



SAPIENZA  
UNIVERSITÀ DI ROMA

## Writing Better Scientific Papers

**Matteo Rini, PhD**

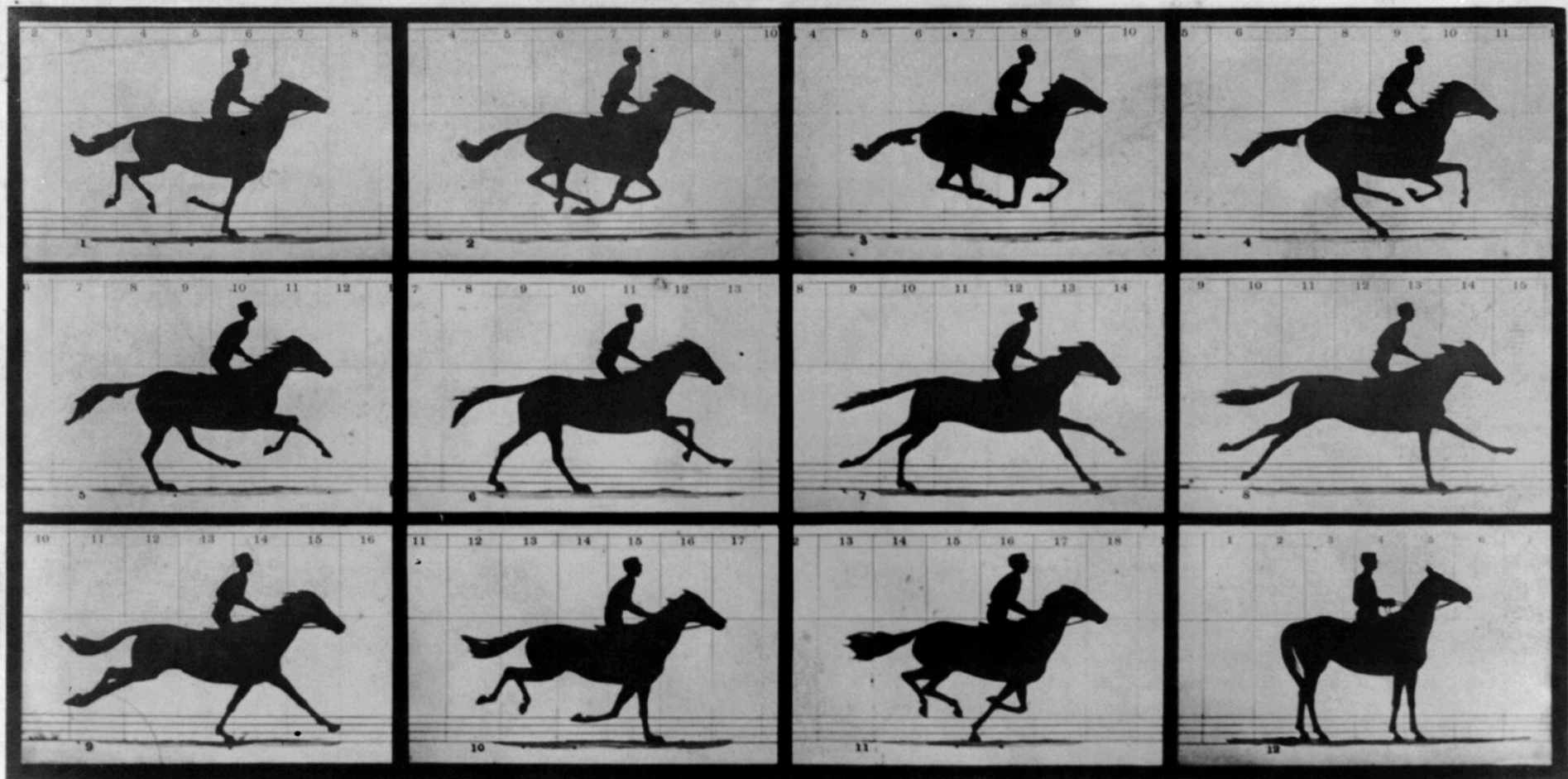
Editor, *Physics Magazine*

Professor of Science Writing & Communication, *NYU*

**As a scientist you are a professional writer**

# Why write well?

- ✓ **get published**
- ✓ **get cited**
- ✓ **get your proposals funded**
- ✓ **communicate with scientists from other fields**
- ✓ **develop communication skills useful in any career path**



Copyright, 1878, by MUYBRIDGE.

MORSE'S Gallery, 417 Montgomery St., San Francisco.

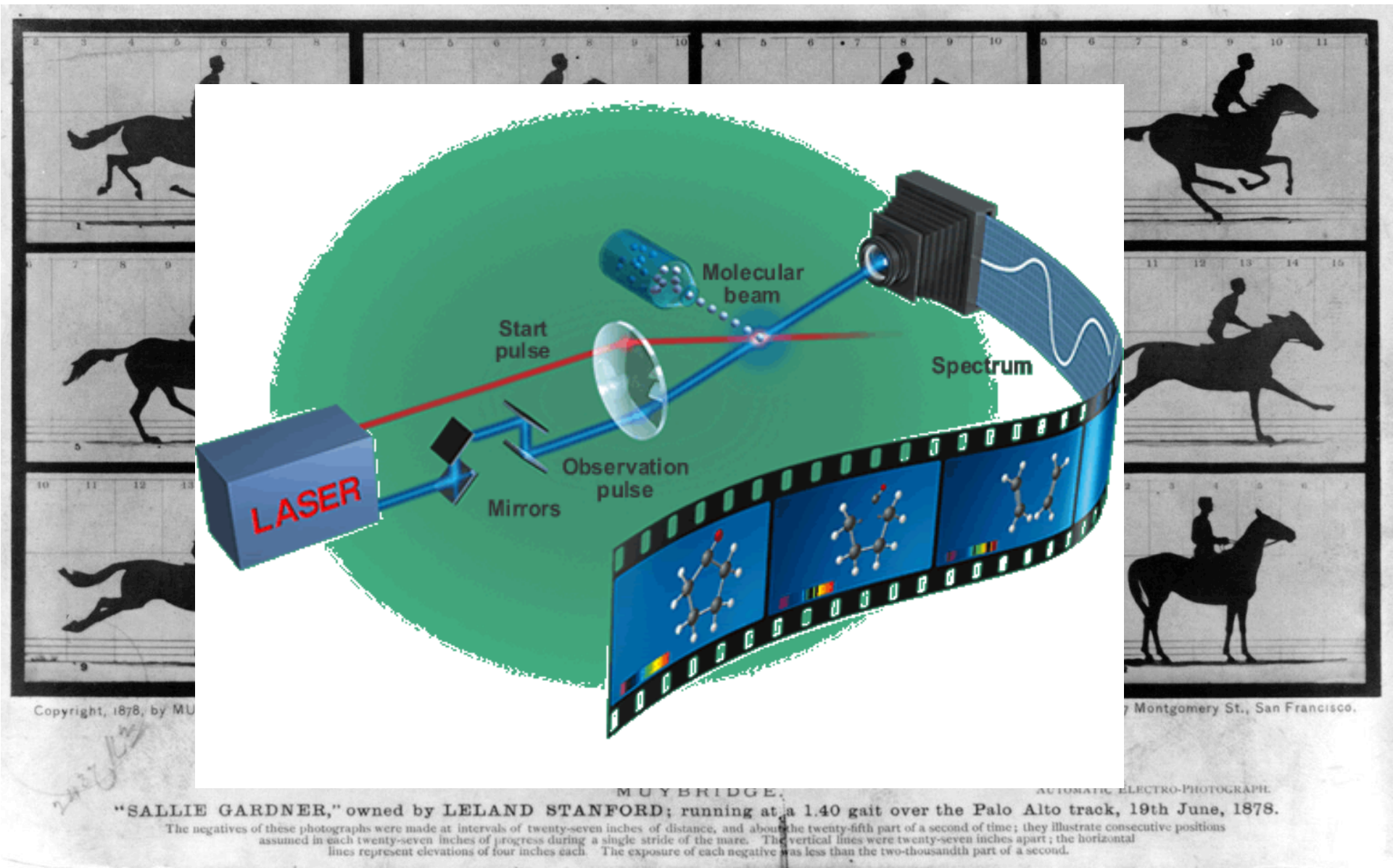
## THE HORSE IN MOTION.

