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# *The Humpty Dumpty Dilemma*

Chemical Biologist Neil Kelleher:  
*Measuring Proteins*

**FINDINGS**

National Institutes of Health  
National Institute of General Medical Sciences

# *Neil Kelleher Weighs in on Proteins*

*Chemical biologist Kelleher wants to find better ways to measure proteins.*

## *Proteins*

- Are central to life
- Begin as genetic instructions
- Can gain or lose mass



*Question:*

What is the unit of mass used to measure proteins?

# *Answer: Dalton*

1 dalton

## Mass

Same as  
smallest atom  
(hydrogen)

## Weight

One trillionth  
of one  
quadrillionth  
of a pound

# Gene-to-Protein Process

- Some genes code for protein-making
- Protein folds into exactly the right shape to do its jobs properly
- There are more proteins than genes that code for them



How many genes do humans have?



What happens if a protein doesn't fold correctly?



Name one reason for this variety.

# *The Humpty Dumpty Method*

## **Step 1:**

Break protein into small pieces.

## **Step 2:**

Convert protein pieces into ions.

## **Step 3:**

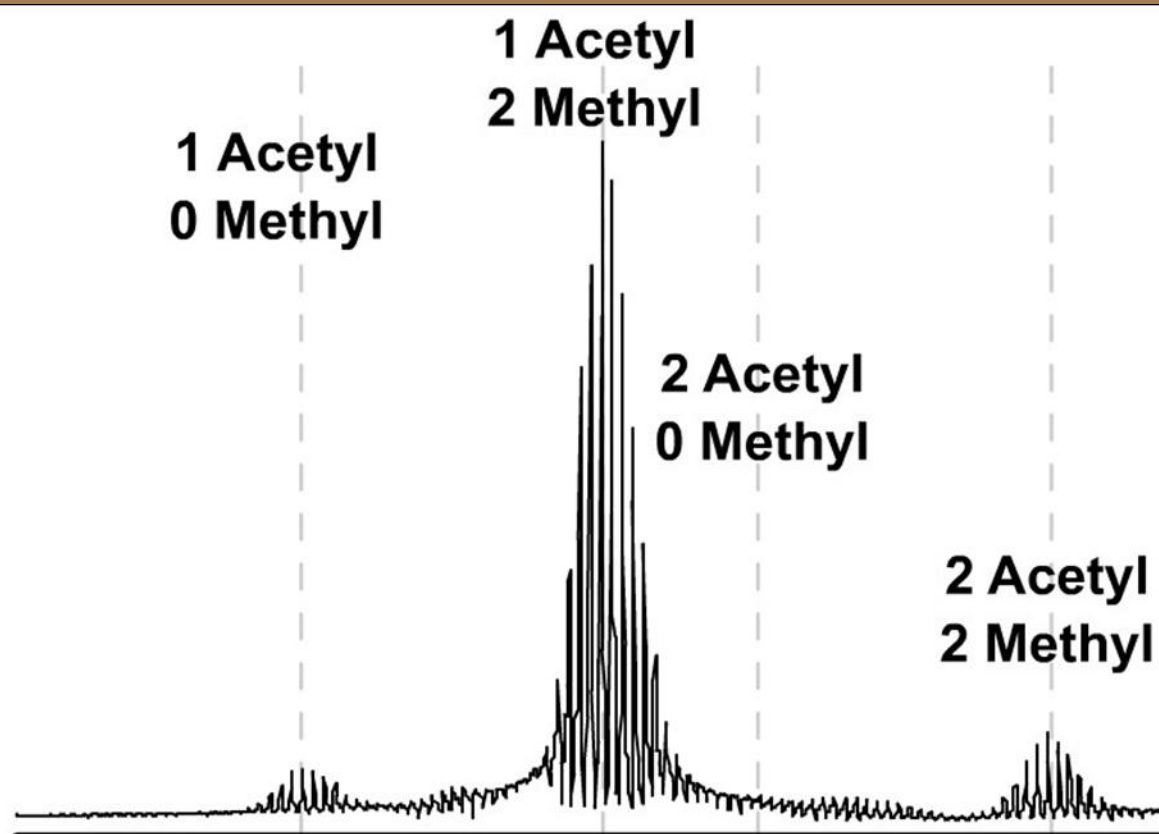
Mass spectrometer sorts ions based on charge and fragments' molecular weight



# The Humpty Dumpty Method (continued)

## **Step 4:**

Computer uses information to create a spectrum that describes protein and its parts



# *Kelleher's Top Down Method*

## **Step 1:**

Use gas-conversion process to collect data on intact protein

## **Step 2:**

Break protein into pieces and analyze them

## **Step 3:**

Custom computer technology finds protein's gene and identifies the chemical changes that help protein do its job

# A Challenging Course

Using  
Mass spectrometry  Imaging technologies

## Chemists

- Analyze larger proteins using Kelleher's top-down approach

## Chemists, cell biologists, and physicists

- Study how molecules work together in living cells
- Track individual molecules

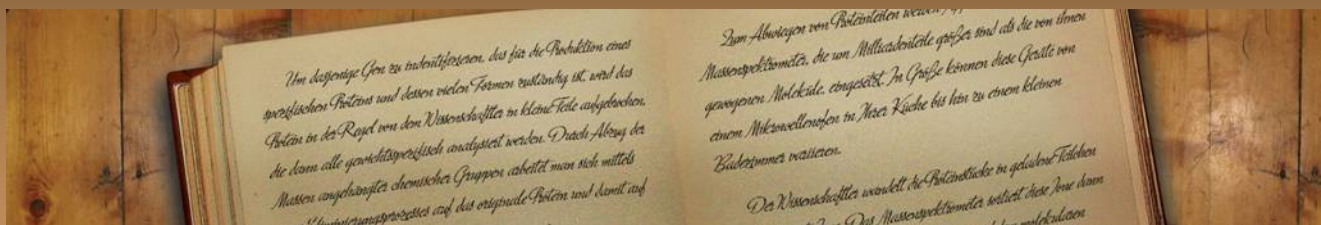
## Researchers

- May learn how to retool molecular reactions to fix disease



# Chemistry: A German Revolution

- Early chemists
  - Worked mainly in metal factories and pharmacies
  - No hands-on lab experiments in school



- German Chemists
  - Justus von Liebig
    - German chemist
    - Set up first lab course in chemistry
  - Friedrich Wöhler
    - Occasionally worked with von Liebig
    - First to convert inorganic compound into an organic one
    - Father of organic chemistry

# *Developments Resulting From Organic Chemistry*

One result of organic chemistry: synthetic dyes used to color fabrics and other textiles



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# *Research Applications*

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In what ways might Kelleher's method be used to explore questions about health and disease?