



TABLE OF CONTENTS



ISSUE

January 2009, Volume 6 No 1 pp1-109

[In This Issue](#)
[Special Feature](#)
[Editorials](#)
[Correspondence](#)
[Research Highlights](#)
[News Feature](#)
[Primer](#)
[Commentary](#)
[Perspective](#)
[Methods to Watch](#)
[News and Views](#)
[Perspective](#)
[Resource](#)
[Analysis](#)
[Brief Communications](#)
[Articles](#)
[Technology Feature](#)
[Errata](#)
[About the cover](#)

IN THIS ISSUE

[PDF](#)

SPECIAL FEATURE

Method of the Year 2008

Special Feature issue: [Jan 2009](#), Volume 6, No 1

[Contents](#)
[Editorial](#)
[News Feature](#)
[Primer](#)
[Commentary](#)

[Perspective](#)
[Methods to Watch](#)
[Movie](#)
[Reader's Choice](#)

Nature Methods' Method of the Year 2008 goes to super-resolution fluorescence microscopy. This series of articles—and the related [movie](#)—showcase how these novel imaging methods came into their own in 2008 and the incredible impact they promise to have in biological research. The Methods to Watch feature provides a glimpse of future Methods of the Year and the Reader's Choice shows methods nominated by readers and editors, and the votes that they received.

EDITORIALS

Special Feature: Method of the Year Method of the Year 2008 p1

[doi:10.1038/nmeth.f.244](#)

With its tremendous potential for understanding cellular biology now poised to become a reality, super-resolution fluorescence microscopy is our choice for Method of the Year.

[Abstract](#) | [Full Text](#) | [PDF \(53 KB\)](#)

Maturing interactions p2[doi:10.1038/nmeth0109-2](https://doi.org/10.1038/nmeth0109-2)

The maturation of large-scale protein-protein interaction methodologies calls for improved methods to assess performance and data quality.

[Abstract](#) | [Full Text](#) | [PDF \(52 KB\)](#)

CORRESPONDENCE

Predicting free energy changes using structural ensembles pp3 - 4

Alexander Benedix, Caroline M Becker, Bert L de Groot, Amedeo Caflisch & Rainer A Böckmann

[doi:10.1038/nmeth0109-3](https://doi.org/10.1038/nmeth0109-3)

[Full Text](#) | [PDF \(431 KB\)](#) | [Supplementary information](#)

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RESEARCH HIGHLIGHTS

Targeted translational profiling p7

Nicole Rusk

[doi:10.1038/nmeth0109-7](https://doi.org/10.1038/nmeth0109-7)

Tagging ribosomes in a cell type-specific way allows the isolation of mRNAs that are being translated in these cells.

[Abstract](#) | [Full Text](#) | [PDF \(421 KB\)](#)

Paving the path to single-molecule structures pp8 - 9

Allison Doerr

[doi:10.1038/nmeth0109-8a](https://doi.org/10.1038/nmeth0109-8a)

A new generation of brilliant X-ray laser sources will be coming online within the next few years. Researchers now show that using these lasers to determine the structures of single molecules should be possible.

[Abstract](#) | [Full Text](#) | [PDF \(143 KB\)](#)

Global instability pp8 - 9

Amy Donner

[doi:10.1038/nmeth0109-8b](https://doi.org/10.1038/nmeth0109-8b)

Scientists create a high-throughput platform for proteome-scale assessment of protein stability.

[Abstract](#) | [Full Text](#) | [PDF \(143 KB\)](#)

News in brief p9[doi:10.1038/nmeth0109-9](https://doi.org/10.1038/nmeth0109-9)

[Full Text](#) | [PDF \(80 KB\)](#)

Good news travels fast p10

Michael Eisenstein

[doi:10.1038/nmeth0109-10](https://doi.org/10.1038/nmeth0109-10)

A new spin on a popular imaging technique allows researchers to accurately visualize tumors deep within the tissues of live mice.

[Abstract](#) | [Full Text](#) | [PDF \(134 KB\)](#)**They know why the caged bird sings... slower p12**

Allison Doerr

[doi:10.1038/nmeth0109-12](https://doi.org/10.1038/nmeth0109-12)

A device to cool localized areas of the zebra finch brain allows researchers to investigate how the timing of birdsong is controlled.