Illustrated by  
MUYBRIDGE.

AUTOMATIC ELECTRO-PHOTOGRAPH.

"SALLIE GARDNER," owned by LELAND STANFORD; running at a 1.40 gait over the Palo Alto track, 19th June, 1878.

The negatives of these photographs were made at intervals of twenty-seven inches of distance, and about the twenty-fifth part of a second of time; they illustrate consecutive positions assumed in each twenty-seven inches of progress during a single stride of the mare. The vertical lines were twenty-seven inches apart; the horizontal lines represent elevations of four inches each. The exposure of each negative was less than the two-thousandth part of a second.



Copyright, 1878, by MU

Montgomery St., San Francisco.

**MUYBRIDGE**      **AUTOMATIC ELECTRO-PHOTOGRAPH**  
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## TODAY'S HEADLINES

July 21, 2003

Volume 81, Number 29

CENEAR 81 29 p. 7

ISSN 0009-2347

## SCIENCE

# TWO FAST STUDIES OF LIQUID WATER

Experiments explore ion solvation and proton transfer in water

## LOUISA DALTON

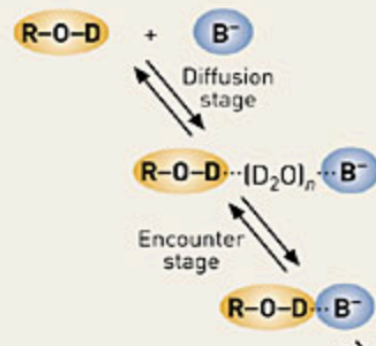
Water can be slippery. Despite centuries of study, experimental details about its rapidly shifting hydrogen-bond network remain elusive. Two reports this week make headway by using rapid-fire femtosecond spectroscopy to probe basic water phenomena: transferring a proton and dissolving a salt.

Researchers in Germany and Israel measured the speed of proton transfer from acid to base in water and propose a detailed mechanism [*Science*, **301**, 349 (2003)].

This "simple and elementary process" has historically been divided into three steps, notes coauthor Matteo Rini, a

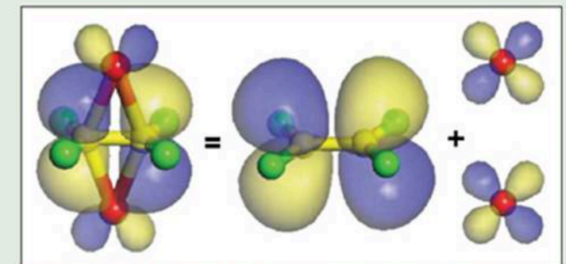
### BRIEF INTERLUDE

Proton-transfer model includes an extra encounter stage



## PHYSICAL REVIEW LETTERS

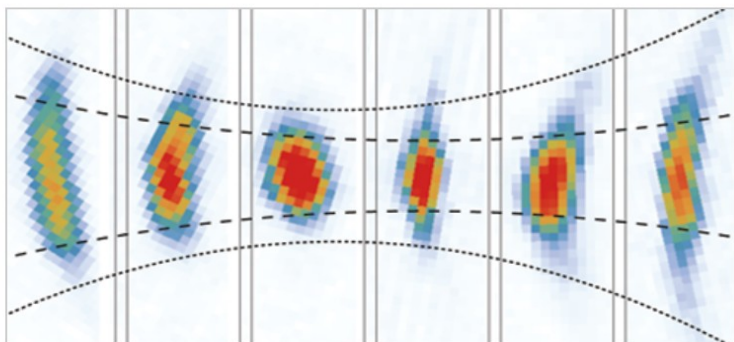
Articles published week ending  
1 DECEMBER 2006  
Volume 97, Number 22



Electron orbitals for the bonding of transition metal atoms (Ti: red) to ethylene (C<sub>2</sub>H<sub>4</sub>: yellow and green). The resulting complex (left) is capable of absorbing up to ten hydrogen molecules.

# Bringing Science to Politics



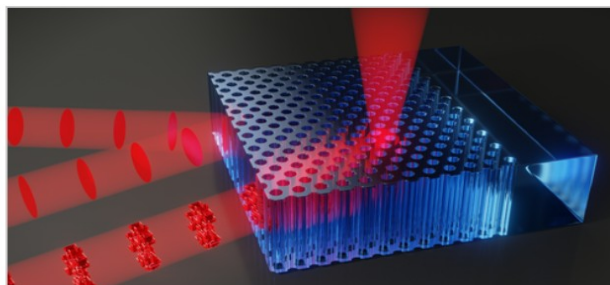


SYNOPSIS

# How to Focus a Bose-Einstein Condensate in a Waveguide

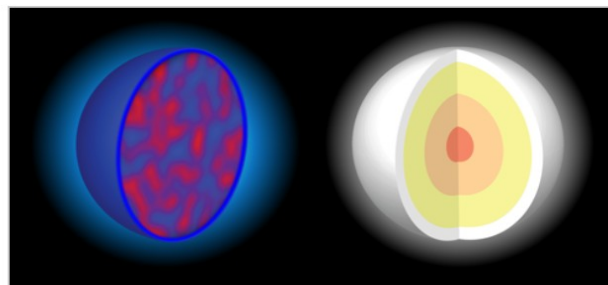
April 28, 2021

A new “lensing” technique counters the spreading of an ultracold cloud of atoms inside a tiny waveguide. [Read More »](#)



