Using multimedia principles to reduce visual complexity of transcriptional regulation in cancer

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ABSTRACT

Research studies on the general public's understanding of genetics have demonstrated a poor grasp of genetic concepts, a finding that also appears in undergraduate genetics students, medical students, and practicing physicians. As genetic discoveries are generating more interest from the medical community and the public, creating effective visuals is of increasing importance. Visual learning studies and multimedia design principles have established methods for improving comprehension of biomedical topics. Animation in particular has the benefit of pairing narration and dynamic visuals, which, when used together, benefit long-term memory more than the use of static images. This project employed visual design strategies (such as content mapping), multimedia learning principles, and 3D molecular animation to effectively communicate a complex genetic topic to audiences with a wide range of background knowledge. The final three-minute animation used audio and visuals to expand individuals' prior knowledge of biology and genetics and to teach a molecular concept with a highly complex information architecture.

BACKGROUND

CONTEXT

As discovery science uncovers the impact of genetics on health and disease, visuals have become integral in explaining these phenomena to a broad audience. The Simpson-Querrey Center for Epigenetics is a new initiative of the Feinberg School of Medicine at Northwestern University, whose scientists 1) study the role of the environment in the regulation of genes and 2) apply this knowledge towards developing disease theories and creating new therapies. Biomedical animation is a valuable and attractive method for them to inform the general public, medical students, cancer physicians, researchers, and potential investors about the type and scope of research that is conducted there.

BIOLOGY

Gene expression regulation most often occurs during transcription *elongation*, or the creation of RNA from a DNA template. Proteins called transcription factors regulate elongation by interacting with RNA Polymerase II (Pol II), the enzyme that catalyzes RNA transcription. Modifications to transcription machinery contribute to a large assortment of cancers[1]. Dr. Ali Shilatifard, the Center's director, studies the transcriptional regulation of tumor-inducing oncogene MYC, a well-known participant in many cancers. An approach to treat MYC-related cancers is to reduce its expression[2] by modifying elongation[3,4].

PURPOSE

A poor grasp of genetic concepts has been observed in the general public[5,6], students[7], and medical professionals[8] - suggesting the importance of properly communicating these topics. Studying the visual methods for communicating complex ideas may benefit the life sciences by providing confidence among stakeholders, encouraging collaboration across life science research centers and medical disciplines, and increasing genetics literacy.

	LEARNING PRINCIPLE	STUDENTS LEARN MORE DEEPLY:
1	**Multimedia principle**	From animation and narration than from narration alone.
2	**Spatial contiguity principle**	When on-screen text is presented next to the portion of the animation that it describes than when it is far from the action.
3	**Temporal contiguity principle**	When corresponding portions of the narration and animation are presented at the same time than when they are separated in time.
4	**Coherence principle**	When extraneous words, sounds, and video are excluded rather than included.
5	**Modality principle**	From animation and narration than from animation and on-screen text.
6	**Redundancy principle**	From animation and narration than from animation, narration, and on-screen text.
7	**Personalization principle**	When the narration is in conversational rather than formal style.

Table 1: The seven principles of multimedia learning as described by Mayer & Moreno[9]. These principles are key to designing effective animations in biomedical science.

METHODS

A thorough literature review was conducted to understand the interactions of all of the players that might appear in the animation. Figure 1 describes the process of organizing the research systematically into visual and verbal animation information.

Next, a storyboard (SB) and script were developed using this content. In-depth structural research was conducted to ensure the proper depiction of the ~20 molecules in the animation (Figure 2).

The final animation was created using 3ds Max and Adobe After Effects.

