nature methods
Techniques for Life Scientists and Chemists

ABOUT NATURE METHODS

Aims and scope of the journal

Nature Methods is a forum for the publication of novel methods and significant improvements to tried-and tested techniques in the life sciences and related areas of chemistry. This monthly publication is aimed at a broad, interdisciplinary audience of academic and industry researchers actively involved in laboratory practice. It provides them with new tools to conduct their research and places a strong emphasis on the immediate practical relevance of the work presented.

The journal publishes primary research papers as well as overviews of recent technical and methodological developments. We are actively seeking primary methods papers of relevance to the biological and biomedical sciences, including methods grounded in chemistry that have a practical application to the study of biological problems.

To enhance the practical relevance of each paper, description of the method must be accompanied by its validation, its application to an important biological question and results illustrating its performance in comparison to available approaches. Articles are selected for publication that present broad interest, thorough assessments of methodological performance and comprehensive technical descriptions that facilitate immediate application.

Specific areas of interest include, but are not limited to:

- **Methods for DNA cloning, amplification and sequencing**
- **Methods for protein engineering, expression and purification**
- **Methods for proteomics, including separations, chromatography, mass spectrometry, analysis of binding interactions, microarray-based technologies, display techniques, analysis of post-translational modifications, glycobiology and metabolomics**
- **Methods for systems biology, including proteomics approaches, protein interaction analysis methods and genome wide expression and regulation profiling**
- **Biomolecular structural analysis technologies, including NMR and crystallography**
- **Chemical biology techniques, including chemical labeling, methods for expanding the genetic code and directed evolution**
- **Biophysical methods, including single molecule and lab-on-a-chip technologies**
- **Imaging technologies, including labeling methods and reporters, microscopy, optical spectroscopy and *in vivo* imaging techniques**
- **Techniques for the analysis and manipulation of gene expression, including epigenetics, gene targeting, transduction, RNA interference and microarray-based technologies**
- **Methods for cell culture and manipulation, including stem cells, single cell methods and lab-on-a-chip technologies**
- **Immunological techniques, including production of antibodies, antibody-based assays and immunolabeling**
- **Methods for the study of physiology and disease processes including cancer**
- **Methods involving model organisms and their manipulation**

Editorial process

The overview of the journal's manuscript decision process includes submission, editorial decision on whether the paper should be reviewed, peer review, decisions after review, revision, acceptance in principle, final submission and acceptance, proofs, advance online publication and print publication. Before submitting a paper, authors should consult our editorial policies as well as technical tips for using our online submission system.

Please also consult our general guide for manuscript preparation and submission, which includes information on article formats, journal style and figure preparation tips. Note that procedures for initial submission, revision and final submission are slightly different, so please consult the directions before proceeding to the online submission system. Presubmission inquiries are not a prerequisite for the regular submission process, but are intended as a mechanism for authors to receive rapid feedback on whether a manuscript in preparation is likely to be of interest to the journal. We encourage authors who have already prepared their manuscripts to bypass the presubmission inquiry process and upload their papers as a regular submission to the journal.

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Like the other Nature titles, *Nature Methods* has no external editorial board. Instead, all editorial decisions are made by a team of full-time professional editors. For information on their research backgrounds and scientific interests, see About the Editors. A full list of journal staff appears on the masthead.

Relationship to other Nature journals

Nature Methods is editorially independent, and its editors make their own decisions, independent of the other Nature journals. If a paper is rejected from one Nature journal, the authors can use an automated manuscript transfer service to submit the paper to another Nature journal via a link sent to them by the editor handling the manuscript. Authors should note that referees' comments (including any confidential comments to the editor) and identities are transferred to the editor of the second journal along with the manuscript. In that case, the journal editors will take the previous reviews into account when making their decision, although in some cases the editors may choose to take advice from additional or alternative referees. Alternatively, authors may choose to request a fresh review, in which case they should not use the automated transfer link, and the editors will evaluate the paper without reference to the previous review process. More details are available on the manuscript transfer service and on the relationships between Nature titles.

Editorial and publishing policies

Please see authors & referees @ npg for detailed information about author and referee services and publication policies at the Nature family of journals. These journals, including *Nature Methods*, share a number of common policies including the following:

- **Author responsibilities**
- **License agreement and author copyright**
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- **Use of experimental animals and human subjects**
- **Competing financial interests**
- **Availability of materials and data**
- **Digital image integrity and standards**
- **Security concerns**
- **Refutations, complaints and corrections**
- **Duplicate publication**
- **Confidentiality and pre-publicity**
- **Plagiarism and fabrication**

Impact Factor

The 2009 impact factor for *Nature Methods* is 16.874, according to the Thomson Reuters Journal Citation Reports.

