MODEL3D Challenge Tools

SCIENTIFIC LITERACY

Part 1 of 2

1.0 Scientific Writing

An introduction into scientific writing. This guide has been prepared as a brief and to the point guide to help you to communicate scientically. MODEL3D has more complete materials prepared by a professional librarian, and can be found on the MODEL3D website. A brief Listing of applications (standalone and web based) for managing literature and communications and a brief discussion of each are provided. Once the learning team has determined which of the tools the team will use, make sure all team members use the same applications (and versions) to help facilitate the Learning Team communicates and experiences maximum productivity to complete the challenge. (*Working smarter, not harder*).

Communicating as a Scientist

This first unit will help you understand what makes scientific communication effective and will help you identify your purpose and analyze your audience in terms of its level of specialization. It then proposes basic strategies to address less specialized audiences and mixed audiences, whether orally or in writing. A list of useful software tools are provided for your learning team to begin using.

1.1 Understanding Communication

Effective communication is about getting your message across. Specifically, it involves capturing your audience's attention, ensuring your audience understands the idea you are trying to convey, and encouraging your audience to do something with that information, such as remember it, apply it, or provide feedback. A message is not just information; rather, it is the interpretation of the information. It says what the information means for the audience. It is to information what conclusions are to results. If information is the answer to the question What? (as in "What did you find in your research?"), then the message is the answer to the question So what? (as in "What do your findings mean to your audience?").

Effective communication, therefore, is centered on the audience: It is audience-friendly, just as effective software is user-friendly. In your communication, focus on what your audience needs or wants to learn, not on what you feel like telling them. Strive to see things from their perspective. Keep in mind all the potential members of your audience (at least those who matter for your purpose), not just those who have expertise or interests similar to your own.

Taking the medium into account

To select your content, consider not only your audience but also the inherent qualities of the medium you use. Specifically, distinguish between written and oral communication.
Readers of a document do not need to read everything. They can select what they read and when they read it, they can read at their own rhythm, and they can reread parts of the document as many times as they wish. In written documents, you can therefore convince your audience through solid, detailed evidence, and you should structure this evidence to enable selective reading.

In contrast, attendees at a presentation cannot select what they listen to or in what order they listen to it. They are usually less interested in details they could more easily read in a document. On the other hand, they can get to know you (the speaker) as a person and, ideally, they can

interact with you through questions or discussion. In oral presentations, you convince an audience by selecting cogent arguments, by articulating them logically, and, especially, by delivering them effectively. When an oral presentation builds on a written document (such as a conference presentation with a paper in the proceedings, a Ph.D. defense, a grant interview, and so on), you must be much more selective in your presentation than in your document — the idea is not to say out loud everything that you have already put in writing.

Showing respect for your audience

When communicating about science, one main challenge is to respect the intelligence of the audience without overestimating its knowledge of the topic or field. For fear of being insultingly simple, conference speakers often make their presentations too complicated. Many attendees may wish the presentation were aimed at a lower level, although their pride may prevent them from admitting this to the speaker. In contrast, few attendees will complain that a presentation was “too simple” for them. Still, attendees react negatively to speakers who address them as if they are stupid. Perhaps the one thing an audience never forgives is a lack of respect.

Respect is about how you say things (your tone) more than about what you say. In general, dare to say things the way they are. If you need something from your supervisor, go ahead and ask for it. If your experiments failed, say so. If you receive an off-topic question, feel free to flag it as such. As you do so, however, strive to help (not offend) your audience. Politely ask your supervisor (state why you need what you need). Present useful lessons from your failures. Finally, offer to discuss the off-topic question in private.

Respect and tone are hard to define, but they have more to do with intent than with set rules. For example, if you are a Ph.D. student, it might be appropriate to address your supervisor by his or her first name; it depends on him or her and on the institutional culture (a question of rules). Still, starting an e-mail as Dear Leilah or as Dear Dr. Delmont indicates distance rather than respect per se. You could very well call your supervisor Dr. Delmont and at the same time show disrespect in the way you phrase your e-mail, such as by demanding something instead of asking for it (a question of intent). Given that your intent when communicating about science is to make the audience understand, make it a habit to write and speak in a simple, straightforward way. Instead of striving to imitate the intricate style of many papers, explain things as simply as you would to a colleague, face to face. Show respect to your audience by avoiding undue informality and by crafting and proofreading your text carefully, but do not believe that you have to write or speak in a special way to “sound scientific.” Above all, focus on your purpose: Get your message across.

1.2 Identifying Your Purpose and Audience

When you communicate, your purpose is not what you want to do; instead, it is what you want your audience to do as a result of reading what you wrote or listening to what you said. Thus, it involves the audience. To communicate effectively (that is, to achieve your purpose), you must adapt to your audience. Therefore, you must know your audience.

Knowing your purpose and audience helps determine your strategy. If your purpose or audience is unclear, clarify it as best you can, possibly by asking others. For a public thesis defense, for example, the audience is usually strongly heterogeneous. It includes your jury, your colleagues, your friends, and perhaps your family. The purpose depends largely on how your institution sees the event. Some institutions feel that you must primarily address the jury, no matter who else is in the

room, as it is your only chance to convince them of your worth. Other institutions see the defense as a way to broaden the visibility of your work and will want you to address a larger audience — including the jury.

(by permission from the Nashville Parent)

Audiences vary. They can be small or large. They can be reasonably homogeneous in what they already know or in what they are interested in, or they can be heterogeneous. Some are reasonably well known, as when you address a letter or memo to a specific person; others are less well defined, as when you publish an article in a magazine. Whenever possible, however, distinguish between specialists and nonspecialists, and between primary readers and secondary readers. Readers and listeners vary in how much they know about the topic you discuss and about your broader scientific field. Specialists will likely want more detail. They can apply detailed information in their own work, or they might need it to be convinced of the validity of your conclusions. Nonspecialists, on the other hand, need more basic information, especially in the introduction. Nonspecialists also require more interpretation, typically with the conclusions. They also need simpler vocabulary (or definitions), as they have not mastered the technical terms of your field.

Specialism is relative. Any audience can be seen as including both more specialized and less specialized members, all the more so when it is ill defined. Even a scientific paper published in a journal, which you can see as a specialized publication, will likely be read by newcomers to the field who are less specialized. Even referees on the program committee of a conference cannot have an equal degree of expertise in all the proposals they must evaluate. In other words, do not assume that a scientific audience is necessarily composed of “people like you.” On the contrary, you may well be the most specialized person on the planet in your specific topic. Effective scientific communication, and in particular effective writing, strives not to exclude readers or listeners. A well-written scientific paper makes sense, at least in its broad lines, to anyone with a scientific background.

Readers might also vary in how familiar they are with the context. When you are writing a document (for example, a letter) to a single person or to a small, well-defined group of people, you might be tempted to jump directly to the heart of the matter, assuming context is unnecessary. This person or group of people, who are your primary readers, may indeed know the context. Still, they may not be mindful of it when they read your document. Moreover, your document might end up being read by people you did not identify, such as those who were forwarded your document by a primary reader or perhaps those who will obtain your document in the future. These people, who are your secondary readers, will not know or remember the context. An effective document makes sense to both primary and secondary readers.

1.4 Writing or Speaking for Specific Audiences

As a scientist, you may find it challenging to present your work — or to explain scientific concepts in general — to a less specialized audience. More challenging still, however, is addressing a mixed audience of both specialists and nonspecialists. Here are specific tips for these two situations.

Writing or speaking for nonspecialists

Whether you are addressing specialized or less specialized audience members, it is a good idea to convey early the motivation for the work you report so that they can relate to it — that is, you must bridge the gap between what they know or are interested in and what you will present. With nonspecialists, this gap is wider than with specialists. You might find it harder to convey the motivation for your work.

