# How to hack nature – teacher notes

***Education in Chemistry***January 2019
rsc.li/2LezCiZ

1. Describe, using bullet points or a flow chart, the natural evolution of a protein.
* *genes coding for proteins randomly mutate*
* *the mutation may lead to a better protein*
* *the improved protein improves the survival chances of the organism it inhabits*
* *the mutated gene is passed on the next generation*
* *after many rounds of rare, beneficial mutations that end up being passed on, a perfectly adapted protein eventually evolves.*
1. Why are the enzymes we find in nature nowadays less suited to non-natural applications compared to ancient enzymes?

*Modern natural enzymes are so well adapted to their specific reactions and conditions that they have become less able to catalyse reactions other than the ones they usually catalyse.*

1. Explain why ancient enzymes are more suitable for laboratory or industrial applications, and describe the steps you would need to take to find a suitable ancient enzyme for catalysing a laboratory reaction.

*Ancient enzymes have been through less evolution and so less fine-tuning. They are very evolvable and also more stable (eg to heat).*

*Ancestral sequence reconstruction is needed. This involves calculating the common ancestor gene for a group of enzymes that perform a similar role to the desired one. Computational methods are used for the calculations. The common ancestor gene is then inserted into a bacteria which hopefully produces the right enzyme.*

1. Below is some information about the Diels–Alder reaction. Use this information and the article to answer the questions.



1. Why is the Diels–Alder reaction so important for chemists?

*The article says it is used everywhere. Examples given include in the synthesis of antibiotics and anti-cancer drugs.*

1. Predict the product(s) from the Diels–Alder reaction shown below and suggest why a Diels–Alderase enzyme may be useful in this reaction.

*Solution*



*An enzyme may allow the reaction to take place at a lower temperature. It may also mean one of the products is produced in a higher yield rather than a mixture of products.*

1. The figure below shows sitagliptin.



1. Copy the structure and identify the chiral centre.
2. Compare and contrast the traditional synthesis with the enzyme-catalysed synthesis.

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| --- | --- |
| ***Traditional*** | ***Enzyme*** |
| *Rhodium and iron catalysts**Produces a mixture of enantiomers**Needs chiral purification* | *Transaminase catalyst**Produces a single enantiomer**No chiral purification needed* |