SYNOPSIS

## Steering Light Within a Crystal



VIEWPOINT

## Probing the Skin of a Lead Nucleus



RESEARCH NEWS

## Crackdown on Spying Damages US Science, Says

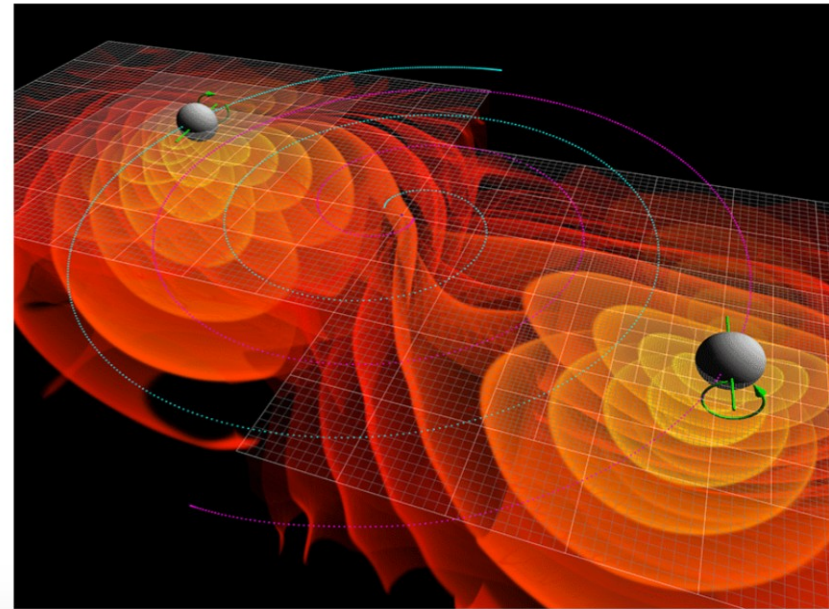


# The First Sounds of Merging Black Holes

**Gravitational waves emitted by the merger of two black holes have been detected, setting the course for a new era of observational astrophysics.**

by Emanuele Berti<sup>\*,†</sup>

For decades, scientists have hoped they could “listen in” on violent astrophysical events by detecting their emission of gravitational waves. The waves, which can be described as oscillating distortions in the geometry of spacetime, were first predicted to exist by Einstein in 1916, but they have never been observed directly. Now, in an extraordinary paper, scientists report that they have detected the waves at the Laser Interferometer Gravitational-wave Observatory (LIGO) [1]. From an analysis of the signal, researchers from LIGO in the US, and their collaborators from the Virgo interferometer in Italy, infer that the gravitational waves were produced by the inspiral and merger of two black holes (Fig. 1), each with a mass that is more than 25 times greater than that of our Sun. Their finding provides the first observational evidence that black hole binary systems can form and merge in the Universe.



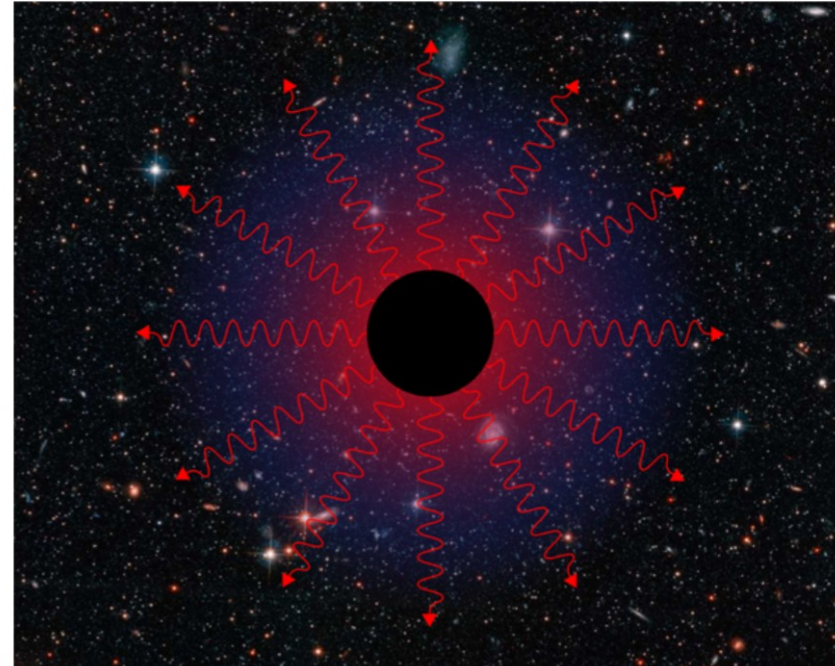
# Black Holes Have Soft Quantum Hair

**A black hole may carry “soft hair,” low-energy quantum excitations that release information when the black hole evaporates.**

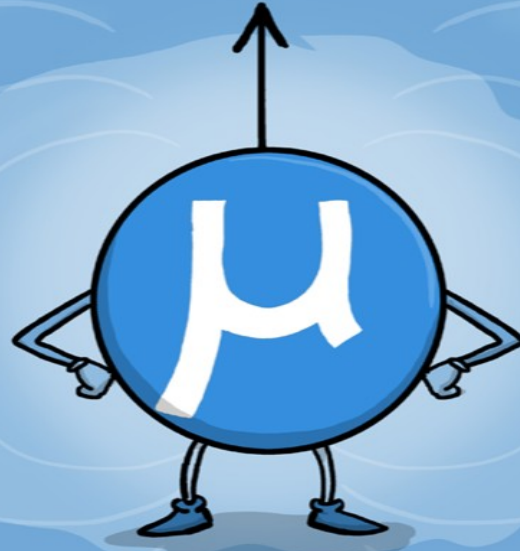
by Gary T. Horowitz\*

**F**our decades ago, Stephen Hawking proposed that black holes could destroy information—a conclusion that is incompatible with standard laws of quantum physics. This idea started a controversy known as the “black hole information problem” that even now has not been resolved. A new study by Hawking himself and Malcom Perry, both at the University of Cambridge, and by Andrew Strominger at Harvard University shows that some of the assumptions that led to the information problem might be wrong [1]. Their results do not completely solve the problem, but point to a promising research direction that might lead to its long-awaited solution.

According to Einstein’s general theory of relativity, stationary black holes are completely determined by just three observable parameters: their mass, charge, and angular momentum. Almost none of the information about what fell into the black hole is visible from the outside. Physicist John



# THE MUON g-2 ANOMALY EXPLAINED

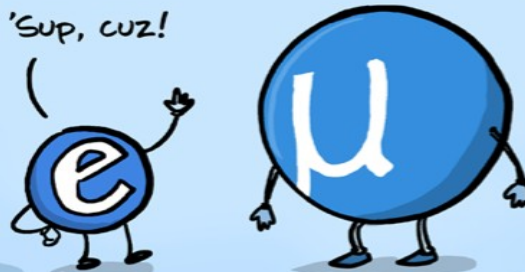


PHD Comics

THE MUON IS THE ELECTRON'S HEAVIER COUSIN.

JUST LIKE THE ELECTRON, IT HAS A MAGNETIC MOMENT THAT COMES FROM ITS CHARGE AND QUANTUM SPIN.

'Sup, cuz!