Nonspecialists lack comparison points. If you mention an absolute value, such as a power consumption of 5 mW, they might not know whether that is a small or a large amount for the device you describe, and they might not even know whether it is little or much in general. You can suggest that the power consumption is low or high by writing something like “as little as 5 mW” or “as much as 5 mW,” but it is more helpful to provide the missing comparison point in the form of a relative value, as in “30 percent less than the most economical device to date” or “three times the average power consumption of devices of type X.” Frequently, you can usefully combine an absolute value with a relative one, as in “5 mW, which is 30 percent less than . . . “

One type of comparison that is useful to all audiences but particularly to less specialized ones, including students, is the analogy. When you draw a parallel between a new concept you are trying to explain and one that is familiar to (or easily grasped by) the audience, you increase the probability that your audience will understand the concept and remember it. For example, you might say that the human genome encoded in DNA is like instructions stored in a library. The power of an analogy depends on how familiar the audience is with the comparison point (here, the library), and also on how consistently you can carry the analogy through your document or presentation. For example, if you can go on to meaningfully compare chromosomes to books in this library and genes to the pages in these books, then you have a more powerful analogy.

Nonspecialists also lack visual references; they cannot automatically picture what you are talking about. Visual material — appropriate for all audiences but crucial for nonspecialists — can include drawings and photographs. Drawings, which can abstract unnecessary details to focus on the essential idea, are best for conceptual explanations. In contrast, photographs, with their visual richness, give a better idea of what the “real thing” looks like. Thus, to explain a new chemical process, use a process flow diagram to discuss the flow of chemicals through the installation, but use a photograph of the pilot plant to provide a feel for size, appearance, and so on. Here, too, provide a comparison point for size, such as including a person in the photograph.

Writing or speaking for a mixed audience

The essential strategy to addressing a mixed audience, from the unavoidable variation in expertise among peers to a mix of scientists and nonscientists, is structure, from the whole document or presentation to the individual sentence. You must distinguish between what everyone needs or wants to learn and what only some of them need or want to learn, and then structure your writing or speaking accordingly.

At the macroscopic level (the whole document or presentation), structure the content in levels of increasing specialization or decreasing interest. For a document such as a report or paper, place first what everyone needs or wants to know, typically in a summary or abstract (first level). Provide more detailed information in the report or paper itself (second level), possibly segregating in appendices what even fewer readers will need or want (third level). For a presentation to both specialists and nonspecialists, and especially when your time is limited, aim for the less specialized audience members in the presentation itself (first level), but foresee enough time afterwards for specialists to ask questions (second level) and perhaps create a companion document with more detailed information (third level). Feel free to include more specialized moments in the presentation itself, so you can hint at your deeper understanding, but make sure that these moments do not prevent less specialized attendees from understanding the remainder of the presentation.

At the microscopic level (the sentence), express in the main clause what is new or interesting to the majority of your audience members and relegate to a subordinate clause what fewer of them want or need to know. For example, consider the following sentences:

We have opted for connectors made of gold. Gold exhibits both high electrical conductivity and excellent resistance to corrosion.

Those who are well aware of the properties of gold might find the second sentence uninteresting or even patronizing, whereas the information is useful to less specialized readers. A better option is to subordinate the second clause, which is new to some audience members, to the first one, which is new to all members of the audience, in this way:

We have opted for connectors made of gold, given its high electrical conductivity and excellent resistance to corrosion.

In this revised version, the properties of gold are not presented independently but as a justification for the choice made. The new, compound sentence is more interesting for all readers, yet no information is lost for the less specialized ones.

1.5 Summary

Communicating is an integral part of being a scientist. To communicate effectively, strive to convey a message (the so what), not just information (the what). Focus on your purpose, which is what you want your audience to do after reading what you wrote or listening to what you said. To this end, be audience-friendly — that is, identify what the audience needs or wants to learn.

Audiences are seldom homogeneous; audience members might be more or less familiar with what you will discuss in terms of both content (they might be more or less specialized) and context (they might be primary or secondary readers). Communication is more effective when it satisfactorily addresses the needs of a broader audience. In particular, a scientific paper should make sense — at least in broad terms — to anyone with a scientific background, both today and in the future. To reach this goal, strive to write or speak in a simple, straightforward way.

Effective communication bridges the gap between the knowledge and interest of the audience and the content of the document or presentation. When your audience is less specialized or less motivated, the gap is wider and bridging it is harder. When writing or speaking specifically for non-

specialists, remember to include the comparison points they lack. Mention relative values instead of or in addition to absolute ones, use analogies, provide visual representations (with an idea of scale), and so on. When writing or speaking for a strongly heterogeneous audience, include first what everyone is primarily interested in and later what only some of the audience needs or wants to learn. In all cases, beware of overestimating the audience's knowledge of your topic or field (a common mistake, in particular in conference presentations), yet always respect its intelligence.

Various software tools to help your learning team communicate more effectively:

Data and document sharing tools-

Google Docs (https://www.google.com/docs/about/)
Full featured free word document processing, supports multiple editing. Share the file to other learning team members.

Google Sheets (https://www.google.com/sheets/about/)
Full featured free spreadsheet environment, supports multiple editing. Share the file to other learning team members.

Google Slides (https://www.google.com/slides/about/)
Full featured free slide making environment, supports multiple editing. Share the file to other learning team members.

Evernote (https://evernote.com/)
A free tool to collect, manage, share and present data across multiple platforms. always available and organized.

qiqqa (http://www.qiqqa.com/)
The essential free research and reference manager. Search for, read and annotate your PDFs. Then review your work, write up and create bibliographies instantly.

Paperpile (https://paperpile.com/)
Manage your research library right in your browser, access your PDFs from anywhere and format citations within Google Docs.

Paper-Box (http://www.paper-box.co/)
A cloud reference manager with Track, Search, Manage, Share, Discuss and Cite Papers Anywhere, on Any Computer

Mendeley (https://www.mendeley.com/)
Mendeley is a free reference manager and academic social network. Make your own fully-searchable library in seconds, cite as you write, and read and annotate your PDFs on any device.

2.0 Writing Scientific Papers

This unit will help you select and organize a paper's content, draft it more effectively, and revise it efficiently. Among others, it offers advice on using verbs optimally, provides general rules for text mechanics (abbreviations, capitalization, hyphens, and so on), and points out frequent shortcomings for speakers of specific language groups. Incorporate the software tools to help your team effeciently work on your scientific paper about your protein.

2.1 Structuring Your Scientific Paper

Scientific papers are for sharing your own original research work with other scientists or for reviewing the research conducted by others. As such, they are critical to the evolution of modern science, in which the work of one scientist builds upon that of others. To reach their goal, papers must aim to inform, not impress. They must be highly readable — that is, clear, accurate, and concise. They are more likely to be cited by other scientists if they are helpful rather than cryptic or self-centered. Scientific papers typically have two audiences: first, the referees, who help the journal editor decide whether a paper is suitable for publication; and second, the journal readers themselves, who may be more or less knowledgeable about the topic addressed in the paper. To be accepted by referees and cited by readers, papers must do more than simply present a chronological account of the research work. Rather, they must convince their audience that the research presented is important, valid, and relevant to other scientists in the same field. To this end, they must emphasize both the motivation for the work and the outcome of it, and they must include just enough evidence to establish the validity of this outcome.

Papers that report experimental work are often structured chronologically in five sections: first, Introduction; then Materials and Methods, Results, and Discussion (together, these three sections make up the paper's body); and finally, Conclusion.

The **Introduction** section clarifies the motivation for the work presented and prepares readers for the structure of the paper.

The **Materials and Methods** section provides sufficient detail for other scientists to reproduce the experiments presented in the paper. In some journals, this information is placed in an appendix, because it is not what most readers want to know first.

The **Results and Discussio**n sections present and discuss the research results, respectively. They are often usefully combined into one section, however, because readers can seldom make sense of results alone without accompanying interpretation — they need to be told what the results mean.

The **Conclusion** section presents the outcome of the work by interpreting the findings at a higher level of abstraction than the Discussion and by relating these findings to the motivation stated in the Introduction.

