“How would you like to live in Looking-glass House, Kitty? I wonder if they’d give you milk, there? Perhaps Looking-glass milk isn’t good to drink…”

Lewis Carroll

In a traditional discussion of optical isomerism at the general chemistry level, one typically notes that most biologically important molecules are chiral and points out that this means that they are therefore not superimposable on their mirror images. While one can explain the concept of and conditions necessary for optical activity in molecules and demonstrate the rotation of plane-polarized light by a glucose solution (I), the discussion tends to lack context. Even the relationship between the left hand and the right can be confusing, and demonstrating the relevance of this idea to molecules can be quite challenging. A recent article by Luján-Upton addresses this topic in the form of a mystery to be solved (2).

As another strategy for engaging the students in this topic and for relating it to the caloric value of food and the identity of organic functional groups, I have asked my students to consider the following open-ended test question. It was offered to them several days ahead of the test to allow them to think about it and with only the restriction that they could not ask me for the answer(s).1

In the book Through the Looking Glass and What Alice Found There by Lewis Carroll (3), Alice (of Alice in Wonderland fame) walks through a mirror into a mirror-image world. Assuming that she is not changed by this transition, her enzymes are still only capable of processing molecules of the handedness of her native world. In short, she has a problem that will severely curtail the duration of her stay because when she gets hungry she can eat, but her body cannot make use of most of the calorie-containing molecules. In a traditional discussion of optical isomerism at the general chemistry level, one typically notes that most biologically important molecules are chiral and points out that this means that they are therefore not superimposable on their mirror images. While one can explain the concept of and conditions necessary for optical activity in molecules and demonstrate the rotation of plane-polarized light by a glucose solution (I), the discussion tends to lack context. Even the relationship between the left hand and the right can be confusing, and demonstrating the relevance of this idea to molecules can be quite challenging. A recent article by Luján-Upton addresses this topic in the form of a mystery to be solved (2).

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In the book Through the Looking Glass and What Alice Found There by Lewis Carroll (3), Alice (of Alice in Wonderland fame) walks through a mirror into a mirror-image world. Assuming that she is not changed by this transition, her enzymes are still only capable of processing molecules of the handedness of her native world. In short, she has a problem that will severely curtail the duration of her stay because when she gets hungry she can eat, but her body cannot make use of most of the calorie-containing molecules such as glucose that exist naturally in the mirror image world. Her enzymes are designed for digesting its enantiomer, D-glucose. So the question is, what can Alice eat in the mirror-image world that provides nutritional value to her?

If this problem were posed to a high-level biochemistry class, the students might consider looking for those digestive enzymes that are sufficiently nondiscriminating to permit the metabolism of nonnative substrates. However, there is a much more clever answer that younger (general or organic chemistry) students could easily comprehend. As further explanation into the nature of the question and answer (without giving it away), one can point out that a compound absolutely necessary for her survival, water, is the same in both worlds. Water is an example of an achiral molecule; it is superimposable on its mirror image. Other necessary compounds such as sodium chloride and dioxygen are also achiral and readily used by her body.

One attractive aspect of this problem is that it draws on several other concepts presented in general chemistry. The caloric value of foods is usually described in the context of thermochemistry and the three major food components, carbohydrates, proteins, and fats (macronutrients [4]), which are discussed along with their respective calorie content. Most textbooks include some elementary biochemistry where the 20 amino acids are presented as the building blocks of proteins. Similarly, the structures of sugars and fats are given, along with a discussion of their organic functional groups. In the lab portion of my particular course, stearic acid (the saturated C_{18} fatty acid) was used for the experimental determination of Avogadro’s number (5), so the students had additional familiarity with the concept of a fatty acid.

It is easy to show with models that of these three components, carbohydrates, typified by glucose (and its polymer, starch) and all but one amino acid, hence essentially all proteins, are not superimposable on their mirror images and are thus not of nutritional value to Alice. However, some fats are achiral, hence useful to Alice because they are exactly the same molecule in both worlds. These would be symmetrically substituted esters of glycerin (triacylglycerols) that possess an internal mirror plane (i.e., the fatty acids attached to carbons 1 and 3 of the glycerin molecule are the same). Obviously, this classification includes all those that have three identical fatty acid groups (simple triacylglycerols), such as tristearin, which has three stearate chains.

