



Applying the 'Models Of' versus 'Models For' Heuristic to support Teachers' Learning of Modelling Practices used in Molecular Biology Research

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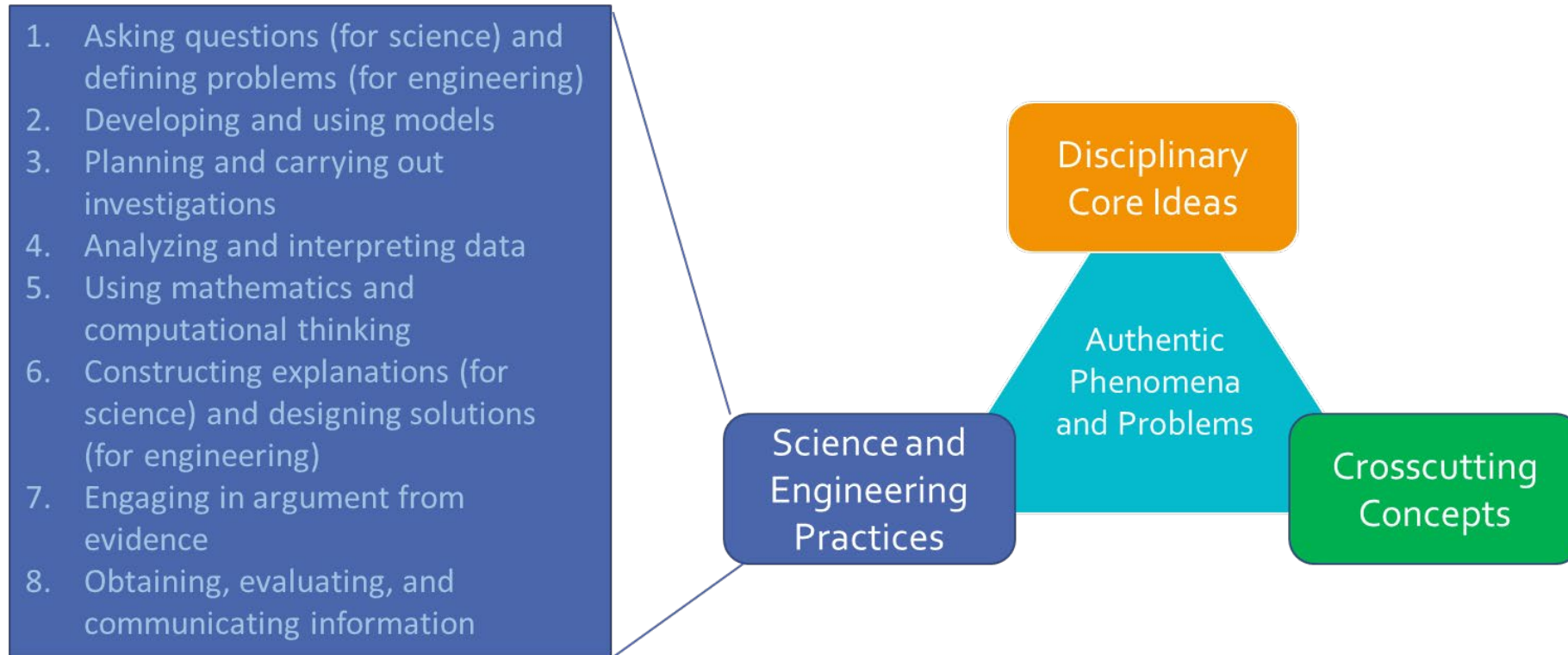
The Pennsylvania State University¹ and Magnolia Consulting²

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Background



- Next Generation Science Standards (NGSS) expects K-12 science teachers to engage students in the practices of scientists and engineers to learn disciplinary core ideas (NRC, 2013).
- These reforms emphasize the importance of not separating the doing from the knowing (Pruitt, 2014).

Background

- Research indicates that relatively few teachers exhibit nuanced understandings of scientific practices that go beyond the rigid, linear scientific method presented in textbooks (Kite et al., 2021).