- 1. Find the best science**
- 2. Communicate it**

# Finding the best science

**MOTIVATION** Why this research?

**OPEN QUESTIONS** What are the specific research needs?

**KEY RESULT** What is really new?

**IMPACT** What are the implications of the result?

# Editing 100s of Scientists

## Some (uncommon) resistance

“...you are simplifying too much. They’ll think I am stupid...”

“...if a scientist does not know what a Lyapunov exponent is, he (and you) should just go back to school. I am not going to waste time explaining it...”

“...you have massacred my text...once again...there is no way to explain this without Hamiltonian equations”

# Challenges

- Talking to your supervisors/competitors/colleagues
  - talking to someone who already knows, jargon
  - talking to impress, to be evaluated
  - communicating the “how”
- The curse of knowledge
- Not relating to the audience



## Overcome these challenges

- Write with the reader in mind
- Practice
  - Clear, effective writing/communication can be learned!
- Read, read, read!

There is little correlation between  
English proficiency and writing skills

# Stages of writing

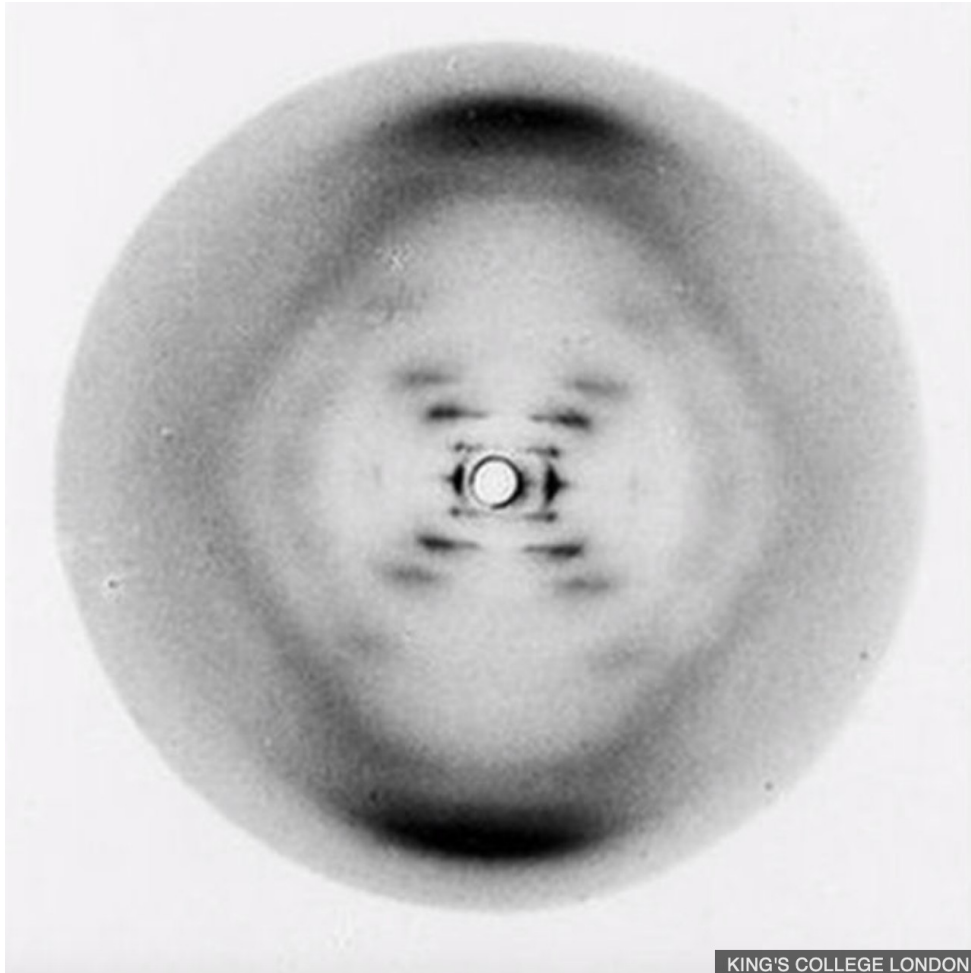
**1. Find your story**

2. Build a story structure

3. Find the best language for the story:

Apply effective writing strategies

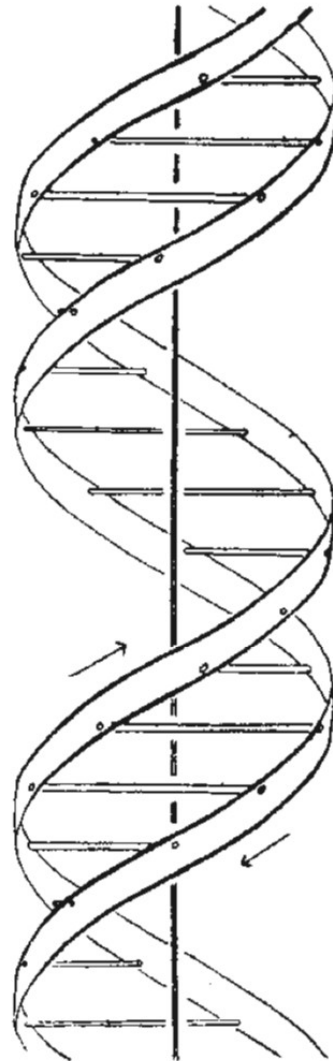
# Data vs Story: DNA



**R. E. Franklin and R. G. Gosling,  
“Molecular Configuration in Sodium  
Thymonucleate,”  
Nature 171 (1953): 740–41.**

“Sodium thymonucleate fibres give  
two distinct types of X-ray diagram.”

# Data vs Story: DNA



**J. D. Watson and F. H. C. Crick,  
“Molecular Structure of Nucleic  
Acids — A Structure for  
Deoxyribose Nucleic Acid,” *Nature*  
171 (1953): 737–38.**

“We wish to suggest a structure  
for the salt deoxyribose nucleic  
acid (DNA). The structure has  
novel features which are of  
considerable biological interest.”

**Every paper tells (not more  
than) one story**

## Stages of writing

1. Find your story

**2. Build a story structure**

3. Find the best language for the story:

Apply effective writing strategies

# Classic structure for a scientific paper

1. Context (the broad  
“why”)

2. Research needs (a more  
specific “why”)

3. What we did and found  
(the “how”)

4. Implications (the “so  
what”)



## Three-dimensional reconstruction of the giant mimivirus particle with an X-ray free-electron laser

Tomas Ekeberg,<sup>1</sup> Martin Svenda,<sup>1</sup> Chantal Abergel,<sup>2</sup> Filipe R. N. C. Maia,<sup>1,3</sup> Virginie Seltzer,<sup>2</sup> Jean-Michel Claverie,<sup>2</sup> Max Hantke,<sup>1</sup> Olof Jönsson,<sup>1</sup> Carl Nettelblad,<sup>1</sup> Gijs van der Schot,<sup>1</sup> Mengqing Liang,<sup>4</sup> Daniel P. De Ponte,<sup>4</sup> Anton Barty,<sup>4</sup> M. Marvin Seibert,<sup>1,5</sup> Bianca Iwan,<sup>1,6</sup> Inger Andersson,<sup>1</sup> N. Duane Loh,<sup>7</sup> Andrew V. Martin,<sup>8</sup> Henry Chapman,<sup>4,9</sup> Christoph Bostedt,<sup>5</sup> John D. Bozek,<sup>5</sup> Ken R. Ferguson,<sup>5</sup> Jacek Krzywinski,<sup>5</sup> Sascha W. Epp,<sup>10</sup> Daniel Rolles,<sup>10</sup> Artem Rudenko,<sup>11</sup> Robert Hartmann,<sup>12</sup> Nils Kimmel,<sup>13,14</sup> and Janos Hajdu<sup>1,15</sup>