(Papers reporting something other than experiments, such as a new method or technology, typically have different sections in their body, but they include the same Introduction and Conclusion sections as described above.)

Although the above structure reflects the progression of most research projects, effective papers typically break the chronology in at least three ways to present their content in the order in which the audience will most likely want to read it. First and foremost, they summarize the motivation for, and the outcome of, the work in an abstract, located before the Introduction. In a sense, they reveal the beginning and end of the story — briefly — before providing the full story. Second, they move

the more detailed, less important parts of the body to the end of the paper in one or more appendices so that these parts do not stand in the readers' way. Finally, they structure the content in the body in theorem-proof fashion, stating first what readers must remember (for example, as the first sentence of a paragraph) and then presenting evidence to support this statement.

The introduction
An effective introduction for a paper
View Full-Size Image
An effective introduction for a paper

The introduction reproduced here exhibits the four components that readers find useful as they begin to read a paper.

In the Introduction section, state the motivation for the work presented in your paper and prepare readers for the structure of the paper. Write four components, probably (but not necessarily) in four paragraphs: context, need, task, and object of the document. **First**, provide some context to orient those readers who are less familiar with your topic and to establish the importance of your work. **Second**, state the need for your work, as an opposition between what the scientific community currently has and what it wants. **Third**, indicate what you have done in an effort to address the need (this is the task). **Finally**, preview the remainder of the paper to mentally prepare readers for its structure, in the object of the document.

Context and need

At the beginning of the Introduction section, the context and need work together as a funnel: They start broad and progressively narrow down to the issue addressed in the paper. To spark interest among your audience — referees and journal readers alike — provide a compelling motivation for the work presented in your paper: The fact that a phenomenon has never been studied before is not, in and of itself, a reason to study that phenomenon.
Write the context in a way that appeals to a broad range of readers and leads into the need. Do not include context for the sake of including context: Rather, provide only what will help readers better understand the need and, especially, its importance. Consider anchoring the context in time, using phrases such as recently, in the past 10 years, or since the early 1990s. You may also want to anchor your context in space (either geographically or within a given research field).
Convey the need for the work as an opposition between actual and desired situations. Start by stating the actual situation (what we have) as a direct continuation of the context. If you feel you must explain recent achievements in much detail — say, in more than one or two paragraphs — consider moving the details to a section titled State of the art (or something similar) after the Introduction, but do provide a brief idea of the actual situation in the Introduction. Next, state the desired situation (what we want). Emphasize the contrast between the actual and desired situations with such words as but, however, or unfortunately.
One elegant way to express the desired part of the need is to combine it with the task in a single sentence. This sentence expresses first the objective, then the action undertaken to reach this objective, thus creating a strong and elegant connection between need and task. Here are three examples of such a combination:

To confirm this assumption, we studied the effects of a range of inhibitors of connexin channels . . . on . . .

To assess whether such multiple-coil sensors perform better than single-signal ones, we tested two of them — the DuoPXK and the GEMM3 — in a field where . . .

To form a better view of the global distribution and infectiousness of this pathogen, we examined 1645 postmetamorphic and adult amphibians collected from 27 countries between 1984 and 2006 for the presence of . . .

Task and object

An Introduction is usually clearer and more logical when it separates what the authors have done (the task) from what the paper itself attempts or covers (the object of the document). In other words, the task clarifies your contribution as a scientist, whereas the object of the document prepares readers for the structure of the paper, thus allowing focused or selective reading.

For the task, use whoever did the work (normally, you and your colleagues) as the subject of the sentence: we or perhaps the authors; use a verb expressing a research action: measured, calculated, etc.; set that verb in the past tense.

The three examples below are well-formed tasks.

To confirm this assumption, **we studied** the effects of a range of inhibitors of connexin channels, such as the connexin mimetic peptides Gap26 and Gap27 and anti-peptide antibodies, on calcium signaling in cardiac cells and HeLa cells expressing connexins.

During controlled experiments, **we investigated** the influence of the HMP boundary conditions on liver flows.

To tackle this problem, **we developed** a new software verification technique called oblivious hashing, which calculates the hash values based on the actual execution of the program.

The list below provides examples of verbs that express research actions:
apply.

We applied Laklöter's principle to . . .

assess	We assessed the effects of larger doses of . . .
calculate	We calculated the photoluminescence spectrum of . . .
compare	We compared the effects of . . . to those of . . .
compute	We computed the velocity predicted by . . .
derive	We derived a new set of rules for . . .
design	We designed a series of experiments to . . .
determine	We determined the complete nucleotide sequence of . . .
develop	We developed a new algorithm to . . .
evaluate	We evaluated the efficacy and biocompatibility of . . .
explore	We explored the relationship between . . .
implement	We implemented a genetic algorithm for . . .
investigate	We investigated the behavior of . . .
measure	We measured the concentration of cadmium in . . .
model	We modeled the diffraction behavior of . . .

For the object of the document,

use the document itself as the subject of the sentence: this paper, this letter, etc.;
use a verb expressing a communication action: presents, summarizes, etc.;
set the verb in the present tense.

The three examples below are suitable objects of the document for the three tasks shown above, respectively.

This paper clarifies the role of CxHc on calcium oscillations in neonatal cardiac myocytes and calcium transients induced by ATP in HL-cells originated from cardiac atrium and in HeLa cells expressing connexin 43 or 26.

This paper presents the flow effects induced by increasing the hepatic-artery pressure and by obstructing the vena cava inferior.

This paper discusses the theory behind oblivious hashing and shows how this approach can be applied for local software tamper resistance and remote code authentication.

The list below provides examples of verbs that express communication actions:

clarify	This paper clarifies the role of soils in . . .
describe	This paper describes the mechanism by which . . .
detail	This paper details the algorithm used for . . .
discuss	This paper discusses the influence of acidity on . . .
explain	This paper explains how the new encoding scheme . . .
offer	This paper offers four recommendations for . . .
present	This paper presents the results of . . .
proposes	This paper proposes a set of guidelines for . . .
provide	This paper provides the complete framework and . . .
report	This paper reports on our progress so far . . .
summarize	This paper summarizes our results for 27 patients with . . .

The body

Even the most logical structure is of little use if readers do not see and understand it as they progress through a paper. Thus, as you organize the body of your paper into sections and perhaps subsections, remember to prepare your readers for the structure ahead at all levels. You already do so for the overall structure of the body (the sections) in the object of the document at the end of the Introduction. You can similarly prepare your readers for an upcoming division into subsections by introducing a global paragraph between the heading of a section and the heading of its first subsection. This paragraph can contain any information relating to the section as a whole rather than particular subsections, but it should at least announce the subsections, whether explicitly or implicitly. An explicit preview would be phrased much like the object of the document: “This section first . . . , then . . . , and finally . . . “

Although papers can be organized into sections in many ways, those reporting experimental work typically include Materials and Methods, Results, and Discussion in their body. In any case, the paragraphs in these sections should begin with a topic sentence to prepare readers for their contents, allow selective reading, and — ideally — get a message across.

Materials and methods

This paragraph of materials and methods expresses the main idea first, in a topic sentence, so readers immediately know what it is about. Most Materials and Methods sections are boring to read, yet they need not be. To make this section interesting, explain the choices you made in your experimental procedure: What justifies using a given compound, concentration, or dimension? What is special, unexpected, or different in your approach? Mention these things early in your paragraph, ideally in the first sentence. If you use a standard or usual procedure, mention that upfront, too. Do not make readers guess: Make sure the paragraph's first sentence gives them a clear idea of what the entire paragraph is about. If you feel you cannot or need not do more than list items, consider using a table or perhaps a schematic diagram rather than a paragraph of text.

Results and discussion

The traditional Results and Discussion sections are best combined because results make little sense to most readers without interpretation.
When reporting and discussing your results, do not force your readers to go through everything you went through in chronological order. Instead, state the message of each paragraph upfront: Convey in the first sentence what you want readers to remember from the paragraph as a whole. Focus on what happened, not on the fact that you observed it. Then develop your message in the remainder of the paragraph, including only that information you think you need to convince your audience.