Most science teachers lack authentic scientific inquiry experiences

Undergraduate labs tend to be confirmatory in nature

Teacher preparation programs do not require science research experiences



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SHAPE MATTERS Program

SHaping Authentic Practices by Engaging in Modelling of
A Research Topic with Teachers to Explore Research in
Science



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SHAPE MATTERS Program



Funded by the National Institute of General Medical Sciences Science Education Partnership Award



Multi-disciplinary team including expertise in from the College of Education, Eberly College of Science, and College of Medicine.



Designed to increase teachers' knowledge of the scientific practices, specifically *Developing and Using Models*, in molecular biology research.



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Why *Developing and Using Models*?



This practice is prevalent in molecular biology research at Penn State.



Teachers' views for how to use models for student learning are highly teacher-centered, mostly describing how they, as teachers, can use models rather than how students can use models for promoting their own learning (Kite et al, 2021).



Teachers frequently view models as teaching tools for representation or explanation but miss using models for developing questions, generating data, making predictions, and communicating ideas (Kite et al. 2021).



SHAPE MATTERS Two-Week Professional Development

- Engaged teachers in *Modelling of* and *Modelling For* (Gouvea & Passmore, 2017) using molecular stories of Diabetes.
- Workshop was intentionally designed to alternate between *modelling of* and *modelling for* such that teachers experienced both approaches and gain a deeper understanding of the way in which scientists develop and use models in authentic research.

Modelling Of

- Focused on mapping between the real molecule and its representation
- Using only modelling of creates a false sense that models simply map onto the real-world in some one-to-one way

Modelling For

- Emphasizes the ways in which models are built and used in science as tools that support inquiry and exploration



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SHAPE MATTERS Workshop Modelling Activities

Sequence of Workshop Activities	Modelling Practice
Water Kit (3-D Molecular Designs)	Modelling of
Process of Crystallizing Molecules	Modelling for
Amino Acid models and Starter Kit (3-D Molecular Designs)	Modelling of
X-ray Crystallography Lab - from crystals to 3-D visualizations	Modelling for
Insulin MRNA to Protein Kit (3-D Molecular Designs)	Modelling of
Exploring the Protein Data Bank	Modelling for
JUDE Tutorials and 3-D Printing Models	Modelling of
Investigation of Designer Insulins	Modelling for
Developing Molecular Stories from Research at Penn State	Modelling for



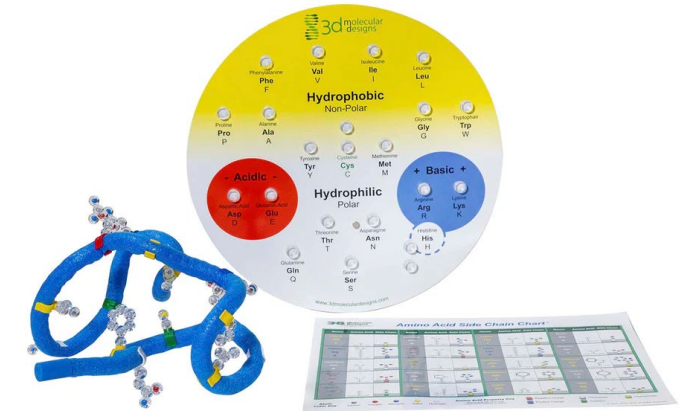
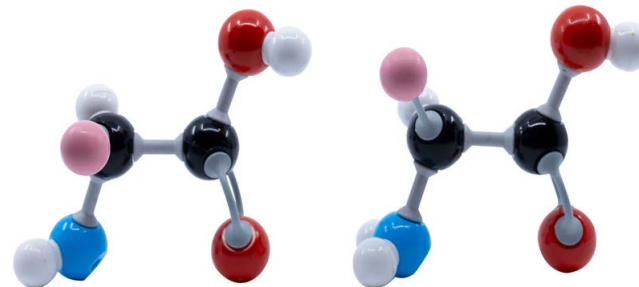
SHAPE MATTERS Workshop Modelling Activities

Water Kit (3-D Molecular Designs)

Process of Crystallizing Molecules

Amino Acid models and Starter Kit (3-D Molecular Designs)