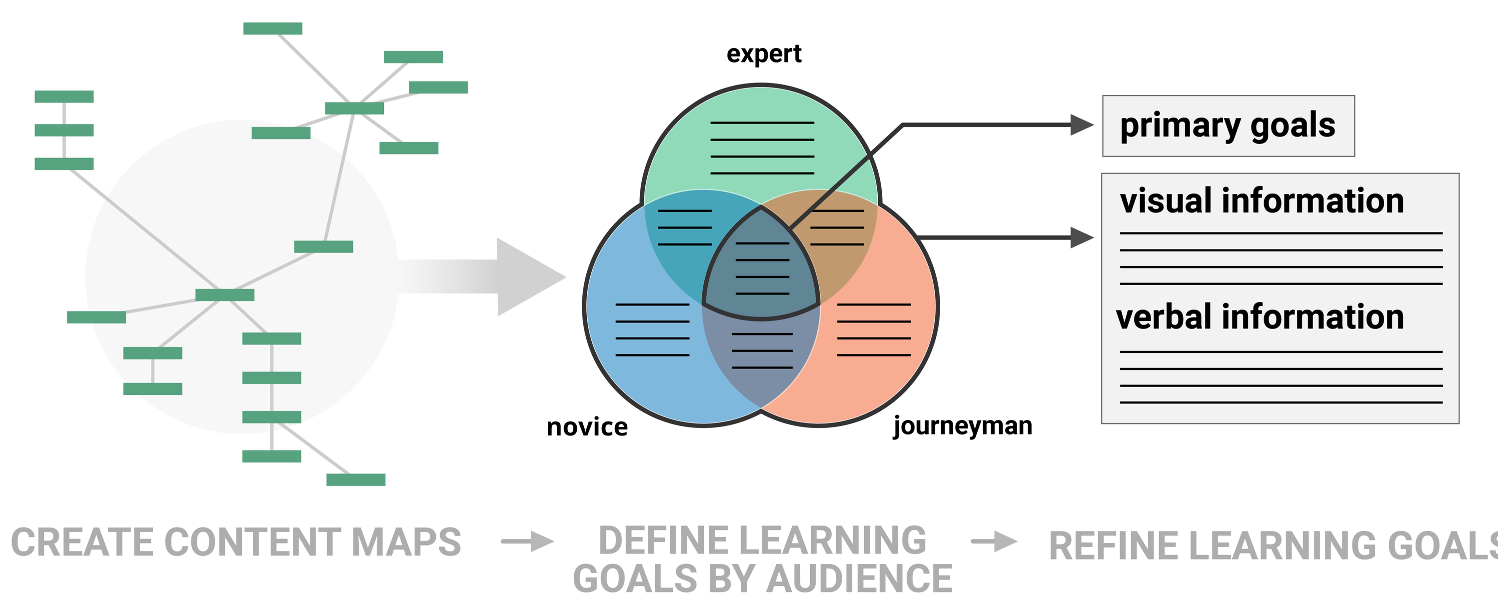


Figure 1: Animation pre-production involved a thorough literature review and content organization. This process began with content mapping, moved into identifying specific learning goals for each audience group (novice, journeyman, and expert), and concluded with a final organization of the learning goals for communicating to a broad audience.

Evaluation took place in two phases. First, the SB was evaluated by 16 UIC Biomedical Visualization students (this population is familiar with SB format and was in the "Journeyman" category - the middle of the three audience subgroups). *(n=16)*

Second, the animation was evaluated by undergraduate students enrolled in the Introduction to Genetics course at UIC. Students were encouraged to share the survey with friends and family in order to capture participants in all three subgroups. *(n=30)*