The conclusion

In the Conclusion section, state the most important outcome of your work. Do not simply summarize the points already made in the body — instead, interpret your findings at a higher level of abstraction. Show whether, or to what extent, you have succeeded in addressing the need stated in the Introduction. At the same time, do not focus on yourself (for example, by restating everything you did). Rather, show what your findings mean to readers. Make the Conclusion interesting and memorable for them.

At the end of your Conclusion, consider including perspectives — that is, an idea of what could or should still be done in relation to the issue addressed in the paper. If you include perspectives, clarify whether you are referring to firm plans for yourself and your colleagues ("In the coming months, we will . . . ") or to an invitation to readers ("One remaining question is . . . ").

If your paper includes a well-structured Introduction and an effective abstract, you need not repeat any of the Introduction in the Conclusion. In particular, do not restate what you have done or what the paper does. Instead, focus on what you have found and, especially, on what your findings mean. Do not be afraid to write a short Conclusion section: If you can conclude in just a few sentences given the rich discussion in the body of the paper, then do so. (In other words, resist the temptation to repeat material from the Introduction just to make the Conclusion longer under the false belief that a longer Conclusion will seem more impressive.)

The Abstract

The readers of a scientific paper read the abstract for two purposes: to decide whether they want to (acquire and) read the full paper, and to prepare themselves for the details presented in that paper. An effective abstract helps readers achieve these two purposes. In particular, because it is typically read before the full paper, the abstract should present what the readers are primarily interested in; that is, what they want to know first of all and most of all.

Typically, readers are primarily interested in the information presented in a paper's Introduction and Conclusion sections. Primarily, they want to know the motivation for the work presented and the outcome of this work. Then (and only then) the most specialized among them might want to know the details of the work. Thus, an effective abstract focuses on motivation and outcome; in doing so, it parallels the paper's Introduction and Conclusion.

Accordingly, you can think of an abstract as having two distinct parts — motivation and outcome — even if it is typeset as a single paragraph. For the first part, follow the same structure as the Introduction section of the paper: State the context, the need, the task, and the object of the document. For the second part, mention your findings (the what) and, especially, your conclusion (the so what — that is, the interpretation of your findings); if appropriate, end with perspectives, as in the Conclusion section of your paper.

Although the structure of the abstract parallels the Introduction and Conclusion sections, it differs from these sections in the audience it addresses. The abstract is read by many different readers, from the most specialized to the least specialized among the target audience. In a sense, it should be the least specialized part of the paper. Any scientist reading it should be able to understand why the work was carried out and why it is important (context and need), what the authors did (task) and what the paper reports about this work (object of the document), what the authors found (findings), what these findings mean (the conclusion), and possibly what the next steps are (perspectives). In contrast, the full paper is typically read by specialists only; its Introduction and Conclusion are more detailed (that is, longer and more specialized) than the abstract.

An effective abstract stands on its own — it can be understood fully even when made available without the full paper. To this end, avoid referring to figures or the bibliography in the abstract. Also, introduce any acronyms the first time you use them in the abstract (if needed), and do so again in the full paper (see Mechanics: Using abbreviations).

2.3 Drafting Your Scientific Paper

Effective writing is readable — that is, clear, accurate, and concise. When you are writing a paper, try to get your ideas across in such a way that the audience will understand them effortlessly, unambiguously, and rapidly. To this end, strive to write in a straightforward way. There is no need to write about science in unusual, complicated, or overly formal ways in an effort to "sound scientific" or to impress your audience. If you can tell a friend about your work, you are off to a good start.
To construct sentences that reflect your ideas, focus these sentences appropriately. Express one idea per sentence. Use your current topic — that is, what you are writing about — as the grammatical subject of your sentence (see Verbs: Choosing between active and passive voice). When writing a complex sentence (a sentence that includes several clauses), place the main idea in the main clause rather than a subordinate clause. In particular, focus on the phenomenon at hand, not on the fact that you observed it.

Constructing your sentences logically is a good start, but it may not be enough. To ensure they are readable, make sure your sentences do not tax readers' short-term memory by obliging these readers to remember long pieces of text before knowing what to do with them. In other words, keep together what goes together. Then, work on conciseness: See whether you can replace long phrases with shorter ones or eliminate words without loss of clarity or accuracy.

The following screens cover the drafting process in more detail. Specifically, they discuss how to use verbs effectively and how to take care of your text's mechanics.

Verbs

Much of the strength of a clause comes from its verb. Therefore, to express your ideas accurately, choose an appropriate verb and use it well. In particular, use it in the right tense, choose carefully between active and passive voice, and avoid dangling verb forms.

Verbs are for describing actions, states, or occurrences. To give a clause its full strength and keep it short, do not bury the action, state, or occurrence in a noun (typically combined with a weak verb), as in "The catalyst produced a significant increase in conversion rate." Instead write, "The catalyst increased the conversion rate significantly." The examples below show how an action, state, or occurrence can be moved from a noun back to a verb.

Instead of	*Write*
Make an examination of . . .	examine
Present a comparison of . . .	compare
Be in agreement . . .	agree
Perform an analysis of . . .	analyze
Produce an improvement in . . .	improve

Using the right tense

In your scientific paper, use verb tenses (past, present, and future) exactly as you would in ordinary writing. Use the past tense to report what happened in the past: what you did, what someone reported, what happened in an experiment, and so on. Use the present tense to express general truths, such as conclusions (drawn by you or by others) and atemporal facts (including information about what the paper does or covers). Reserve the future tense for perspectives: what you will do in the coming months or years. Typically, most of your sentences will be in the past tense, some will be in the present tense, and very few, if any, will be in the future tense.

Past tense

Work done
We collected blood samples from . . .
Groves et al. determined the growth rate of . . .
Consequently, astronomers decided to rename . . .

Work reported
Jankowsky reported a similar growth rate . . .
In 2009, Chu published an alternative method to . . .
Irarrázaval observed the opposite behavior in . . .

Observations
The mice in Group A developed, on average, twice as much . . .
The number of defects increased sharply . . .
The conversion rate was close to 95% . . .

Present tense

General truths
Microbes in the human gut have a profound influence on . . .
The Reynolds number provides a measure of . . .
Smoking increases the risk of coronary heart disease . . .

Atemporal facts
This paper presents the results of . . .
Section 3.1 explains the difference between . . .
Behbood's 1969 paper provides a framework for . . .

Future tense

Perspectives
In a follow-up experiment, we will study the role of . . .
The influence of temperature will be the object of future research . . .

Note the difference in scope between a statement in the past tense and the same statement in the present tense: "The temperature increased linearly over time" refers to a specific experiment, whereas "The temperature increases linearly over time" generalizes the experimental observation, suggesting that the temperature always increases linearly over time in such circumstances.
In complex sentences, you may have to combine two different tenses — for example, "In 1905, Albert Einstein postulated that the speed of light is constant . . . . " In this sentence, postulated refers to something that happened in the past (in 1905) and is therefore in the past tense, whereas is expresses a general truth and is in the present tense.

Choosing between active and passive voice

In English, verbs can express an action in one of two voices. The active voice focuses on the agent: "John measured the temperature." (Here, the agent — John — is the grammatical subject of the sentence.) In contrast, the passive voice focuses on the object that is acted upon: "The temperature was measured by John." (Here, the temperature, not John, is the grammatical subject of the sentence.)

To choose between active and passive voice, consider above all what you are discussing (your topic) and place it in the subject position. For example, should you write "The preprocessor sorts the two arrays" or "The two arrays are sorted by the preprocessor"? If you are discussing the preprocessor, the first sentence is the better option. In contrast, if you are discussing the arrays, the second sentence is better. If you are unsure what you are discussing, consider the surrounding sentences: Are they about the preprocessor or the two arrays?