As an aside, a general triacylglycerol without a mirror plane, such as one prepared from three different fatty acids, is chiral, so its enantiomer in the mirror image world would, in principle, not be of use to Alice. This is simple to demonstrate with a model set. However, many of these enantiomeric pairs are not necessarily so different chemically from each other. A given compound can be related to its mirror image by the exchange of fatty acids on carbons 1 and 3 (Fig. 1), which might be structurally similar (e.g. stearate and palmitate, both saturated hydrocarbon tails of length 18 and 16 carbons, respectively).

Figure 1. Relationship between enantiomeric triacylglycerols.
One might even suppose that some concentration of each enantiomer exists in both worlds. But more importantly, one can infer that some of the enzymes responsible for ester hydrolysis in fats are sufficiently flexible to tolerate both substrates, which would make them both nutritionally valuable (6). Note that the glycerin molecule and each of the free fatty acids are individually achiral, so that after hydrolysis, stereochemistry is no longer an issue.

Several other solutions to the problem were accepted, including the achiral amino acid, glycine, and the most unequivocal and clever answer, ethanol. Consumption of the latter is, of course, a natural topic for college students but a particularly humorous answer considering that Alice is a young child. Vodka is a relatively unadulterated aqueous solution of ethanol, which might be an important consideration; other chiral compounds present of the wrong stereochemistry, such as flavorings and colorings, might happen to be toxic. A metabolic product of ethanol, acetic acid (vinegar), is also a correct answer. Finally, she could also eat other naturally occurring achiral compounds that we don’t ordinarily think of as food per se, but which have caloric value—such as citric acid or glycerin, mentioned before.

To elaborate on this exercise, one could consider biochemical extensions of this question to vitamins that Alice might require. For instance, of those she needs, her own body synthesizes vitamin D, whereas β-carotene (a source of vitamin A) is achiral, as is thiamine (vitamin B₁, Fig. 2). However, ascorbic acid (vitamin C, Fig. 2) is chiral and there would presumably be no source of the enantiomer that she needs in the mirror-image world. Interestingly, whereas only a single stereoisomer of α-tocopherol (d-α-tocopherol) occurs naturally in our world (a form of vitamin E, Fig. 2), research with synthetic α-tocopherol, a mixture of all eight possible stereoisomers,² has shown that the enantiomer of the naturally occurring molecule is also somewhat efficacious (7). So Alice should be able to tolerate mirror-image vitamin E. This is, perhaps, not surprising because the antioxidiant ability of vitamin E is associated with the bicyclic system, not the alkyl tail.

If Alice came down with a headache, acetylsalicylic acid (aspirin) and acetaminophen (Tylenol) are both achiral and hence useful, but naproxen sodium salt (Aleve) is chiral (and the other enantiomer, which would have been the one marketed in the mirror world, is reported to be a liver toxin [8]). Conveniently, ibuprofen (Advil or Motrin) is also chiral but is sold as a racemate (an equal mixture of the two enantiomers), so it would be an equally effective pain reliever for Alice in both worlds (Fig. 3) (9).

Fortunately for Alice, if she’s addicted to her morning coffee, caffeine is achiral; but if it’s cigarettes she’s hooked on, she’s in trouble because nicotine is chiral. In a fascinating twist, because the two enantiomers of carvone and limonene both exist in both worlds and are responsible for distinct flavors, smells (and perhaps tastes) will be inverted. To Alice in the mirror-image world, a caraway seed bagel will taste like spearmint and a stick of spearmint gum will taste like caraway (Fig. 4). Similarly, lemons will smell like oranges and oranges like lemons (10).
Acknowledgments

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Notes

1. This question could also be used as a topic for class discussion.

2. Note that the molecule has three stereocenters, each of which can have two possible absolute configurations: $2^3 = 8$. Natural $d$-$\alpha$-tocopherol has RRR absolute configuration.

Literature Cited

The beautiful spring day made Alice reluctant to go into her dorm. She knew, though, that she had to study hard for her organic chemistry exam Professor Emil Fischer was giving the following day.

As she entered her room, she found her cat, Kitty, eagerly awaiting her arrival. Alice sighed. “I’m sorry, Kitty. I’d love to play with you, but I have to study for my stereochemistry test tomorrow.” Kitty tilted her head as if to say, “What’s that?” Alice smiled at the cat’s reaction, then settled into her favorite soft chair, opened her organic chemistry text, and began to read.