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<sup>2</sup>Génomique & Structurale - IGS - UMR 7256, CNRS, Aix-Marseille Université, Institut de Microbiologie de la Méditerranée, Parc Scientifique de Luminy, Case 934, 13288 Marseille Cedex 9, France

<sup>3</sup>NERSC, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA

<sup>4</sup>Center for Free-Electron Laser Science, DESY, Notkestrasse 85, 22607 Hamburg, Germany

<sup>5</sup>LCLS, SLAC National Accelerator Laboratory, 2575 Sand Hill Road, Menlo Park, CA 94025, USA

<sup>6</sup>Attophysics Group, CEA-Saclay, 91191 Gif sur Yvette Cedex, France

<sup>7</sup>Centre for BioImaging Sciences, National University of Singapore, 14 Science Drive 4 Blk S1A, Singapore 117546

<sup>8</sup>The University of Melbourne, Parkville, 3010 VIC Australia

<sup>9</sup>University of Hamburg, Notkestrasse 85, 22607 Hamburg, Germany

<sup>10</sup>Max Planck Advanced Study Group, Center for Free Electron Laser Science, Notkestrasse 85, 22607 Hamburg, Germany

<sup>11</sup>J.R. Macdonald Laboratory, Department of Physics, Kansas State University, 116 Cardwell Hall, Manhattan, KS 66506, USA

<sup>12</sup>PNSensor GmbH, Römerstr. 28, 80803 München, Germany

<sup>13</sup>Max-Planck-Institut Halbleiterlabor, Otto-Hahn-Ring 6, 81739 München

<sup>14</sup>Max-Planck-Institut für extraterrestrische Physik, Giessenbachstrasse, 85741 Garching, Germany

<sup>15</sup>European XFEL, Albert-Einstein-Ring 19, 22761, Hamburg, Germany

We present a proof-of-concept three-dimensional reconstruction of the giant Mimivirus particle from experimentally measured diffraction patterns from an X-ray free-electron laser. Three-dimensional imaging requires the assembly of many two-dimensional patterns into an internally consistent Fourier volume. Since each particle is randomly oriented when exposed to the X-ray pulse, relative orientations have to be retrieved from the diffraction data alone. We achieve this with a modified version of the expand, maximize and compress (EMC) algorithm and validate our result using new methods.

### 1 INTRODUCTION

X-ray free-electron lasers provide femtosecond X-ray pulses with a peak brilliance ten billion times higher than any available X-ray source. Such a large jump in physical quantity is very rare, and can have far-reaching implications for several areas of science. It has been suggested that such pulses could outrun key damage processes and allow structure determination without the need for crystallization[1]. In 2006 came the first verification of this “diffraction before destruction” method with the reconstruction of a silicon nitride nanostructure created with a focused ion beam (FIB) and exposed to the FLASH free-electron laser in Hamburg[2].

So far, imaging applications at FELs have mainly been limited to nanocrystallography and to two-dimensional projections of single particles while 3D reconstructions from single particles have remained elusive.

Nanocrystallography[1][3] is an extension to protein crystallography where the high intensity and short pulse duration of a FEL allow for the use of very small crystals. Some proteins only produce small crystals. However, the fundamental problem that some samples are hard or impossible to crystallize is still valid. For this reason, single-

particle imaging was a key part of the scientific case for building X-ray free-electron lasers.

2D imaging with FELs such as the imaging of live cells[4][5], organelles[6] and viruses[7] is a promising method for imaging irreproducible samples. A resolution down to 21 nm have been achieved on Carboxysomes in a recent study[6]. There is also one application where a 2D image from a single-shot FEL experiment was compared to regular X-ray diffraction tomography performed at a synchrotron[8]. In a recent paper the structure of simple gold nanostructures were recovered in 3D from one single diffraction patterns[9]. This technique is however restricted to structurally simple and strongly scattering structures with a high degree of symmetry.

Several fundamental challenges exist for a general method of 3D single-particle imaging. First, 3D imaging requires the assembly of diffraction patterns from many identical copies of a reproducible object. Many of the applications of 2D imaging so far have been dealing with cells or other particles where each sample is structurally unique. Second, there is no way to directly measure the orientation of the sample when it was hit in the X-ray pulse. Instead the orientation of each sample particle has

to be recovered from the noisy signal of the diffraction patterns.

Solving these problems not only gives more information about the sample by presenting the structure in 3D, it is also a necessity for extending signal from weakly scattering samples such as proteins and small viruses. For these samples the scattering from a single particle may be too weak for reconstructing a 2D projection image and increasing the signal to noise ratio (SNR) by merging many patterns could allow for phasing even in this case.

A solution to the orientation problem was proposed by Duane Loh and Veit Elser in 2009 with the expand, maximize and compress (EMC) algorithm [10] which was verified for simulated diffraction patterns in the original publication. Later the algorithm was also tested for an artificial sample although at a resolution that was too low to allow for phase retrieval[11]. This paper presents the first application of the algorithm to a biological sample.

The sample used in this study was the Mimivirus (Acanthamoeba polyphaga mimivirus) particle[12][13][14]. Mimivirus is one of the largest known viruses. The viral capsid is about 450 nanometers in diameter and is covered by a layer of thin fibres. A 3D structure of the viral capsid exist[14] but the 3D structure of the inside is currently unknown.

### 2 EXPERIMENTAL SETUP AND DATA PREPROCESSING

These particles were aerosolized and then focused into a particle stream using an aerodynamic lens. The particle stream was intersected with the pulse train from the Coherent Light Source (LCLS). Diffracted patterns were collected on a detector placed 0.7 m downstream from the interaction region. At this distance the collected diffraction signal corresponds to the amplitude squared of a slice through the Fourier transform of the electron density of the sample. Mimivirus particles that were not hit by the FEL were shown to remain infectious after the injection process suggesting that they were not harmed by the injection process. A detailed description of the setup can be found in the Supplemental Material. A total of 198 diffraction patterns were selected and pre-processed and a subset of 25 of these are shown in FIG. 1. The selection preprocessing and selection is explained in supplemental material.