The 2009 impact factor represents the number of citations in 2009 to papers published in 2007 and 2008, divided by the total number of papers published in 2007 and 2008. A more detailed explanation of impact factors appears on the Thomson Reuters website.

Editorial blogs

We encourage community participation in all Nature journal blogs. Methagora is *Nature Methods*' blog. Nautilus is a blog for authors and aspiring authors of Nature Publishing Group journals. Peer-to-Peer is a blog for reviewers and is about peer review. Other Nature Publishing Group blogs can be found on the blog index page.

Abbreviation

The correct abbreviation for abstracting and indexing purposes is *Nat. Methods*.

ISSN and EISSN

The international standard serial number (ISSN) for *Nature Methods* is 1548-7091, and the electronic international standard serial number (EISSN) is 1548-7105.

Further editorial information

Please see the following editorials for more information on various aspects of journal policy.

Why did we launch *Nature Methods*?

Nature Methods and the interface between biology and chemistry.

Purpose of the Correspondence section.

Results of first readers' survey.

What constitutes pre-publication and how to avoid it.

Guidelines for images used in publications.

How *Nature Methods* peer reviews papers.

Relationship between *Nature Methods* and *Nature Protocols*.

The importance of declaring conflicts of financial interest.

Availability of custom-designed software used in publications.

Introducing the online Methods section at *Nature Methods*.

ARTICLE TYPES IN NATURE METHODS

Primary research formats

An **Article** is a technical report of primary research data on a new technique that is likely to be influential. This format is not a review of technology, but its primary report in the literature. Articles include a detailed description of the method, including all the technical details necessary to its reproducibility, and the results of a validation study. In order to guarantee immediate practical relevance, Articles must show an application of the new method to an important biological question and demonstrate its advantage over existing approaches. Validation of the new method and demonstration of its superiority over existing techniques most often involve novel biologically relevant data. However since the focus is on the technology, providing significant new insight into a biological problem is not a requirement.

Articles begin with an unreferenced abstract (typically 150 words) and are divided into separate sections for Introduction, Results, Discussion and Methods. Introduction and Discussion are brief and focused, the Results section usually contains a general description of the method followed by its validation, and the Methods section provides all technical details necessary for the independent reproduction of the methodology, without referring to a chain of bibliographical references. The main text (excluding abstract, Methods, references and figure legends) is 2,500 – 3500 words. Articles have no more than 6 display items (figures and tables). The Results and Methods should be divided by topical subheadings; the Discussion may contain subheadings at the editors' discretion. If statistical testing was used to analyze the data, the Methods section must contain a subsection on statistical analysis. References are typically no more than 30.

Articles include received/accepted dates. They may be accompanied by supplementary information. Articles are peer reviewed, and authors must provide a competing financial interests statement before publication.

A **Brief Communication** is a more concise format used typically to report a significant improvement to a tried-and-tested method, its modification and adaptation to an important original application, or an important new tool or resource of broad interest for the scientific community. This format typically does not exceed 3 printed pages. Brief Communications begin with a brief unreferenced abstract (3 sentences, no more than 70 words), which will appear on Medline. The title is limited to 10 words (or 90 characters). The main text is typically 1,000–1,500 words, including the abstract and contains no headings with the exception of a single heading for Methods to point readers to the online Methods section. Brief Communications normally have no more than 2 display items, although this may be flexible at the discretion of the editor, provided the page limit is observed. References are limited to 15. Article titles are omitted from the reference list.

Brief Communications include received/accepted dates. They may be accompanied by supplementary information. Brief Communications are peer reviewed, and authors must provide a competing financial interests statement before publication.

An **Analysis** article reports comprehensive comparative analyses of technologies, methods or reagents of key importance for a field of research, leading to important practical conclusions about their performances. Analysis articles may also report new analysis of existing large datasets that lead to a novel, exciting or arresting conclusion. The main text (excluding abstract, Methods, references and figure legends) is approximately 3,000 words. The abstract is typically 100-150 words, unreferenced. Analyses have no more than 6 display items (figures and/or tables). An introduction (without heading) is followed by sections headed Results, Discussion and Methods. The Results and Methods should be divided by topical subheadings; the Discussion does not contain subheadings. If statistical testing was used to analyze the data, the Methods section must contain a subsection on statistical analysis. References are limited to 50.

Analyses include received/accepted dates. They may be accompanied by supplementary information. Analyses are peer reviewed, and authors must provide a competing financial interests statement before publication.