Alice’s stereochemistry reading went well for a while, but the hypnotic effect of the cat’s purring and the long day had their inevitable effect. The text began to blur, and Alice’s head nodded more and more frequently.

Alice found herself staring at her image in the full-length mirror hanging in her room.

“We’re always talking about mirror images in my organic course, Kitty. I think that I’ll see what life is like on the other side of the mirror.” And with that, Alice stepped magically through the looking glass and entered Mirror Image Land.

* * * * *

“Who are you?” asked a startled old man wearing a rumpled tweed jacket.

“I’m Alice, from the other side of the mirror. Who are you?” asked Alice.

“I am Professor Rehcsif Lime, an organic chemist. May I ask why you came here?”

“I came here because I want to see what life is like in Mirror Image Land.”

“I see,” said the Professor. “I think that you will find that life is quite different here. Would you like a stick of sugar-free spearmint gum?”

“Why yes, thank you,” replied Alice. She unwrapped the gum and started to chew.

“Bleeeech!” exclaimed Alice as she spit the gum out. “It tastes like sweet rye bread.”
“Yes, I thought that would be the case. You are not like us, you see,” said Professor Lime, grinning like the Cheshire cat.

“What do you mean?” asked Alice, still trying to get rid of the terrible taste in her mouth.

“Well, the spearmint plant in your world makes l-carvone, which is associated with the smell and taste of spearmint. But this is a mirror image world, and our spearmint plants make its mirror image, d-carvone. Because your taste buds and scent receptors are still the same, you perceive our spearmint gum to smell and taste like caraway, which is associated with d-carvone.”

“I still don’t understand,” said Alice. “Is everything going to be different on this side?”

“Well, no. Take baseballs, for instance. They’re the same in our world as in yours. But the gloves, now they’re different. The mirror image of a right-handed glove from your world doesn’t fit onto your right hand very comfortably. We say that balls are achiral, but gloves are chiral, that is, not superimposable on their mirror images. Of course, the mirror image of a right-handed glove fits your left hand perfectly.”

The Professor looked sad as he added, “I’m afraid you can’t stay here for very long Alice or you’ll run into problems.”

“Problems? But why? I’m able to walk and breathe just as if I were at home. Could I eat when I got hungry?”

“I’m afraid that would be the difficulty for you, Alice. All of your enzymes are mirror images of our enzymes, and yours aren’t adapted for digesting our food. Here, everything is the mirror image isomer, the enantiomer, of what exists in your world. Your enzymes won’t allow you to use any of our proteins, because our amino acids are mirror images of yours. Enzymes and the molecules that they act on have to fit together in a lock-and-key fashion for the enzymes to catalyze reactions. Your enzymes just aren’t arranged to process some of our molecules.”

“I study organic chemistry,” said Alice, “so I know that my enzymes only fit L-amino acids, but won’t they work with yours too?”

“No,” said Professor Lime. “Our amino acids are mirror images of yours. They are D-isomers, and that is all that my enzymes will digest. Here you could digest only one amino acid. It would be unlikely that you could derive nutritional value from any of the others.”

“Could I eat starches here?”

Professor Lime shook his head glumly. “No, you couldn’t. Think about what your starches are composed of compared to ours. Eating our starches wouldn’t help you. You’d soon starve.”

“Couldn’t I eat fats?”

“Excellent. You may have something there. You could eat some fats, but not others. You would have to be very careful just what fats you choose to eat or your enzymes will not be able to digest them. You would have to limit yourself to eating fats that are the same in both worlds.”
Alice was puzzled by Professor Lime’s comments.

“Professor, this is beginning to give me a terrible headache.”

“Oh dear, you must be careful what you take as a pain killer. Some that would help you in your world would not work here, and others would be effective both here and there. Also, the mirror images of some drugs that help in your world would be poisonous. You would have to choose very carefully.”

“But how can I know which ones will help me and which will not?”

Professor Lime furrowed his brow, thought for a moment, and then said, “Well, you can breathe the air here, can’t you?”

“Yes.”

“Well, there is your answer. Because our air works for you, you can use anything that is like our air.”

Alice’s headache grew steadily worse as she puzzled over Professor Lime’s latest pronouncement. She said, “But I can’t eat air. Whatever do you mean?”