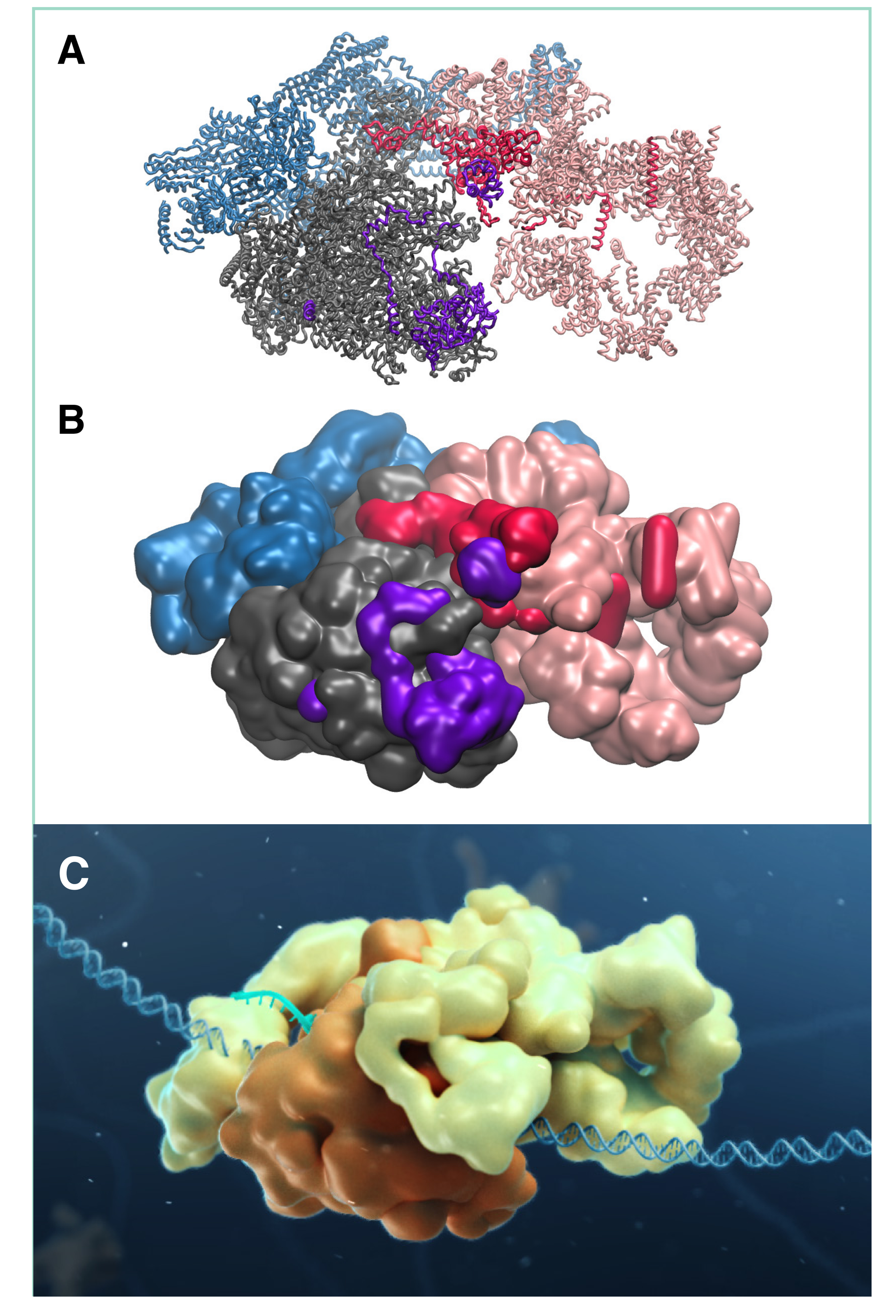


Figure 2: Identifying and assembling molecular structures is an important part of pre-production. Here, the pre-initiation complex is shown A) using its secondary structure via VMD, B) in its surface representation via VMD, and C) as it appears in the final animation. PDB ID 5OQM.

RESULTS

Watch the final animation.

PHASE 1: STORYBOARD

- Increase in knowledge: 63%-85% *(p=0.001)*
- Insights into learning issues (see ex. below)

PHASE 2: ANIMATION

- Increase in knowledge: 63%-74% *(p=0.017)*
- Examined separately, the Novice and Expert groups significantly increased their knowledge *(p<0.01)*; the Journeyman group's increase in pre- and post-test scores was not significant, despite being the highest increase among the three groups.