### 3 ORIENTATION RECOVERY

Three-dimensional structure determination requires the assembly of many 2D diffraction-patterns into an internally consistent 3D Fourier volume. A diffraction pattern presents an Ewald-sphere slice through the 3D

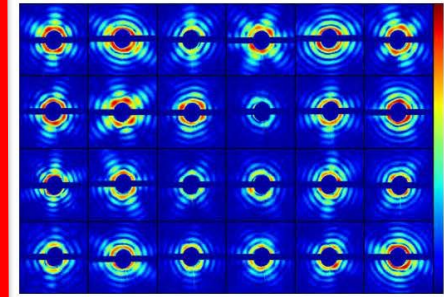


FIG. 1. 24 of the 198 diffraction patterns that were included in the analysis. The central region is missing due to a hole in the detector that lets the beam through. Patterns were selected for having signal to beyond  $83 \text{ nm}^{-1}$  but not saturating the detector.

Fourier-transform of the electron density. Since each particle is randomly orientated when exposed to the X-ray pulse, the relative orientations of the particles have to be retrieved from the diffraction data alone. This was done using a modified version of the EMC algorithm[10]. This algorithm has been verified for simulated data[10] and has been experimentally tested using artificial “nanorice” particles at a resolution too low to permit phase retrieval[11].

In the EMC algorithm a 3D diffraction space is iteratively updated to comply with the experimental data in the three steps expand, maximize and compress. In the expand step the current diffraction space is expanded into tomograms by taking slices through the diffraction space at a discrete sampling of all rotations. In the maximize step all tomograms are compared to all experimental diffraction patterns by calculating the probability of detecting the experimental pattern while treating the tomograms as expectation values. New tomograms are then created by summing together all diffraction patterns weighted by the respective calculated probability. In the compress step a new 3D diffraction space is assembled from the new tomograms.

For this study we introduce a new similarity function in the maximize step that is based on a Gaussian model:

$$L(K, M) = \prod_i e^{-\frac{(M_i - K_i)^2}{2\sigma_i^2}} \quad (1)$$

where  $K$  is the diffraction pattern,  $M$  is the slice through the 3D diffraction space,  $i$  is the pixel index and  $\sigma_i$  is the standard deviation of the Gaussian. We set  $\sigma_i = A\sqrt{M_i}$  where  $A$  is a constant. This similarity function balances well the contribution from the few but high-intensity central pixels and the numerous low-intensity outer pixels.

## Paragraphs

Make the paragraph the unit of composition.

— Strunk and White, *Elements of Style*

Each paragraph should convey a coherent “**unit of thought,**” which might be summarized in a “**focal sentence**”. Two important options:

Point-first paragraph

Point-last paragraph

## Point-First Paragraph

**The basic features of GW150914 point to it being produced by the coalescence of two black holes**—i.e., their orbital inspiral and merger, and subsequent final black hole ringdown. Over 0.2 s, the signal increases in frequency and amplitude in about 8 cycles from 35 to 150 Hz, where the amplitude reaches a maximum. The most plausible explanation for this evolution is the inspiral of two orbiting masses,  $m_1$  and  $m_2$ , due to gravitational-wave emission. At the lower frequencies, such evolution is characterized by the chirp mass [11]

of wetland complexes, including the Birds of Paradise wetland field complex that is five times larger than earlier remote and ground survey had indicated, and revealed a previously unknown wetland field complex that is even larger. The field systems date mainly to the Maya Late and Terminal Classic (~1,400–1,000 y ago), but with evidence from as early as the Late Preclassic (~1,800 y ago) and as late as the Early Postclassic (~900 y ago). Previous study showed that these were polycultural systems that grew typical ancient Maya crops including maize, arrowroot, squash, avocado, and other fruits and harvested fauna. The wetland fields were active at a time of population expansion, landscape alteration, and droughts and could have been adaptations to all of these major shifts in Maya civilization. These wetland-farming systems add to the evidence for early and extensive human impacts on the global tropics. Broader evidence suggests a wide distribution of wetland agroecosystems across the Maya Lowlands and Americas, and we hypothesize the increase of atmospheric carbon dioxide and methane from burning, preparing, and maintaining these field systems contributed to the Early Anthropocene.

lidar | ancient Maya | wetland agroecosystems

**P**recolumbian Maya civilization persisted from ~3,000 to 1,000 or 500 calibrated years before present (BP), building vast numbers of cities, farms, roads, and reservoirs. Over the last decade, lidar (light detection and ranging) imagery has greatly expanded our estimate of ancient infrastructure that ground survey had laboriously identified for more than a century (1, 2). This massive

herently difficult to excavate, and widespread recent plowing, draining, and deforestation are destroying many relict field systems (28). Fortunately, tropical forest cover is still extensive in some areas such as Guatemala's Petén, where a recent *Science* article estimated 67 km<sup>2</sup> of seasonally wet, canalized fields based on lidar mapping with some ground validation beneath the forest canopy (1). These Petén field systems and canals will require further extensive validation, excavation, dating, and multiple proxy evidence to confirm their uses, chronologies, and extents over Maya history.

We report here the verification of widespread ancient Maya wetland fields in the Rio Bravo watershed of Belize based on lidar data and many excavations with multiple lines of evidence for cultivars, formation, and chronology (Fig. 1). These ancient wetland systems occur in four main areas within the watershed. We focus on the area with the most evidence thus far, the Birds of Paradise (BOP) fields (26, 27), to present a synthesis of formation, use, and chronology based on 42 radiocarbon ages, including 15 from six wetland excavations (Fig. 2 and *SI Appendix, Table S1*; these include all radiocarbon ages amassed for the BOP fields and

### Significance

Understanding agricultural subsistence is vital for understanding past complex societies. Lidar data are indicating widespread ancient Maya infrastructure. Wetland agriculture was crucial to ancient cultures, but no previous study coupled lidar with multiproxy evidence to demonstrate the extent and uses of Maya wetland fields. We conducted a lidar survey

## Stages of writing

1. Find your story
2. Build a story structure
- 3. Find the best language for the story:  
Apply effective writing strategies**

# Economy and lightness

- Do not speak in a stuffy manner for a judgmental audience
- Economy

“**The secret of good writing is to strip every sentence to its cleanest components.** Every word that serves no function, every long word that could be a short word, every adverb that carries the same meaning that’s already in the verb, every passive construction that leaves the reader unsure of who is doing what—these are the thousand and one adulterants that weaken the strength of a sentence.”

William Zinsser in *On Writing Well*, 1976

## Quickness & lightness

- **Recognizing and cutting clutter**  
“This work sheds new light on the physics of nuclear fusion...”
- **Adverbs are often useless**  
very, really, quite, basically, generally, significantly, remarkably...
- **Use jargon only when needed**  
The avian species -> Birds?
- **Active vs passive voicing**  
Passive voicing leaves an open question (who did it?)

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# Quickness and lightness

- **Cut all unnecessary words**  
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very, really, quite, basically, generally, significantly, remarkably...
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The avian species -> Birds?
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Passive voicing leaves an open question (who did it?)

# Use short sentences!

Techniques for the direct phase modulation of laser diodes, typically based on the control of the applied current or voltage and always associated with a very dramatic amplitude and/or frequency modulation of the emitted light, have been available for decades, while being insufficiently reliable for high-bit-rate communications and quantum key distribution applications.

# Use short sentences!

Techniques for modulating the phase of laser diodes have have been available for decades.

They are typically based on the control of the applied current or voltage.