[Abstract](#) | [Full Text](#) | [PDF \(82 KB\)](#)**NEWS FEATURE**

Special Feature: Method of the Year**Super-resolution microscopy: breaking the limits pp15 - 18**

Kelly Rae Chi

[doi:10.1038/nmeth.f.234](https://doi.org/10.1038/nmeth.f.234)

After a long period of measured development and a recent surge of technical advances driven by physicists, super-resolution fluorescence microscopy emerged in 2008 as a powerful tool for biologists. Kelly Rae Chi reports.

[Abstract](#) | [Full Text](#) | [PDF \(765 KB\)](#)**PRIMER**

Special Feature: Method of the Year**Primer: fluorescence imaging under the diffraction limit pp19 - 20**

Daniel Evanko

[doi:10.1038/nmeth.f.235](https://doi.org/10.1038/nmeth.f.235)

A brief description of the theory and methods behind super-resolution fluorescence imaging.

[Abstract](#) | [Full Text](#) | [PDF \(355 KB\)](#)**COMMENTARY**

Special Feature: Method of the Year**Putting super-resolution fluorescence microscopy to work pp21 - 23**

Jennifer Lippincott-Schwartz & Suliana Manley

[doi:10.1038/nmeth.f.233](https://doi.org/10.1038/nmeth.f.233)

Super-resolution microscopy is poised to revolutionize our understanding of the workings of the cell. But the technology still has some limitations, and these must be taken into consideration if widespread application is to yield biological insight.

[Abstract](#) | [Full Text](#) | [PDF \(371 KB\)](#)**PERSPECTIVE**

Special Feature: Method of the Year**Microscopy and its focal switch pp24 - 32**

Stefan W Hell

[doi:10.1038/nmeth.1291](https://doi.org/10.1038/nmeth.1291)[Abstract](#) | [Full Text](#) | [PDF \(513 KB\)](#)**METHODS TO WATCH**

Special Feature: Method of the Year**Induced pluripotency p33**

Natalie de Souza

[doi:10.1038/nmeth.f.236](https://doi.org/10.1038/nmeth.f.236)

Methods to reprogram somatic cells to pluripotency have improved and will improve further; more biological studies of these cells are forthcoming.

[First Paragraph](#) | [Full Text](#) | [PDF \(420 KB\)](#)

Special Feature: Method of the Year
Synthetic life p33

Nicole Rusk

[doi:10.1038/nmeth.f.237](#)

After constructing a synthetic genome, the challenge is to prove its functionality.

[First Paragraph](#) | [Full Text](#) | [PDF \(420 KB\)](#)

Special Feature: Method of the Year
Imaging through automation p34

Daniel Evanko

[doi:10.1038/nmeth.f.238](#)

Automated imaging has the power to transform microscopy into a more quantitative technique with new capabilities.

[First Paragraph](#) | [Full Text](#) | [PDF \(312 KB\)](#)

Special Feature: Method of the Year
Quantitative mass spectrometry p34

Allison Doerr

[doi:10.1038/nmeth.f.239](#)

Quantitative mass spectrometry-based proteomics is now being applied on a large scale to address interesting biological questions.

[First Paragraph](#) | [Full Text](#) | [PDF \(312 KB\)](#)

Special Feature: Method of the Year
Membrane protein structures p35

Allison Doerr

[doi:10.1038/nmeth.f.240](#)

New methods addressing the challenges in membrane protein expression, solubilization and crystallization promise to yield many more atomic structures.

[First Paragraph](#) | [Full Text](#) | [PDF \(163 KB\)](#)

Special Feature: Method of the Year
Optical imaging in thick samples p35

Natalie de Souza

[doi:10.1038/nmeth.f.241](#)

Optical methods to image deep into thick samples make it increasingly possible to watch biological processes *in vivo*.

[First Paragraph](#) | [Full Text](#) | [PDF \(163 KB\)](#)

Special Feature: Method of the Year
Experimental micro-matchmaking p36

Nicole Rusk

[doi:10.1038/nmeth.f.242](#)

Although microRNA target predictions are continually improving, high-throughput validation of direct interaction is still needed.