The desire to be objective in scientific writing has led to an overuse of the passive voice, often accompanied by the exclusion of agents: “The temperature was measured” (with the verb at the end of the sentence). Admittedly, the agent is often irrelevant: No matter who measured the temperature, we would expect its value to be the same. However, a systematic preference for the passive voice is by no means optimal, for at least two reasons.

For one, sentences written in the passive voice are often less interesting or more difficult to read than those written in the active voice. A verb in the active voice does not require a person as the agent; an inanimate object is often appropriate. For example, the rather uninteresting sentence “The temperature was measured . . . “ may be replaced by the more interesting “The measured temperature of 253°C suggests a secondary reaction in . . . .” In the second sentence, the subject is still temperature (so the focus remains the same), but the verb suggests is in the active voice. Similarly, the hard-to-read sentence “In this section, a discussion of the influence of the recirculating-water temperature on the conversion rate of . . . is presented” (long subject, verb at the end) can be turned into “This section discusses the influence of . . . . “ The subject is now section, which is what this sentence is really about, yet the focus on the discussion has been maintained through the active-voice verb discusses.

As a second argument against a systematic preference for the passive voice, readers sometimes need people to be mentioned. A sentence such as “The temperature is believed to be the cause for . . . “ is ambiguous. Readers will want to know who believes this — the authors of the paper, or the scientific community as a whole? To clarify the sentence, use the active voice and set the appropriate people as the subject, in either the third or the first person, as in the examples below.

Biologists believe the temperature to be . . .
Keustermans et al. (1997) believe the temperature to be . . .
The authors believe the temperature to be . . .
We believe the temperature to be . . .

Avoiding dangling verb forms

A verb form needs a subject, either expressed or implied. When the verb is in a non-finite form, such as an infinitive (to do) or a participle (doing), its subject is implied to be the subject of the clause, or sometimes the closest noun phrase. In such cases, construct your sentences carefully to avoid suggesting nonsense. Consider the following two examples.

To dissect its brain, the affected fly was mounted on a . . .
After aging for 72 hours at 50°C, we observed a shift in . . .

Here, the first sentence implies that the affected fly dissected its own brain, and the second implies that the authors of the paper needed to age for 72 hours at 50°C in order to observe the shift. To restore the intended meaning while keeping the infinitive to dissect or the participle aging, change the subject of each sentence as appropriate:

To dissect its brain, we mounted the affected fly on a . . .
After aging for 72 hours at 50°C, the samples exhibited a shift in . . .

Alternatively, you can change or remove the infinitive or participle to restore the intended meaning:

To have its brain dissected, the affected fly was mounted on a . . .

After the samples aged for 72 hours at 50°C, we observed a shift in . . .

Mechanics

In communication, every detail counts. Although your focus should be on conveying your message through an appropriate structure at all levels, you should also save some time to attend to the more mechanical aspects of writing in English, such as using abbreviations, writing numbers, capitalizing words, using hyphens when needed, and punctuating your text correctly.

Using abbreviations

Beware of overusing abbreviations, especially acronyms — such as GNP for gold nanoparticles. Abbreviations help keep a text concise, but they can also render it cryptic. Many acronyms also have several possible extensions (GNP also stands for gross national product).
Write acronyms (and only acronyms) in all uppercase (GNP, not gnp).

Introduce acronyms systematically the first time they are used in a document. First write the full expression, then provide the acronym in parentheses. In the full expression, and unless the journal to which you submit your paper uses a different convention, capitalize the letters that form the acronym: “we prepared Gold NanoParticles (GNP) by . . . “ These capitals help readers quickly recognize what the acronym designates.
Notes:

Do not use capitals in the full expression when you are not introducing an acronym: “we prepared gold nanoparticles by… “

As a more general rule, use first what readers know or can understand best, then put in parentheses what may be new to them. If the acronym is better known than the full expression, as may be the case for techniques such as SEM or projects such as FALCON, consider placing the acronym first: “The FALCON (Fission-Activated Laser Concept) program at…”

In the rare case that an acronym is commonly known, you might not need to introduce it. One example is DNA in the life sciences. When in doubt, however, introduce the acronym.

In papers, consider the abstract as a stand-alone document. Therefore, if you use an acronym in both the abstract and the corresponding full paper, introduce that acronym twice: the first time you use it in the abstract and the first time you use it in the full paper. However, if you find that you use an acronym only once or twice after introducing it in your abstract, the benefit of it is limited — consider avoiding the acronym and using the full expression each time (unless you think some readers know the acronym better than the full expression).

Writing numbers

In general, write single-digit numbers (zero to nine) in words, as in three hours, and multidigit numbers (10 and above) in numerals, as in 24 hours. This rule has many exceptions, but most of them are reasonably intuitive, as shown hereafter.

Use numerals for numbers from zero to nine

when using them with abbreviated units (3 mV);
in dates and times (3 October, 3 pm);
to identify figures and other items (Figure 3);
for consistency when these numbers are mixed with larger numbers (series of 3, 7, and 24 experiments).

Use words for numbers above 10 if these numbers come at the beginning of a sentence or heading ("Two thousand eight was a challenging year for . . . "). As an alternative, rephrase the sentence to avoid this issue altogether ("The year 2008 was challenging for . . . ").

Capitalizing words

Capitals are often overused. In English, use initial capitals

at beginnings: the start of a sentence, of a heading, etc.;
for proper nouns, including nouns describing groups (compare physics and the Physics Department);
for items identified by their number (compare in the next figure and in Figure 2), unless the journal to which you submit your paper uses a different convention;
for specific words: names of days (Monday) and months (April), adjectives of nationality (Algerian), etc.

In contrast, do not use initial capitals for common nouns: Resist the temptation to glorify a concept, technique, or compound with capitals. For example, write finite-element method (not Finite-Element Method), mass spectrometry (not Mass Spectrometry), carbon dioxide (not Carbon Dioxide), and so on, unless you are introducing an acronym (see Mechanics: Using abbreviations).

Using hyphens to clarify meaning

Hyphens can be tricky in English, especially in long expressions. Here is a more detailed example. Use hyphens in English to clarify relationships in chains of words. Thus, low temperature impact (without a hyphen) suggests a low impact of the temperature, whereas low-temperature impact (with a hyphen) suggests the impact of or at low temperature. Such hyphens, useful for (nouns used as) adjectives, are unnecessary for adverbs. For example, a highly interesting paper does not need a hyphen; in this phrase, highly can only qualify interesting (not paper).

In general, do not use a hyphen with a prefix, namely an element that is not a word in itself and that is added at the beginning of a word to modify its meaning. Thus, write multichannel, nonlinear, preamplifier, postdoctoral, realign, etc. As an exception to this rule, use a hyphen to separate vowels that would otherwise be read together, as in pre-embryo, or when the original word is written with a capital, as in pre-Columbian.

Punctuating text

Punctuation has many rules in English; here are three that are often a challenge for non-native speakers.

As a rule, insert a comma between the subject of the main clause and whatever comes in front of it, no matter how short, as in "Surprisingly, the temperature did not increase." This comma is not al-

ways required, but it often helps and never hurts the meaning of a sentence, so it is good practice. In series of three or more items, separate items with commas (red, white, and blue; yesterday, today, or tomorrow). Do not use a comma for a series of two items (black and white).

In displayed lists, use the same punctuation as you would in normal text (but consider dropping the and).

The system is fast, flexible, and reliable.

The system is
fast,
flexible,
reliable.

2.4 Revising Your Scientific Paper

Writing is an iterative process. Do not hope to write a perfect paper in one pass. Instead, work in several passes, focusing on progressively smaller aspects of your document in each pass. First, focus on selecting the right content for your paper and on structuring this content effectively from the document as a whole all the way down to individual paragraphs. Next, refine your writing at the sentence level to convey your ideas in a clear, accurate, and concise way. Finally, ensure that your document is correct: Check not only the grammar and spelling, but also the numbering of figures and tables, the validity of cross-references, the accuracy of dates, etc.