However, because such methods are always associated with a dramatic amplitude and/or frequency modulation, they are unsuitable for high-bit-rate communications and quantum key distribution applications.

## Few Examples

### Clunky phrase

- A majority of
- A number of
- Are of the same opinion
- At the present moment
- By means of
- Less frequently occurring
- small/large in size

### Equivalent

most  
many  
agree  
now  
by  
rare  
small/large

**Do we need to depersonalize science?**

844 Sitzung der physikalisch-mathematischen Klasse vom 25. November 1915

# Die Feldgleichungen der Gravitation.

VON A. EINSTEIN.

In zwei vor kurzem erschienenen Mitteilungen habe ich gezeigt, wie man zu Feldgleichungen der Gravitation gelangen kann, die dem Postulat allgemeiner Relativität entsprechen, d. h. die in ihrer allgemeinen Fassung beliebigen Substitutionen der Raumzeitvariablen gegenüber kovariant sind.

Der Entwicklungsgang war dabei folgender. Zunächst fand ich Gleichungen, welche die NEWTONSCHE Theorie als Näherung enthalten

**BEFORE TITLE: On the breakdown of the Born-Oppenheimer approximation for conical intersections of potential-energy surfaces of the same symmetry**

**AFTER TITLE: Diabolical Conical Intersections**



**“I have observed that the Hamiltonian philosophy is like avocado: you either like it or you don’t”**

**[P.J. Morrison, Rev. Mod. Phys. 70, 467 (1998)].**

**“Radiative fluxes from 1987A are still changing on time scales short compared to journal publication time scales”**  
[Virginia Trimble, Rev. Mod Phys. 60, 859 (1988)].

**“The difference between the two types of variables can be elucidated by describing two ways of watching fish. In the Eulerian picture one stays at a point and watches whatever fish happen by; in the Lagrangian picture one picks out a particular fish and keeps track of where it goes”**  
[P. J. Morrison, Rev. Mod. Phys. 70, 467 (1998)].

# Visibility

“...a basic human faculty: the power of ... thinking in terms of images.”  
(I. Calvino)

**Let the figures tell the story!**

“We wish to suggest a structure for the salt deoxyribose nucleic acid (DNA). The structure has novel features which are of

equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Disc* part in making the observations.

- <sup>1</sup> Young, F. B., Gerrard, H., and Jevons, W. (1920).
- <sup>2</sup> Longuet-Higgins, M. S., *Mon. Not. Roy. Astr.* 5, 285 (1949).
- <sup>3</sup> Von Arx, W. S., *Woods Hole Papers in Phys.* (3) (1950).
- <sup>4</sup> Ekman, V. W., *Arkiv. Mat. Astron. Fysik.* (S)

## MOLECULAR STRUCTURE OF DEOXYRIBOSE NUCLEIC ACID

### A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid. The structure has novel features which are of biological interest.

A structure for nucleic acid has been proposed by Pauling and Corey<sup>1</sup>. Their manuscript available to us before publication. Their model consists of two twined chains, with the phosphate groups on the axis, and the bases on the outside. This structure is unsatisfactory for the following reasons: (1) We believe that the material shown in the X-ray diagrams is the salt, not the free acid. If the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining  $\beta$ -D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furber's model No. 1, but it is



## Tips:

- Build the paper around figures
- Do figures & captions tell a clear story?

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally<sup>3,4</sup> that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data<sup>5,6</sup> on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set

### Three-dimensional reconstruction of the giant mimivirus particle with an X-ray free-electron laser

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- <sup>12</sup>PNSensor GmbH, Römerstr. 28, 80803 München, Germany
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- <sup>14</sup>Max-Planck-Institut für extraterrestrische Physik, Giessenbachstrasse, 85741 Garching, Germany
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We present a proof-of-concept three-dimensional reconstruction of the giant Mimivirus particle from experimentally measured diffraction patterns from an X-ray free-electron laser. Three-dimensional imaging requires the assembly of many two-dimensional patterns into an internally consistent Fourier volume. Since each particle is randomly oriented when exposed to the X-ray pulse, relative orientations have to be retrieved from the diffraction data alone. We achieve this with a modified version of the expand, maximize and compress (EMC) algorithm and validate our result using new methods.

1

#### INTRODUCTION

X-ray free electron lasers provide femtosecond X-ray pulses with a brilliance ten billion times higher than any available X-ray source. Such a large jump in X-ray flux is very rare, and can have far-reaching implications for several areas of science. It has been shown that such a high intensity of X-ray pulses can be used to study structural transitions without the need for crystallization[1]. In 2006 came the first verification of this “diffraction before destruction” method with the reconstruction of a silicon nitride nanostructure created with a focused ion beam (FIB) and exposed to the FLASH free-electron laser in Hamburg[2].

So far, imaging applications at FELs have mainly been limited to nanocrystallography and to two-dimensional projections of single particles while 3D reconstructions from single particles have remained elusive.

Nanocrystallography[1][3] is an extension to protein crystallography where the high intensity and short pulse duration of a FEL allow for the use of very small crystals.

# Every researcher

particle imaging was a key part of the scientific case for building X-ray free-electron lasers.

2D imaging with FELs such as the imaging of live cells[4][5], organelles[6] and viruses[7] is a promising method for imaging irreproducible samples. A resolution down to 21 nm have been achieved on Carboxysomes in a recent study[6]. There is also one exception that such a high intensity of X-ray pulses can be used to study structural transitions without the need for crystallization[1]. In 2006 came the first verification of this “diffraction before destruction” method with the reconstruction of a silicon nitride nanostructure created with a focused ion beam (FIB) and exposed to the FLASH free-electron laser in Hamburg[2].

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2

#### EXPERIMENTAL SETUP AND DATA PREPROCESSING

The particles were aerosolized and then focused into a particle stream using an aerodynamic lens. The particle stream was intersected with the pulse train of the Coherent Light Source (LCLS). Diffracted patterns were collected on a detector placed 0.7 m downstream from the interaction region. At this distance the collected diffraction signal corresponds to the amplitude squared of a slice through the Fourier transform of the electron density of the sample. Mimivirus particles that were not hit by the FEL were shown to remain infectious after the injection process suggesting that the damage is caused by the injection process.

The experimental setup can be found in the supplemental material. The total of 198 diffraction patterns were preprocessed and a subset of 24 patterns was selected for the reconstruction. The selection preprocess is in supplemental material.

3

#### ORIENTATIONAL DETERMINATION

Three-dimensional structure determination requires

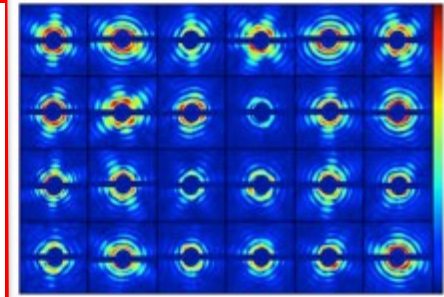


FIG. 1. 24 of the 198 diffraction patterns that were included in the analysis. The central region is missing due to a hole in the detector that lets the beam through. Patterns were selected for having signal to beyond 83 nm<sup>-1</sup> but not saturating the detector.