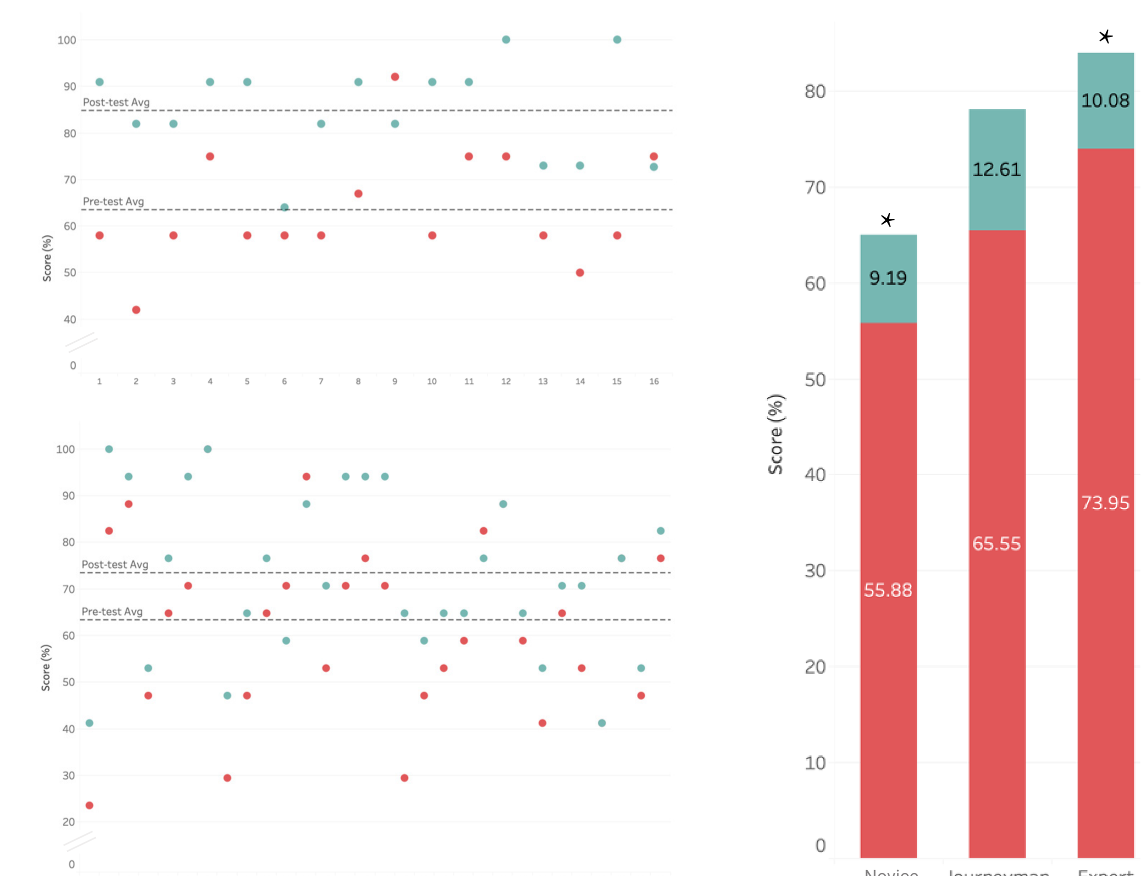
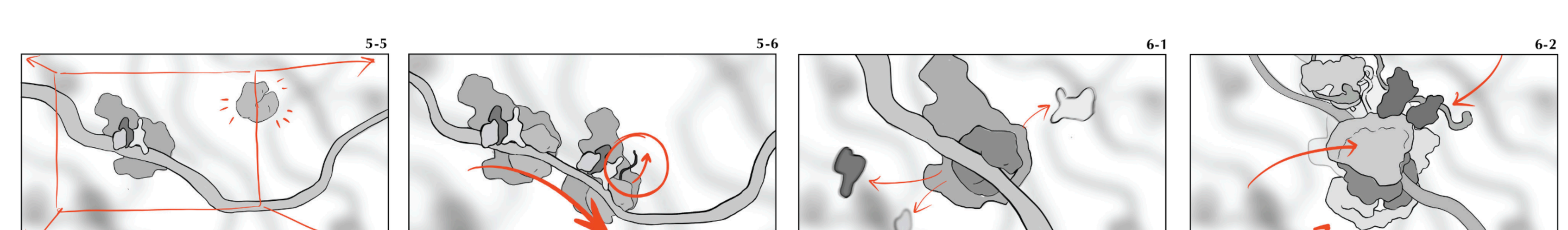