A **Resource** presents a large data set (such as a comprehensive list of proteins in an organelle or tissue, a genome-wide antibody library, coordinated analysis of cells or reagents by several different laboratories) of broad utility, interest and significance to the community. The main text (excluding abstract, Methods, references and figure legends) is approximately 3,000 words. The abstract is typically 100-150 words, unreferenced. Resources have no more than 6 display items (figures and/or tables). An introduction (without heading) is followed by sections headed Results, Discussion and Methods. The Results and Methods should be divided by topical subheadings; the Discussion does not contain subheadings. If statistical testing was used to analyze the data, the Methods section must contain a subsection on statistical analysis. References are limited to 50.

Resources include received/accepted dates. They may be accompanied by supplementary information. Resources are peer reviewed, and authors must provide a competing financial interests statement before publication.

Other Formats

Correspondence is a flexible format providing readers with the opportunity to comment on papers published in a previous issue of the journal, to present resources of broad interest to *Nature Methods* readership (such as databases) or to desccribe a further methodological development to a method previously published in *Nature Methods*. A Correspondence may describe primary research data, but is not intended for full presentation of data. Correspondence should never be more than one printed page and one figure. The total length is typically 250–450 words. The number of references should not exceed 6 for either the Correspondence or its Reply, and article titles are omitted from the reference list. Titles for correspondence are supplied by the editors.

In cases where a correspondence is critical of a previous research paper, the authors are normally given the option of publishing a brief reply. Criticism of opinions or other secondary matter does not involve an automatic right of reply.

Authors must provide a competing financial interests before publication. Refutations are always peer reviewed. Other types of Correspondence may be peer reviewed at the editors' discretion.

News and Views are by prior arrangement only. They may be linked to articles in *Nature Methods*, or they may focus on papers of exceptional significance that are published elsewhere. Unsolicited contributions will not normally be considered, although prospective authors are welcome to make proposals. News and Views are not peer reviewed. Authors must provide a competing financial interests statement before publication.

A **Review** is an authoritative, balanced and scholarly survey of methodological approaches to a technology or a specific aspect of a technology. These Reviews should have a strong functional component, highlight practical questions that are likely to arise for researchers undertaking the application of the technology, and provide information to guide their choices. The requirement for balance need not prevent authors from proposing a specific viewpoint, but authors must also present alternative approaches. Reviews are normally 3,000–4,000 words, and illustrations are strongly encouraged. References are limited to 100. Citations should be selective and, in the case of particularly important studies (≤10% of all the references), we encourage authors to provide short annotations explaining why these are key contributions. The scope of a Review should be broad enough that it is not dominated by the work of a single laboratory, and particularly not by the authors' own work.

Review authors must provide a competing financial interests statement before publication. Received/accepted dates are not included. Reviews are always peer reviewed to ensure factual accuracy, appropriate citations and scholarly balance.

Perspective is a format for scholarly reviews and discussions of the primary research literature that do not meet the criteria for a Review—either because the scope is too narrow, or because the author is advocating a controversial position or a speculative hypothesis or discussing work primarily from one group. Perspectives can also accommodate two side-by-side reviews advocating opposite sides of a research controversy. The text should not normally exceed 3,000 words and may be much shorter. References are limited to 50.

The related format **Historical Perspective** is a more technical account of a particular scientific development. Like other Perspectives, and in contrast to Historical Commentary, Historical Perspectives are scholarly reviews, including citation of key references, aiming to present a balanced account of the historical events, not merely personal opinions or reminiscences.

Perspective authors must provide a competing financial interests statement before publication. Received/accepted dates are not included. Perspectives are always peer reviewed.

Commentary is a very flexible format; Commentaries may be on policy, science and society or purely scientific issues. The main criteria are that they should be of immediate interest to a broad readership and should be written in an accessible, non-technical style. Their length is typically 1–4 pages, although some may be longer. Because the content is variable, the format is also flexible. Commentaries do not normally contain primary research data, although they may present 'sociological' data (funding trends, demographics, bibliographic data, etc.). References are limited to 25, and article titles are omitted from the reference list.

The related format **Historical Commentary** is a journalistic treatment of the history of a particular discovery or technical development. These pieces may be a personal account by one of the participants or may present strong personal opinions. This format does not necessarily seek scholarly balance, and it should be journalistic and accessible rather than scholarly in style.

Commentary authors must provide a competing financial interests statement before publication. Commentaries may be peer reviewed at the editors' discretion.

Application Notes are advertorials which allow product manufacturers to present interesting new products or innovative applications of a laboratory technology. Application Notes are not peer-reviewed and are marked as an advertisement. Authors of Application Notes must be members of the manufacturer's organization. If independent researchers contribute

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For further information on the review process and how editors make decisions, please see the manuscript decisions page.