X-ray Crystallography Lab - from crystals to 3-D visualizations



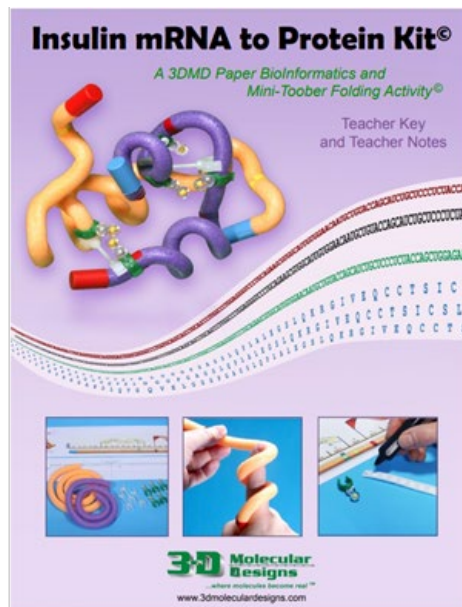
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SHAPE MATTERS Workshop Modelling Activities

Insulin mRNA to Protein Kit (3-D Molecular Designs)

Exploring the Protein Data Bank

JUDE Tutorials and 3-D Printing Models



8. Adding Bonds:

JUDE has the ability to render different bonds within the protein like Hydrogen Bonds and Disulfide Bonds between Cysteine amino acids. If you wanted to 3D print your protein, you could also add additional structural supports called Struts.

One important feature of our insulin protein is the presence of disulfide bonds. In order to show all of the disulfide bonds in insulin, you will need to select all.

To select all:

```
select all
```

To show your disulfide bonds at 1.0 angstrom thickness:

```
ssbonds 1.0
```

Disulfide bonds occur between two cysteine amino acids. Your disulfide bonds currently look like they are floating, because the backbone format only shows the position of the alpha carbon.

To set your disulfide bonds in the backbone:

```
set ssbonds backbone
```

To color the disulfide bond yellow:

```
color ssbonds yellow
```

To see explore to add how to add and format hydrogen bonds, check the JUDE commands page here.



Modeling 'of'
Insulin mRNA to
protein kit




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SHAPE MATTERS Workshop Modelling Activities

Investigation of Designer Insulins


Developing Molecular Stories from Research at Penn State



2021-2022

Can you turn an Adenine Riboswitch into a Guanine Riboswitch?

Heather Jones - Beverly Hills Middle School
Daniel Williams - Shelter Island High School
Dr. Philip Bevilacqua, Lauren McKinley and Jacob Sieg - Penn State Eberly College of Science, Department of Chemistry



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Eberly College of Science

Introduction

Ribonucleic acid (RNA) is a single stranded molecule made up of alternating sugar (ribose) and phosphate groups. Attached to each sugar is one of four bases - Adenine (A), Guanine (G), Uracil (U) and Cytosine (C). RNA is more than just a messenger - more than 30 other classes of RNA are known and some small RNAs have been found to be involved in regulating gene expression.

Riboswitches are recently discovered RNA sequences that can turn gene expression on or off. Riboswitches form complex, folded structures that selectively bind ligands (3). Riboswitches are widespread in bacteria and understanding their mechanisms can help us target infectious bacteria and develop antibacterial agents.

Dr. Bevilacqua and his lab are interested in the discovery of new riboswitches and being able to "deorphanize" predicted riboswitches by identifying the ligand they bind. Purine riboswitches (A,G) are great examples of riboswitch structural changes and RNA evolution.

Secondary and Tertiary structure

Adenine riboswitch **Guanine riboswitch**

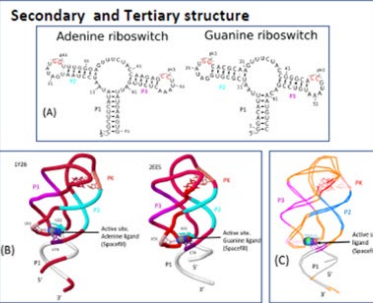


Fig. 2: (A) Secondary structure of Adenine and Guanine Riboswitches, displaying the P1, P2 and P3 complementary Watson/Crick base pairing regions and the pseudoknot (PK) binding region. (B) Tertiary structure of the Adenine (pdb 1Y26) and Guanine (pdb 2EES) Riboswitches, displaying the P1, P2 and P3 complementary Watson/Crick base pairing regions (colored backbone) and the pseudoknot (PK) region (wireframe G/C nucleotides). Also highlighted are the two active sites with Adenine and Guanine displayed (spacefill). (C) Pymol alignment of 1Y26 and 2EES showing the almost complete similarity of the two different riboswitches, displaying the P1, P2 and P3 complementary Watson/Crick base pairing regions, the pseudoknot (PK) region and the active site.