Figure 3: Panels A and B show the data from testing the storyboard (A) and the final animation (B). In both cases, the average test scores demonstrated an increase in knowledge from viewing the visual materials. Panel C shows the difference in performance (teal) across different subgroups after viewing the final animation.

EXAMPLE

Problem areas were identified and corrected after intermediate stage feedback to evaluate the story and visuals (i.e. Phase I: SB). An example of this is shown below. A question about the important stages of initiation and elongation was the lowest-answered question during phase I testing. This was corrected for with subtle multimedia principle changes and resulted in the same question being the highest-answered question in phase II testing. These changes were cues for saliency and the better use of the temporal contiguity principle.



AUDIO: Transcription begins when the enzyme RNA polymerase II, known as Pol II, is recruited to an available gene ...

AUDIO: ... by initiation proteins, where it pauses at the transcription start site.

AUDIO: After initiation, these factors dissociate ...

AUDIO: ... and are replaced by elongation factors that help with RNA production.

Watch the final animation segment, with appropriate edits.

DISCUSSION

This project explored the use of animation to explain the interactions of Pol II, MYC, and the assortment of transcription factors that assist in modulating the rate of elongation, to a broad audience of life science researchers, physicians, and the public.

The effectiveness of this animation was dependent on 1) incorporating the principles of multimedia learning and 2) designing a visual hierarchy that scaffolds the complex content. The Coherence Principle (Figure 1 & 4) was most impactful and took the most time to develop.

For broad audiences, this project shows value in creating custom learning goals for prior knowledge, even if it requires separating the audience into subgroups. By systematic pre-production planning, we were able to increase knowledge across a broad audience. In addition, viewers said the animation was "engaging" and "concise", and had "visual appeal".

High-level biomedical science is important to visualize to increase the public's knowledge of genetics and epigenetics. The lack of understanding of genetics topics in the general public is well-known, and thoughtful visualizations can help solve this problem.

		INCORPORATION / USE IN FINAL ANIMATION:
1	**Multimedia principle**	The animation visually and verbally describes the mechanism of transcription elongation.
2	**Spatial contiguity principle**	While describing factors that influence gene expression, the label and image is presented next to the node that is described in the narration.
3	**Temporal contiguity principle**	The animation coordinated the narration with information presented visually, as when the proteins involved in elongation are being described.
4	**Coherence principle**	Unnecessary information about specific transcription factors was removed; instead, factors were grouped into "initiation factors", "inhibitory elongation factors", and "activating elongation factors"
5	**Modality principle**	The important factors in transcriptional regulation are described with visual cues and narration, for example when elongation factors are described visually (glow and short label) and verbally.
6	**Redundancy principle**	Text was used sparingly to highlight the most important structures for the purpose of recall; for example, the SEC is described with narration, visual cues (glow and text).
7	**Personalization principle**	The inclusion of phrases such as "Let's take a look at the role of transcription in cancer" make the animation personal, rather than conversational.

Figure 4: Final incorporation of the principles of multimedia learning with examples.

CONCLUSIONS

- Created, to our knowledge, the first animation depicting Pol II, MYC, the complex movement of Pol II, and the assortment of transcription factors that assist in initiation-elongation pause release
- Systematically organized a complex biomedical topic into a visual-verbal narrative to optimize learning for a broad audience
- Used multimedia principles to effectively communicating a novel, specific, and highly complex topic in the biomedical sciences
- Demonstrated that, through careful pre-production planning, a complex biomedical animation can increase understanding in people with a wide range of biomedical background knowledge

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