A high priority of *Nature Methods* is that all papers be accessible to nonspecialists. Manuscripts are subject to substantial editing to achieve this goal. After acceptance, a copy editor may make further changes so that the text and figures are readable and clear to those outside the field, and so that papers conform to our style. Contributors are sent proofs and are welcome to discuss proposed changes with the editors, but *Nature Methods* reserves the right to make the final decision about matters of style and the size of figures.

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Submission of a signed competing financial interests statement is required for all content of the journal. This statement will be published at the end of all papers, whether or not a competing financial interest is reported. In cases where the authors declare a competing financial interest, a short statement to that effect is published at the end of article, which is linked to a more detailed version available online.

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Authors of accepted papers are encouraged to submit images for consideration as a cover. Cover images are not necessarily

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Nature Methods is read by scientists from diverse backgrounds. In addition, many are not native English speakers. Authors should therefore give careful thought to how their findings may be communicated clearly. Although a shared basic knowledge of biology and chemistry may be assumed, please bear in mind that the language and concepts that are standard in one subfield may be unfamiliar to nonspecialists. Thus, technical jargon should be avoided as far as possible and clearly explained where its use is unavoidable. Abbreviations, particularly those that are not standard, should also be kept to a minimum. The background, rationale and main conclusions of the study should be clearly explained. Titles and abstracts in particular should be written in language that will be readily intelligible to any scientist. We strongly recommend that authors ask a colleague with different expertise to review the manuscript before submission, in order to identify concepts and terminology that may present difficulties to nonspecialist readers.

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Manuscripts reporting new structures should contain a table summarizing structural and refinement statistics. Templates for such tables describing NMR and X-ray crystallography data are available on our website. To facilitate assessment of the quality of the structural data, a stereo image of a portion of the electron density map (for crystallography papers) or of the superimposed lowest energy structures (>10; for NMR papers) should be provided with the submitted manuscript. If the reported structure represents a novel overall fold, a stereo image of the entire structure (as a backbone trace) should also be provided.

Please use American English spelling throughout.

Acknowledgments should be brief, and should not include thanks to anonymous referees and editors, or effusive comments. Grant or contribution numbers may be acknowledged. *Nature Methods* requires an Author Contribution statement as described in the Authorship section of our joint Editorial policies.

The Methods section of original research articles will appear online only. Print readers will be directed to the online version of the paper for detailed methods and associated references. Please provide a Methods section with subsections detailing all the methods used in the paper. Exceptions to this are chemical synthesis descriptions, equation-heavy sections or methods used to acquire data that only appears as supplementary information. These exceptions should be presented in supplementary information. The Methods section should be placed at the very end of the manuscript, after the Acknowledgments, Author Contributions, figure legends and tables, but before the references.

A single list of references should be provided, with any new citations that appear in the Methods section numbered consecutively beginning after the last reference cited in the main text, figure legends and tables. The combined reference number in the main text, figure legends, tables and online Methods should not exceed 30 for Brief Communications, 50 for Articles or 70 for Analyses or Resources.

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Figure legends for Articles begin with a brief title for the whole figure and continue with a short description of each panel and the symbols used; focusing on describing what is shown in the figure and de-emphasizing methodological details. Each legend should total no more than 250 words. Brief Communications have short figure legends (generally less than 100 words), which may include details of methods.

Gene nomenclature

Authors should use approved nomenclature for gene symbols, and use symbols rather than italicized full names (*Ttn*, not *titin*). Please consult the appropriate nomenclature databases for correct gene names and symbols. A useful resource is LocusLink. Approved human gene symbols are provided by HUGO Gene Nomenclature Committee (HGNC), e-mail: hgnc@genenames.org; see also www.genenames.org. Approved mouse symbols are provided by The Jackson Laboratory, e-mail: nomen@informatics.jax.org; see also http://www.informatics.jax.org/mgihome/nomen.

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Avoid listing multiple names of genes (or proteins) separated by a slash, as in '*Oct4/Pou5f1*', as this is ambiguous (it could

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Every article that contains statistical testing should state the name of the statistical test, the *n* for each statistical analysis, the comparisons of interest, a justification for the use of that test (including, for example, a discussion of the normality of the data when the test is appropriate only for normal data), the alpha level for all tests, whether the tests were one-tailed or two-tailed, and the actual *P* value for each test (not merely "significant" or "$P < 0.05$"). Randomization procedures, or other ways to eliminate bias in sampling (in particular for experiments involving animals), should be clearly described. It should be clear what statistical test was used to generate every *P* value. In the case of Brief Communications, these details should be reported in the text or the figure captions.