Active Site - Ligand Binding

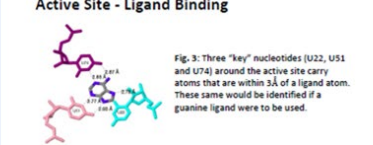


Fig. 3: Three "key" nucleotides (U22, U51 and U74) around the active site carry atoms that are within 3Å of a ligand atom. These same would be identified if a guanine ligand were to be used.

Data collection and analysis:

Shape

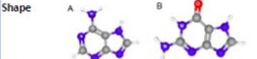


Fig. 4: Fig. 4: Shape of (A) Adenine Ligand (B) Guanine Ligand

Size

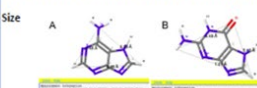


Fig. 5: Size of Adenine Ligand and Guanine Ligand (A) Adenine Ligand size measurement along the Watson/Crick Face, Sugar Face, Hoogsteen Face (B) Guanine Ligand size measurement along the Watson/Crick Face, Sugar Face, Hoogsteen Face

Hydrogen bonding

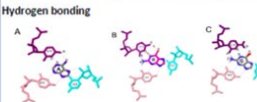


Fig. 6: Hydrogen bonding of Adenine Ligand and Guanine Ligand (A) Hbonds of U74 with Adenine Ligand (B) Hbonds of U74 with Guanine Ligand (C) Hbonds of C74 with Guanine Ligand

Summary

A modest change of the nucleotide in position 74 of the RNA molecule from a Uracil to a Cytosine allowed an Adenine riboswitch to act as a Guanine riboswitch, this needs to be experimentally verified in the lab.

In the future we can also model and experimentally test the pyrimidine riboswitches (Cytosine and Uracil) to see if they behave in the same fashion as the purine riboswitches.

Finally, we can examine other mutations in the active site to see if they can bind other nucleotides.

This research is significant in many ways. It can help us in understanding regulation of genes in bacteria, system manipulation that can be used to drug development, understanding how ligands bind RNA to develop drugs and control gene expression.

This research is also important to the RNA world hypothesis, self-replicating RNA multiplied before the evolution of DNA and proteins, we can use this to study the origin of life.

Finally, with this research, we have a new lens into molecular evolution in which the change of just one nucleotide can automatically cause a new riboswitch ligand interaction.

Molecular Story

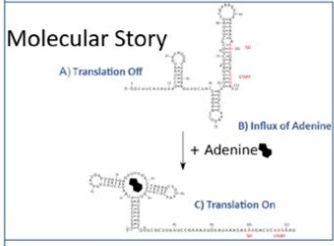


Fig. 1: (A) Folded, mainly ds mRNA from bacteria can not be translated as the Shine-Dalgarno (SD) site and the start codon are base paired and not accessible, translation is off. (B) A cellular process increases the concentration of adenine (DNA degradation or NT salvage). (C) Adenine binds to the riboswitch inducing a major conformational change, the Shine-Dalgarno (SD) site and the start codon are now as mRNA, accessible to the ribosome, translation is now on.

Lys_{B28}Pro_{B29}-human insulin HumalogTM Aka lispro

Mutation: inversion of position 28 and 29 amino acids at the C-terminal end of B chain

How does this structural change lend to a functional change?

Eliminates hydrophobic interactions to weaken terminal B-sheets hydrogen bonds that stabilize the dimer

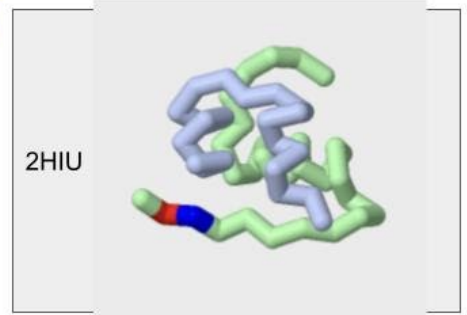
How does your model represent this change?