Beyond a good dictionary and a good grammar reference, you can use several types of software tools to check your document for correctness. Your text processor likely includes a spelling checker and perhaps a grammar checker. You can also build a personal list of attention points and look for these in your paper using simple or complex text searches. Finally, you can regard the Web as a corpus and search it — discerningly — for usage.

Automated spelling and grammar checkers do not understand what you write: They only check your text for symptoms of problems. Consequently, use them prudently. Closely examine the words or sentences they flag, but do not accept their proposed alternatives too readily. For example, if you wrote mouses instead of mice (the plural of mouse), a spelling checker may propose mousse and mouse's as alternatives (neither of which would be correct here), but not mice. You would then have to look up mouse in a dictionary to find the correct plural. Grammar checkers are typically even less accurate at proposing correct alternatives: Unless you know the language well, they may be more confusing than helpful.

To check the grammar and many more aspects of your text, a useful approach is to build your own personal list of attention points over time, then use your text processor's Find function to search for these points in your paper. For example, if you tend to focus on the observation of phenomena rather than the phenomena themselves — by using sentences such as "An increase of the temperature was observed" — you might add the word observe to your list. Then, each time you find observe in your text, you can decide whether to revise your sentence (for example, by writing "The temperature increased"). If your text processor allows you to search for patterns in addition to phrases, you can perform even more powerful checks. For example, you might search for the pattern "it is . . . that" to find suboptimal main clauses such as "It is clear that," "It is evident that," and "It is a surprise to us that" (best replaced by "Clearly," "Evidently," and "Surprisingly").

You can verify correct or idiomatic use of English via Web search. For example, if you wonder whether to write “we participated to a meeting” or “we participated in a meeting,” you can search the Web for both phrases (with quotation marks) to see whether one is found significantly more often than the other (here, it would be the second one). This method is, of course, not authoritative — popular does not necessarily mean correct — but it can be helpful if used carefully. You may find a more representative sample by shortening the phrases you search for (in this example, perhaps by dropping the word we). If you do, be careful not to lose the relevance by shortening a phrase too much. For example, if you search for “participated to” only, your search will count irrelevant instances, such as “we participated to the best of our abilities.” In any case, do not trust the counts alone: Look at the search results themselves to make sure they are relevant. Finally, include enough alternatives in your search. If you regard a meeting as a location rather than an activity, you may prefer to write “we participated at the meeting,” an option you would, of course, not have found by searching for the initial two phrases.

2.5 Advice for Specific Language Groups

A foreign language is all the more difficult to master when it differs from one’s native language in unexpected ways. The following three situations are particularly challenging:

The foreign language uses concepts not present in the native language. Examples include inflection (as in whom versus who), conjugation (he does, we do, we did, etc.), and gender (he, she, it), which are not employed in all languages.

The foreign language uses concepts that are present in the native language in a different way or to a different extent. Examples include prepositions (used differently in different languages), gender (a word that is masculine in one language may not be so in another), and moods and tenses (not all moods or tenses of one language are necessarily present in another, and, if they are, they may be used differently).

The foreign and native languages use words that have similar forms but different meanings (so-called false friends), or the foreign language uses two different words for two meanings rendered by the same word in the native language (such as make and do, both rendered by the same word in many languages).

English has many false friends with Germanic and Romance languages. Probably the most common are actually (meaning in fact rather than currently), and eventually (meaning in the end rather than possibly). Other examples are become (meaning begin to be rather than get, as in the German bekommen), high school (designating grades 9 through 12 rather than college or university, as in the French haute école), and fabric (meaning cloth rather than factory, as in the Spanish fábrica). You can search the Web for more examples that exist between English and your native language, or you might start a personal list of words you often confuse. Then, every time someone corrects such a confusion in your writing, you can add that false friend to your list.

Among the words often confused in English because they translate to the same word in other languages are the following five pairs.

Lend/borrow (both translating as *ausleihen* in German and *lenen* in Dutch)	Can I borrow your calculator for a minute? Sure, I will lend it to you.
Then/than (both translating as *dan* in Dutch)	If x is larger than y and y is larger than z, then x is larger than z.
If/when	If I decide to join you, I will meet you at noon. [= in the event that] When I make up my mind, I will let you know. [= at the time that]
Must not/need not	You must not use your calculator. [= are not allowed to] You need not bring anything. [= are not required to]
Since/for	I have been working on this problem since 2008. I have been working on this problem for two years.

Advice for speakers of German and Dutch

In addition to the false friends and often confused words mentioned earlier, speakers of German and Dutch must pay special attention to several other common mistakes.
Mind the difference between the following related words:

Teach/learn	I teach quantum mechanics to first-year students. I learned this material from two Nobel laureates.
Experience/experiment	I learned a lot from experience. (I am an experienced researcher.) To test our hypothesis, we performed three experiments (according to our group's standard experimental procedure).
Remember/remind	I must remember to send her a copy of my paper. Please remind me to do so.
Make/do	If I make a mistake, I will have to do the experiment all over again. (Usage for *make* and *do* is complex. When in doubt about your planned use, look it up in the dictionary or verify usage through a discerning Web search.)
Less/fewer	In less time, I will be able to complete fewer experiments. (*Time* is uncountable, *experiments* are countable. The same comment applies to the use of *much* [uncountable] and *many* [countable].)

Beware of Dutch constructions that are uncommon or incorrect in English, such as the use of also as the first word of a sentence. Thus, the Dutch sentence “Ook de temperatuur heeft een invloed op . . . “ does not translate as “Also the temperature has an influence on . . . “ A more correct rendering in English is “The temperature, too, has an influence on . . . “

Be alert for unnecessary hyphens, such as a hyphen between an abbreviation used as an adjective and a noun. Write, for example, the FFT algorithm (not the FFT-algorithm) and the Web application (not the Web-application or the Webapplication).

Finally, beware of **abusive abbreviations**. Do not carry over into English the Dutch habit of abbreviating expressions such as onder andere (o.a.), met betrekking tot (m.b.t.), and ter attentie van (t.a.v.). In English, it is uncommon to write a.o. for among others, w.r.t. for with respect to, or f.a.o. for for the attention of.

In English, abbreviations such as the ones above are used mostly for Latin expressions, as in e.g. for exempli gratia, i.e. for id est, or b.i.d. for bis in die. Still, these Latin expressions are probably best replaced by their English equivalents (for example, that is, and twice daily).

Advice for speakers of French, Spanish, and other Romance languages

In addition to the false friends and often confused words mentioned earlier, speakers of Romance languages must pay special attention to several other common mistakes.
Beware of noun phrases that use chains of prepositions, in particular the preposition of. Thus, rather than “the variation of the temperature of the surface of the sea,” write “the variation in sea-surface temperature.”

Speakers of Romance languages tend to write in indirect ways, often burying the main idea in several layers of subordinate clauses. Spanish, in particular, overuses constructions such as “A estas alturas, se podría decir sin riesgo a equivocarse que . . . ,” which can usually be removed entirely in both the original language and the English rendering. Use subordinate clauses to convey subordinate ideas, not to hide the message.

In many Romance languages (French being a notable exception), the subject pronoun can be dropped. Remember to always include subject pronouns in English, in particular the impersonal it. For instance, write “It is interesting,” not “Is interesting.”

Finally, do not insert a space in front of any punctuation mark in English the way you sometimes would in French. Similarly, do not insert a space before the percent (%) and degree (°) signs.

Advice for speakers of Chinese and Japanese

Conceptual differences between English and Chinese or Japanese are numerous: Native speakers of Chinese or Japanese easily make mistakes with singular versus plural forms, subject-verb agreement, and articles. Speakers of Chinese may further be challenged by genders and verb tenses. Although these broad issues cannot be summarized here, another area of frequent confusion is worth noting: the order of a person’s first and last names.

