engagement within genome editing, bringing together those with experience of engaging (or supporting others to engage) the public in genome editing and related fields, to synthesise learning, create tools to be shared, and to encourage high quality public engagement. GEPES was commissioned and funded by Wellcome.

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