Kink near c terminus of 1LPH due to inversion near one end of B-sheet in dimer may destabilize bonds of B sheets

May weaken hexameric structure contributing to faster acting properties

Research question:

Compare distances between sidechains across B-sheets for both insulins



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Teacher Participants

- 24 teachers total over three different cohorts
- Most teachers taught high school (grades 9-12)
- 88% of teachers had a Master's degree
- 63% taught in Pennsylvania schools
- Credentialed in:
 - 75% Biology
 - 34% Chemistry
 - 34% General Sciences

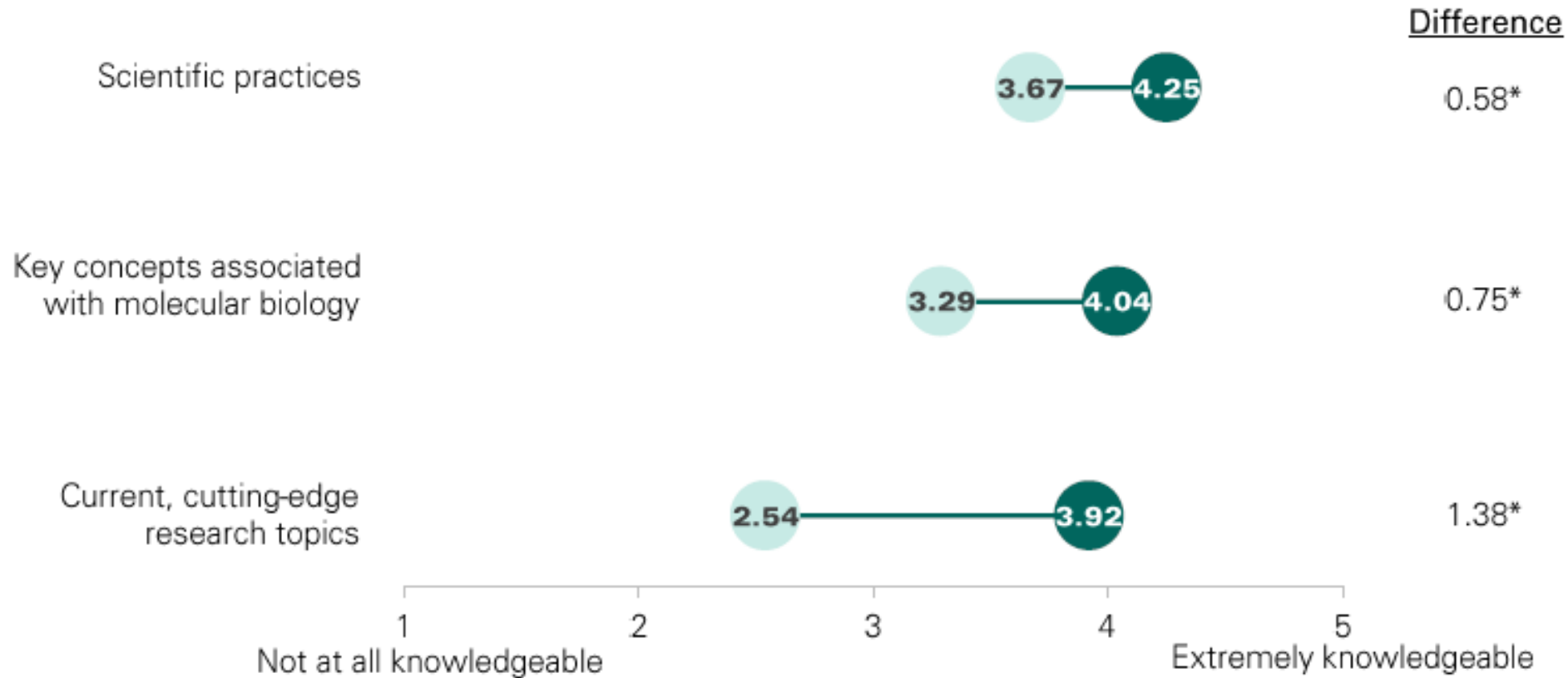
Evaluation Methods

- Mix-methods formative and summative evaluation
- Multiple data collection methods
 - Teacher Surveys (Summer Workshop Survey and Molecular Modelling Survey)
 - Project Team interviews
 - Teacher interviews and focus groups
 - Review of documents and existing data
- Data analyzed
 - Quantitative- descriptive statistics on closed-ended survey items, paired samples t-tests
 - Qualitative – Open ended survey items and interviews analyzed using open coding and thematic analysis, Triangulation of findings.