In English, and as the terms indicate, a person’s first (or given) name comes first, and his or her last (or family) name comes last. For publications and other administrative purposes in English-speaking contexts, remember to write and say your first name first. Independent of this formal sequence, feel free to indicate to other people what you would like to be called in conversation, especially if you prefer not to be called by your first name, as is typical in informal settings in other cultures. Indicating what you would like to be called is helpful to your peers, who often feel insecure about what to call their colleagues from China or Japan.

2.6 Summary

Scientific papers, like any other form of professional communication, are about getting messages across. To make sure you focus on the so what, create your scientific paper in a top-down fashion. First, work on the macrostructure: Select the content for your paper and organize it in a reader-friendly way, paying special attention to the beginning and the end. Then, work on the mid-level structure: Deliver one message with each paragraph using clear, accurate, and concise sentences. Finally, work on the microstructure: Polish your paper all the way down to the smallest details of the language.

At the macrostructure level, present the content in the order in which the audience will most likely want to read it. In particular, place first in an abstract what readers are primarily interested in, that is, the beginning of the story (the motivation), in the form of a context, a need, a task, and an object of the document; and the end of the story (the outcome), in the form of findings, conclusions, and perhaps perspectives. Write your abstract so that it can be understood even by the least specialized of your target readers, independent of the full paper.

With the full paper, strive to convince your audience that your work is important, valid, and relevant. In the Introduction section, emphasize again the motivation for your work. Structure this section like the first half of the abstract (context, need, task, and object of the document), but in more detail. In the Conclusion section, emphasize the outcome of your work. Structure this section like the second half of the abstract (findings if needed, conclusions, and perspectives), but with more detail. In the body of the paper, present just enough evidence to establish the validity of this outcome.

At the paragraph level, present first (typically in the very first sentence) what you want your readers to remember before developing this message in the rest of the paragraph. With each sentence, convey one idea: Structure the sentence in a way that reflects your idea, with the topic in the subject position, the action in the verb, and the main information in the main clause. Use verbs well: Choose the right verb, put it in the right tense and voice, and make sure it has a meaningful subject.

After you have designed and drafted your paper, revise it for correctness using whatever tools are most helpful to you. Beyond spelling and grammar checkers, consider text searches, both in your paper (searching for your own list of attention points) and on the Web (checking usage discerningly through popularity).

More to Come, look for the last installment of this section, it will include the following:

Unit 3 Writing Correspondence
Unit 4 Giving Oral Presentations
Unit 5 Interacting During Conference Sessions
Unit 6 Communicating in the Classroom

THE JOURNAL OF BIOLOGICAL CHEMISTRY
© 2005 by The American Society for Biochemistry and Molecular Biology, Inc.

Vol. 280, No. 4, Issue of January 28, pp. 2990–2997, 2005
Printed in U.S.A.

The Crystal Structure of the Herpes Simplex Virus 1 ssDNA-binding Protein Suggests the Structural Basis for Flexible, Cooperative Single-stranded DNA Binding*[S]

Received for publication, June 17, 2004, and in revised form, October 25, 2004
Published, JBC Papers in Press, October 26, 2004, DOI 10.1074/jbc.M406780200

Title Page

Marina Mapelli‡§, Santosh Panjikar‡, and Paul A. Tucker¶

From the European Molecular Biology Laboratory, Hamburg Outstation, c/o DESY, Notkestrasse 85, D-22603 Hamburg, Germany

Abstract

All organisms including animal viruses use specific proteins to bind single-stranded DNA rapidly in a non-sequence-specific, flexible, and cooperative manner during the DNA replication process. The crystal structure of a 60-residue C-terminal deletion construct of ICP8, the major single-stranded DNA-binding protein from herpes simplex virus-1, was determined at 3.0 Å resolution. The structure reveals a novel fold, consisting of a large N-terminal domain (residues 9–1038) and a small C-terminal domain (residues 1049–1129). On the basis of the structure and the nearest neighbor interactions in the crystal, we have presented a model describing the site of single-stranded DNA binding and explaining the basis for cooperative binding. This model agrees with the bended morphology observed in electron micrographs.

Viruses of the *Herpesviridae* family infect almost all vertebrates, including man, causing a variety of diseases. Of the seven viruses identified as human infectious agents, herpes simplex virus-1 (HSV-1)[1] is the prototype of the alphaherpesvirus subfamily and of the family as a whole. The HSV-1 single-stranded DNA (ssDNA)-binding protein (SSB), ICP8, is a nuclear protein that, along with the six other HSV replication proteins (the viral polymerase (UL30) and its accessory factor (UL42), the trimeric helicase-primase complex (UL5-UL8-UL52), and the origin-binding protein (OBP), coded by the gene ul9), is required for viral DNA replication (1) during lytic infection. Replication has been thought to proceed by a rolling circle mechanism (2) partly because the replication product is a concatamer, although the observation of highly branched replication intermediates could be explained by other mechanisms

that would link recombination and replication. ICP8 is a 128-kDa multifunctional zinc metalloprotein (3) encoded by the ul29 gene. It preferentially binds ssDNA over double-stranded DNA in a non-sequence-specific and cooperative manner (4). ICP8 has been reported to interact either directly or indirectly with several other viral proteins. There is evidence that it binds to the C terminus of the OBP and stimulates its helicase activity (5, 6), that it promotes the helicase activity of the viral helicase-primase complex (UL5-UL8-UL52) (7), and that it modulates the processivity of the viral polymerase (UL30) (8). Before viral DNA replication commences, these proteins are thought to be co-localized with ICP8 at small punctuate foci called prereplicative sites. With the onset of viral genome amplification, these proteins become redistributed into a larger globular replication compartment (9) whose location is defined by the preexisting host cell nuclear architecture, most probably at the periphery of the nuclear matrix-associated ND10 domains where the viral transactivator ICP0 and the viral input genome are believed to migrate in the early stages of infection (10). ICP8 is also involved in several other events of the DNA metabolism. It can promote DNA strand transfer (11), catalyze strand invasion in an ATP-independent manner (12), and renature complementary DNA strands (13), which indicates that ICP8 plays an important role in HSV genome recombination. The replication of HSV-1 DNA is also associated with a high degree of homologous recombination. Recently it was shown that ICP8 works together with alkaline nuclease (UL12), which is a 5′- 3′-exonuclease, to effect strand exchange (14). In addition to its role in DNA synthesis, ICP8 has been shown to regulate viral gene expression by repressing transcription from the parental genome (15) and stimulating late gene expression from progeny genomes (16).

Genetic and biochemical analyses have failed to identify functionally independent domains within ICP8. Even the extent of the minimal DNA binding region has remained unclear. It has been placed in the C-terminal half of the protein (17) or in regions spanning residues 564–1110 (18) or 300–849 (19). The C-terminal 60 amino acid residues were shown to account for most of the cooperative behavior in ssDNA binding (20), possibly modulated by the two cysteines 254 and 455 (21). It has also been shown that the C-terminal 28 amino acids contain a nuclear localization signal (22), that the residues between 499 and 512 host a zinc binding motif (3), and that the residues from 1082–1169 are also important for the stimulation of late gene expression (18).

Here we have reported the first crystal structure of an ssDNA-binding protein of the *Herpesviridae*, a 60-amino acid C-terminal deletion mutant of ICP8, at 3.0 Å resolution. The structure consists of an unexpectedly large N-terminal folding unit and a small C-terminal α-helical domain, both with novel folds. In addition, it

* The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

[S] The on-line version of this article (available at http://www.jbc.org) contains supplemental figures.

The atomic coordinates and structure factors (code 1UNJ) have been deposited in the Protein Data Bank, Research Collaboratory for Structural Bioinformatics, Rutgers University, New Brunswick, NJ (http://www.rcsb.org/).

‡ Both authors contributed equally to this work.

§ Present address: European Institute of Oncology, Via Ripamonti 435, 20141 Milano, Italy.

¶ To whom correspondence should be addressed. Tel.: 49-40-8998-2129; Fax: 49-40-8998-2149; E-mail: tucker@embl-hamburg.de.