Fourier-transform of the electron density. Since each particle is randomly orientated when exposed to the X-ray pulse, the relative orientations of the particles have to be retrieved from the diffraction data alone. This was done using a modified version of the EMC algorithm[10]. This algorithm has been verified for simulated data[10] and has been experimentally tested using artificial “nanorice” particles at a resolution too low to permit phase retrieval[11].

In the EMC algorithm a 3D diffraction space is iteratively updated to comply with the experimental data in three steps: expand, maximize and compress. In the expand step the current diffraction space is expanded into tomograms by taking slices through the diffraction space at a discrete sampling of all rotations. In the maximize step all tomograms are compared to all experimental diffraction patterns by calculating the probability of detecting the experimental pattern while treating the tomograms as expectation values. New tomograms are then created by summing together all diffraction patterns weighted by the respective calculated probability. In the compress step the 3D diffraction space is assembled

using a new similarity function on a Gaussian model:

$$\frac{M_i - \langle M_i \rangle^2}{\sigma_i^2} \quad (1)$$

$M_i$  is the slice through the pixel index and  $\sigma_i$  is the standard deviation of the Gaussian. We set  $\sigma_i = A\sqrt{M_i}$  where  $A$  is a constant. This similarity function

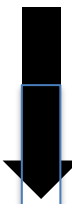
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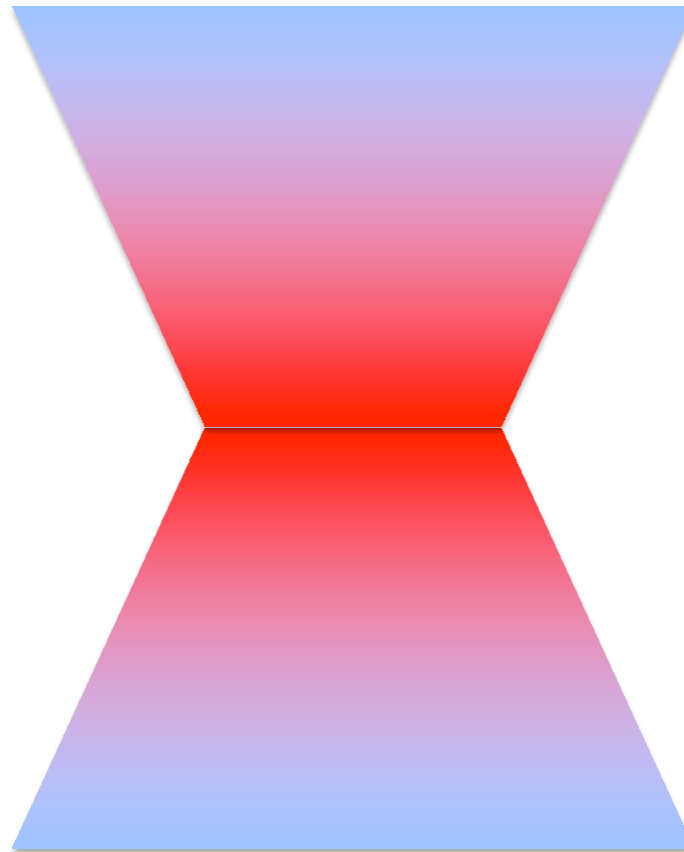
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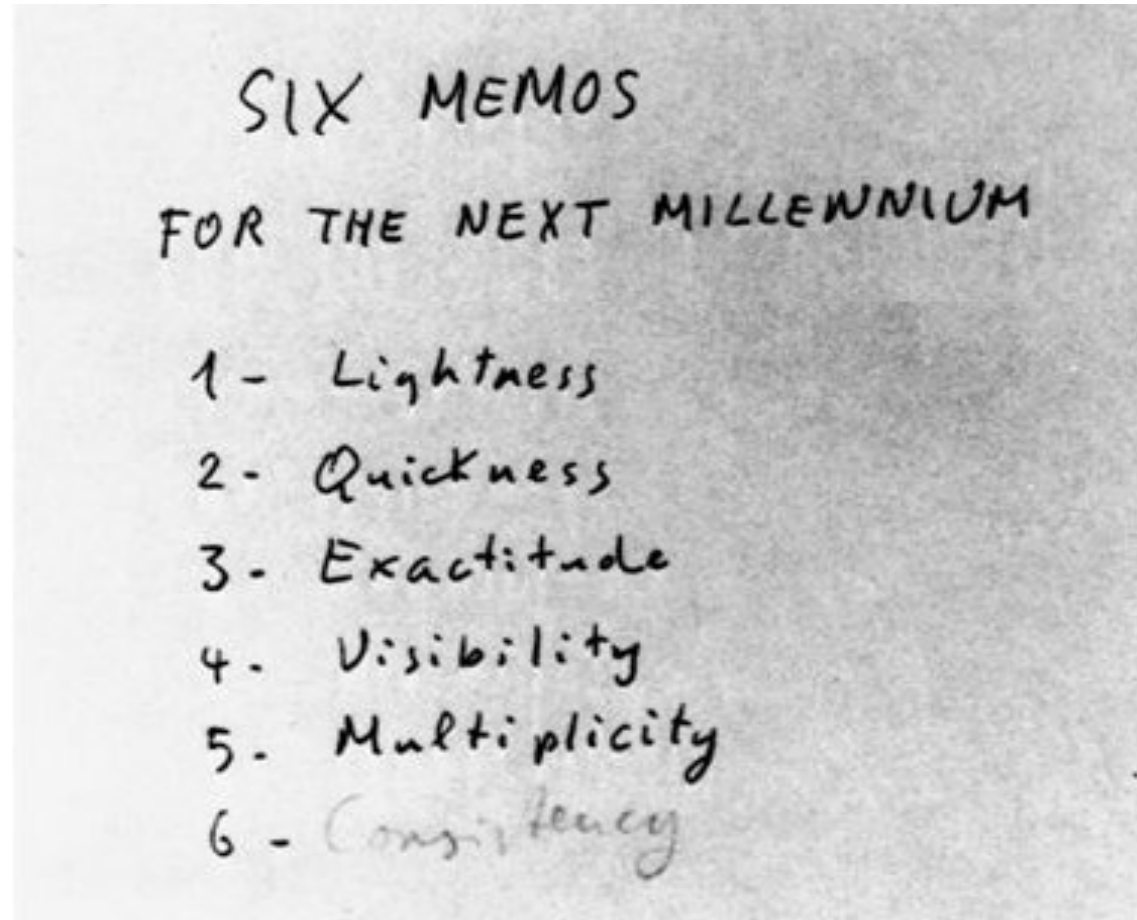
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# 6 memos for the author of a scientific paper



\* Italo Calvino's *Six Memos for the Next Millennium* (Charles Eliot Norton Lectures at Harvard)

## Consistency

**As a scientist  
you are a professional writer**

**Find your own voice!**



# Review of Modern Physics: Style guide

## APPENDIX A: Writing a better scientific article

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