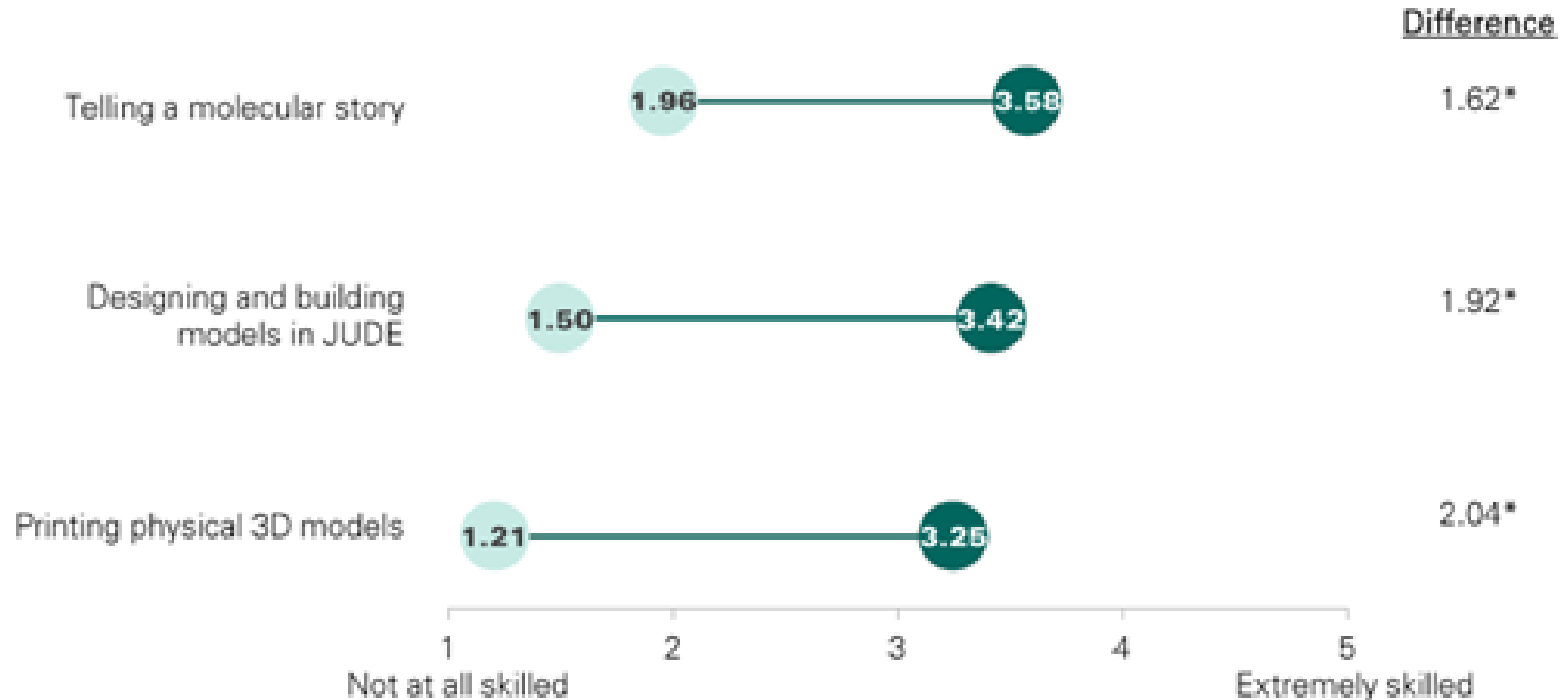
Teachers' self-rated knowledge before and after workshop

(light green) (dark green)