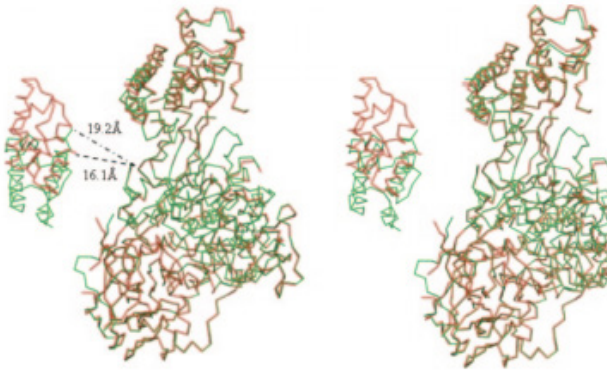
[1] The abbreviations used are: HSV, herpes simplex virus; ssDNA, single-stranded DNA; SSB, ssDNA-binding protein; OBP, origin-binding protein; SeMet, selenomethionine; MAD, multiwavelength anomalous diffraction; MMA, methyl mercury acetate; OB, oligonucleotide/oligosaccharide binding; HsmSSB, human mitochondrial SSB.

Authors statement (are there any conflict of interests?)

Various graphics and diagrams can provide a wealth of information about your protein of interest and don't forget to record pertenant references tht you might use in your paper and enter them in your reference manager for later use.

Crystal Structure of the ssDNA-binding Protein of HSV-1

. Orientation of the C termi- stereopair showing the structural sition of the N-terminal domains wo independent molecules, illus- the difference in relative orienta- their C-terminal domains. These nal domains would dock onto the lecule in the protein chain as in- in Fig. 3. The relative orientation d N-terminal domains is probably ned to some degree by the packing rotein chains in the solid state.



If you use information from a graphic drawn or represented in a paper, be sure to provide a reference for that, so others can find that information if they need it.

Vol. 280, No. 4, Issue of January 28, pp. 2990–2997, 2005
Printed in U.S.A.

REFERENCES

1. Challberg, M. D. (1986) *Proc. Natl. Acad. Sci. U. S. A.* **83,** 9094–9098
2. Skaliter, R., and Lehman, I. R. (1994) *Proc. Natl. Acad. Sci. U. S. A.* **91,** 10665–10669
3. Gupte, S. S., Olson, J. W., and Ruyechan, W. T. (1991) *J. Biol. Chem.* **266,** 11413–11416
4. Lee, C. K., and Knipe, D. M. (1985) *J. Virol.* **54,** 731–738
5. Makhov, A. M., Boehmer, P. E., Lehman, I. R., and Griffith, J. D. (1996) *J. Mol. Biol.* **258,** 789–799
6. He, X., and Lehman, I. R. (2001) *Proc. Natl. Acad. Sci. U. S. A.* **98,** 3024–3028
7. Falkenberg, M., Elias, P., and Lehman, I. R. (1998) *J. Biol. Chem.* **273,** 32154–32157
8. Hernandez, T. R., and Lehman, I. R. (1990) *J. Biol. Chem.* **265,** 11227–11232
9. Quinlan, M. P., Chen, L. B., and Knipe, D. M. (1984) *Cell* **36,** 857–868
10. Lukonis, C. J., Burkham, J., and Weller, S. K. (1997) *J. Virol.* **71,** 4771–4781
11. Bortner, C., Hernandez, T. R., Lehman, I. R., and Griffith, J. (1993) *J. Mol. Biol.* **231,** 241–250
12. Nimonkar, A. V., and Boehmer, P. E. (2003) *J. Biol. Chem.* **278,** 9678–9682
13. Dutch, R. E., and Lehman, I. R. (1993) *J. Virol.* **67,** 6945–6949
14. Reuven, N. B., Staire, A. E., Myers, R. S., and Weller, S. K. (2003) *J. Virol.* **77,** 7425–7433
15. Godowski, P. J., and Knipe, D. M. (1986) *Proc. Natl. Acad. Sci. U. S. A.* **83,** 256–260
16. Chen, Y. M., and Knipe, D. M. (1996) *Virology* **221,** 281–290
Read, R. J., Rice, L. M., Simonson, T., and Warren, G. L. (1998) *Acta Crystallogr. Sect. D Biol. Crystallogr.* **54,** 905–921
33. Laskowski, R. A., MacArthur, M. W., Moss, D. S., and Thornton, J. M. (1993) *J. Appl. Crystallogr.* **26,** 283–291
34. Kraulis, P. J. (1991) *J. Appl. Crystallogr.* **24,** 946–950
35. De Lano, W. L. (2002) *Pymol User Manual*, DeLano Scientific, San Carlos, CA
36. Merritt, E. A., and Murphy, M. E. P. (1994) *Acta Crystallogr. Sect. D Biol. Crystallogr.* **50,** 869–873
37. Raghunathan, S., Kozlov, A. G., Lohman, T. M., and Waksman, G. (2000) *Nat. Struct. Biol.* **7,** 648–652
38. Yang, C., Curth, U., Urbanke, C., and Kang, C. (1997) *Nat. Struct. Biol.* **4,** 153–157
39. Agrawal, V., and Kishan, K. V. (2003) *Curr. Protein Pept. Sc.* **4,** 195–206
40. Holm, L., and Sander, C. (1993) *J. Mol. Biol.* **233,** 123–138
41. Murzin, A. G. (1993) *EMBO J.* **12,** 861–867
42. Tucker, P. A., Tsernoglou, D., Tucker, A. D., Coenjaerts, F. E., Leenders, H., and van der Vliet, P. C. (1994) *EMBO J.* **13,** 2994–3002
43. White, E. J., and Boehmer, P. E. (1999) *Biochem. Biophys. Res. Commun.* **264,** 493–497
44. Gao, M., Bouchey, J., Curtin, K., and Knipe, D. M. (1988) *Virology* **163,** 319–329
45. Casas-Finet, J. R., and Karpel, R. L. (1993) *Biochemistry* **32,** 9735–9744
46. Boehmer, P. E., Craigie, M. C., Stow, N. D., and Lehman, I. R. (1994) *J. Biol. Chem.* **269,** 29329–29334
47. Taylor, T.J., and Knipe, D. M., (2004) *J. Virol.* **78,** 5856–5858

Look up references cited in the text of the paper so you can obtain more background on your protein. Google them and see if they are free to download, if not, then ask the librarian how you can log onto JSTOR or services like this one to gain access to paid articles. Older references might provide more historical information that might make your story more interesting. Look up the references in the older papers and track the development history. Remember to enter any reference you think you might use in your paper. waiting to the last minute to do references, is **not** a good idea.

Conclusions section usually at end before the reference.

leased from DNA and processive replication ensues.

Potential Protein-Protein Interaction Sites—We have identified the function of head, neck, and the C-terminal helical region of ICP8; however, a large part of the shoulder region is not, according to our model, involved in cooperative ssDNA binding. It is unlikely that such a large part of the N-terminal domain would have no functional role, because the necessity of packaging the viral genome should tend to enhance the evolution of multifunctional proteins and reduce the likelihood of producing non-functional coding regions. Regulation of late gene expression could involve the ssDNA binding region, but presumably nuclear positioning involves the exposed part of the protein chain. Recent work (47) has identified, by immunocoprecipitation, a number of cellular proteins that co-localize with ICP8. Some of these co-localizations are not dependent on mediation by DNA and are involved in (cellular) DNA replication, repair, and recombination. Structurally there are two regions that are likely to be involved in some of these interactions. The first is a deep pocket (Fig. 5*B*) with conserved aromatic residues (Tyr^{20}, Phe^{61}, Tyr^{90}) at the base and capped by the hydrogen bonding interaction between Glu^{58} and Arg^{193}. The second is a cleft (Fig. 5*C*) containing the fully conserved Cys^{116} and Arg^{120}, both on $\alpha 2$, at the side.

Acknowledgments—We thank Lisa L. Keefe and Andy Herrard of