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Authors must justify the use of a particular test and explain whether their data conform to the assumptions of the tests. Three errors are particularly common.

- *Multiple comparisons:* **When making multiple statistical comparisons on a single data set, authors should explain how they adjusted the alpha level to avoid an inflated Type I error rate, or they should select statistical tests appropriate for multiple groups (such as ANOVA rather than a series of *t*-tests).**
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- *Small sample size:* **When the sample size is small (less than about 10), authors should use tests appropriate to small samples or justify their use of large-sample tests.**

There is a checklist available to help authors minimize the chance of statistical errors.

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Figures should be uploaded upon submission via our online submission system, in one of our preferred formats, if possible. Please use the smallest file size that provides sufficient resolution, preferably less than 1 MB, so that referees do not have to download extremely large files. When a paper is accepted, the editors will request high-resolution files suitable for publication.

Unnecessary figures and parts (panels) of figures and tables should be avoided: data presented in small tables or histograms, for instance, can generally be stated briefly in the text instead. Figures should not contain more than one panel unless the parts are logically connected; each panel of a multipart figure should be sized so that the whole figure can be reduced by the same amount and reproduced on the printed page at the smallest size at which essential details are visible. When a manuscript is accepted for publication, we will ask for high-resolution figure files, possibly in a different electronic format. This information will be included in the acceptance letter.

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Figures divided into parts should be labeled with a lower-case, bold a, b and so on, in the same typesize as used elsewhere in the figure. Lettering in figures should be in lower-case type, with only the first letter of each label capitalized. Units should have a single space between the number and the unit, and follow SI nomenclature (for example, ms rather than msec) or the nomenclature common to a particular field. Thousands should be separated by commas (1,000). Unusual units or abbreviations should be spelled out in full or defined in the legend. Scale bars should be used rather than magnification factors, with the length of the bar defined in the legend rather than on the bar itself. In general, please use visual cues rather than verbal explanations, such as "open red triangles," in the legend.

Authors are encouraged to consider the needs of colorblind readers (a substantial minority of the male population) when choosing colors for figures. Many colorblind readers cannot interpret micrographs presented in green and red, for example. Thus, we encourage authors to submit micrographs in color combinations other than green and red.

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MANUSCRIPT DECISIONS

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The corresponding author is notified by e-mail when the editor decides to send a paper for review. Authors may indicate a limited number of scientists who should not review the paper. Excluded scientists must be identified by name. Authors may also suggest referees; these suggestions are often helpful, although they are not always followed. By policy, referees are not

identified to the authors or to anyone else outside the journal's editorial office, except at the request of the referee.

Conceptually similar manuscripts are held to the same editorial standards as far as possible, and so they are often sent to the same referees. However, each of the cosubmitted manuscripts must meet the criteria for publication without reference to the other paper. Thus if one paper is substantially less complete or convincing than the other, it may be rejected, even if the papers reach the same conclusion.

Decision after review and revision

When making a decision after review, editors consider not only how good the paper is now, but also how good it might become after revision.

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In either case, the revised manuscript should be accompanied by a cover letter that includes a point-by-point response to referees' comments and an explanation of how the manuscript has been changed.

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Final submission and acceptance

A request for final submission is sent when the paper is nearly ready to publish, possibly requiring some text changes but no revisions to the data or conclusions. These letters are accompanied by detailed editorial advice for preparing the final revision. A high priority of *Nature Methods* is that all papers be accessible to nonspecialists. Manuscripts are subject to substantial editing to achieve this goal. After acceptance, a copy editor may make further changes so that the text and figures are readable and clear to those outside the field, and so that papers conform to our style.

For the final revision, authors should use the revision link to the online submission system provided in the decision letter to upload a final version of the text with all the requested format changes. Electronic files of the final figures, at high resolution, should be sent separately on disk or via ftp.

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Decisions are reversed on appeal only if the editors are convinced that the original decision was a serious mistake, not merely a borderline call that could have gone either way. Further consideration may be merited if a referee made substantial errors of fact or showed evidence of bias, but only if a reversal of that referee's opinion would have changed the original decision. Similarly, disputes on factual issues need not be resolved unless they were critical to the outcome. Thus, after careful consideration of the authors' points, most appeals are rejected by the editors.

If an appeal merits further consideration, the editors may send the authors' response or the revised paper to one or more referees, or they may ask one referee to comment on the concerns raised by another referee. On occasion, particularly if the editors feel that additional technical expertise is needed to make a decision, they may obtain advice from an additional referee.

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