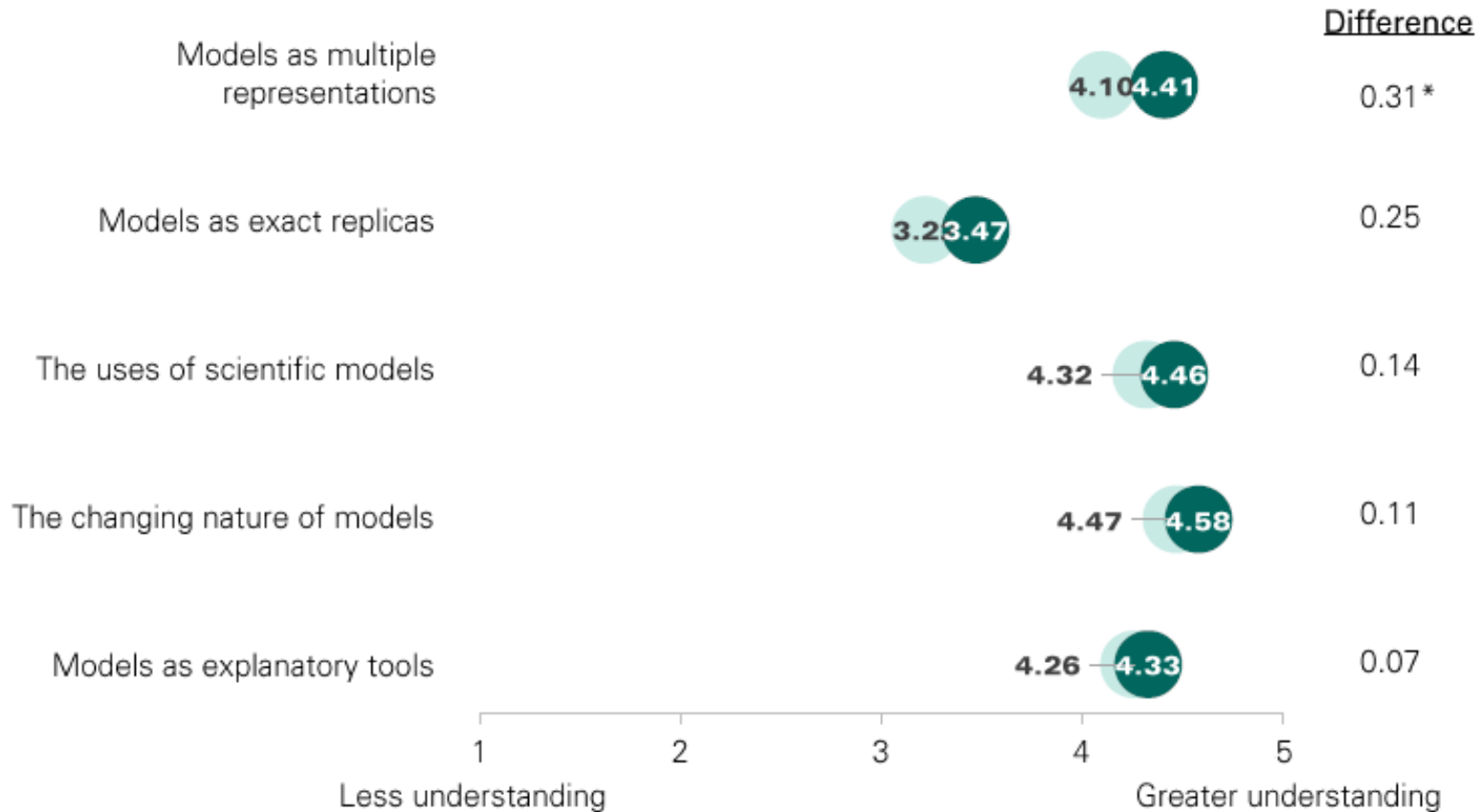
*Statistically significant paired samples *t*-test at $p < .05$.

Teachers' self-rated skills before and after workshop



*Statistically significant paired samples t-test at $p < .05$.

Teachers' knowledge of molecular modelling before and after workshop



*Statistically significant paired samples *t*-test at $p < .05$.

Discussion and Conclusions

- Professional development focused on the practice of developing and using models by leveraging the expertise of the multi-disciplinary team of science researchers and science education faculty.
- Alternating back and forth between modelling of and modelling for helped teachers to gain a better understanding of the modelling practice.
 - Evaluation shows statistically significant growth in their understanding of the modelling practice.
- The findings are limited to a small sample size of teachers and the knowledge findings are all self-reported.



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Thank you.

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