“Of course you can’t eat air. I only meant that you could consume things that have the same characteristics as air. You can drink our water, for example.”

“Professor Lime, water isn’t like air. Water is a liquid and air is a gas. What do they have in common? What do you mean?”

Ignoring Alice’s question, the Professor continued, “Then, of course, vitamins would be a problem for you too. You could take some of ours, but others would do you no good.”

Her frustrations mounting, to say nothing of her headache, Alice said, “You’re right, Professor Lime. I enjoyed meeting you, but I’m afraid that life in Mirror Image Land is too much for me to handle. I’m going back through the mirror where things fit me better. Besides, I have to study for my stereochemistry test.”

“Goodbye, Alice. I enjoyed meeting you too. Good luck on your examination.”

With that, Alice found herself back in her room, seated in her favorite chair, with Kitty purring on her lap. She knew that she had been dreaming, but it all seemed so real.

“You know, Kitty,” she said, “I guess I have been dreaming, but someone that I met in my dreams may have helped me to think about stereochemistry in a whole new way.”

**Questions**

Note that all of these questions and their answers assume that Alice is unchanged when she steps through the mirror.

1. Professor Lime tells Alice that she could digest only one of the amino acids found in Mirror Image Land
(mil), but couldn't digest any of the proteins found there. Which amino acid could Alice eat? If she can eat an amino acid, why can't she eat mil proteins?

2. In our world, starch is a polymer formed from a single monomer unit, D-glucose. How would mil starch differ from our starch? Draw the structure of the monomer unit that would be present in mil starch.

3. Professor Lime tells Alice that she could eat some mil fats, but not others. We will limit our consideration of fats to mono-, di-, and triglycerides that are formed from glycerol and various achiral fatty acids. The general structures for these compounds and glycerol, are shown below:

Assuming that the fatty acids represented by the R-groups may be the same or different, and further assuming that they are not themselves stereogenic (chiral), decide which glycerides (fats) Alice could safely eat in mil.

4. The structure of carvone is shown below, but its stereochemistry is not specified.

![structure of glycerol, 1-monomoglyceride, 2-monomoglyceride, 1,2-dimoglyceride, 1,3-dimoglyceride, triglyceride]

Literature sources (cf. S. Budavari, ed., *The Merck Index*, 1996) indicate that l-carvone (the R-isomer) smells like spearmint, and d-carvone (the S-isomer) smells like caraway. Draw the structures of the two carvone enantiomers and correctly label each. Specify the priorities that you have assigned to the groups attached to the stereogenic carbon atom.
5. The sweetener in the sugar-free gum that the Professor gives to Alice is a carbohydrate named xylitol.

\[
\begin{align*}
\text{O} & \\
\text{\includegraphics[width=0.2\textwidth]{xylitol.png}} & \\
\end{align*}
\]

What can you say about the chirality of xylitol?

6. Professor Lime cautions Alice that she must be careful what pain reliever she chooses to take to relieve her headache. Shown below are the structures of four commonly used analgesics. If we assume that only the mirror image isomers of these compounds were available to Alice in MIL, which of these compounds would be good choices for Alice to take?

7. Alice is confused when Professor Lime tells her that because she can breathe in MIL she can eat anything that is “like our air.” He also includes water in the things that Alice could use safely in MIL. Explain the Professor’s reasoning when he made these statements to Alice.

8. The Professor cautions Alice that she would be able to use some MIL vitamins, but that others would not work for her. The structures of β-carotene and three important vitamins are shown below. Which of these could Alice use, and which would be ineffective for her in MIL?

\[
\begin{align*}
\text{Acetylsalicylic acid (aspirin)} & \\
\text{Ibuprofen} & \\
\text{Acetaminophen} & \\
\text{Naproxen sodium salt} & \\
\end{align*}
\]
This case is based on an article that considered the problems that would arise if a person were to cross over into a mirror-image environment (G.T. Yee, "Through the Looking Glass and What Alice Ate There," *Journal of Chemical Education* 79:569–571). Some of the stereochemistry problems posed in that article are woven into this case study.

![Chemical structures](image.png)

**Image Credits:** Story graphics adapted from John Tenniel's illustrations for Lewis Carroll's *Alice's Adventures in Wonderland* and *Through the Looking Glass.*