[First Paragraph](#) | [Full Text](#) | [PDF \(182 KB\)](#)

Special Feature: Method of the Year
Controlling cell function with light p36

Daniel Evanko

[doi:10.1038/nmeth.f.243](https://doi.org/10.1038/nmeth.f.243)

The use of light for active cellular control rather than just passive observation continues to make headway.

[First Paragraph](#) | [Full Text](#) | [PDF \(182 KB\)](#)

NEWS AND VIEWS

Inhibiting microRNA function *in vivo* pp37 - 38

Pedro P Medina & Frank J Slack

[doi:10.1038/nmeth0109-37](https://doi.org/10.1038/nmeth0109-37)

A new strategy is presented to functionally knock down microRNAs in a mouse.

[Abstract](#) | [Full Text](#) | [PDF \(154 KB\)](#)

PERSPECTIVE

Literature-curated protein interaction datasets pp39 - 46

Michael E Cusick, Haiyuan Yu, Alex Smolyar, Kavitha Venkatesan, Anne-Ruxandra Carvunis, Nicolas Simonis, Jean-François Rual, Heather Borick, Pascal Braun, Matija Dreze, Jean Vandenhaute, Mary Galli, Junshi Yazaki, David E Hill, Joseph R Ecker, Frederick P Roth & Marc Vidal

[doi:10.1038/nmeth.1284](https://doi.org/10.1038/nmeth.1284)

[Abstract](#) | [Full Text](#) | [PDF \(261 KB\)](#) | [Supplementary information](#)

RESOURCE

Empirically controlled mapping of the *Caenorhabditis elegans* protein-protein interactome network pp47 - 54

Nicolas Simonis, Jean-François Rual, Anne-Ruxandra Carvunis, Murat Tasan, Irma Lemmens, Tomoko Hirozane-Kishikawa, Tong Hao, Julie M Sahalie, Kavitha Venkatesan, Fana Gebreab, Sebiha Cevik, Niels Klitgord, Changyu Fan, Pascal Braun, Ning Li, Nono Ayivi-Guedeoussou, Elizabeth Dann, Nicolas Bertin, David Szeto, Amélie Dricot, Muhammed A Yildirim, Chenwei Lin, Anne-Sophie de Smet, Huey-Ling Kao, Christophe Simon, Alex Smolyar, Jin Sook Ahn, Muneesh Tewari, Mike Boxem, Stuart Milstein, Haiyuan Yu, Matija Dreze, Jean Vandenhaute, Kristin C Gunsalus, Michael E Cusick, David E Hill, Jan Tavernier, Frederick P Roth & Marc Vidal

[doi:10.1038/nmeth.1279](https://doi.org/10.1038/nmeth.1279)

High-throughput yeast two-hybrid screening is used to generate the largest *C. elegans* interactome resource available thus far. Using an empirical quality control framework presented in Venkatesan *et al.*, also online, the data set is evaluated for quality and is used to estimate the total size of the worm interactome.

[Abstract](#) | [Full Text](#) | [PDF \(631 KB\)](#) | [Supplementary information](#)

ANALYSIS

Cost-effective strategies for completing the interactome pp55 - 61

Ariel S Schwartz, Jingkai Yu, Kyle R Gardenour, Russell L Finley Jr & Trey Ideker

[doi:10.1038/nmeth.1283](https://doi.org/10.1038/nmeth.1283)

Different experimental designs for protein interaction mapping are modeled to compare their efficiency in completing an interactome map. Testing of the strategy that minimized the final experimental cost in an ongoing *Drosophila melanogaster* interactome project found 450 high-confidence interactions using only 47 microtiter plates.

[Abstract](#) | [Full Text](#) | [PDF \(538 KB\)](#) | [Supplementary information](#)

BRIEF COMMUNICATIONS

Stable knockdown of microRNA *in vivo* by lentiviral vectors pp63 - 66

Bernhard Gentner, Giulia Schira, Alice Giustacchini, Mario Amendola, Brian D Brown, Maurilio Ponzoni & Luigi Naldini

[doi:10.1038/nmeth.1277](https://doi.org/10.1038/nmeth.1277)

To study microRNA function *in vivo*, the authors optimize lentiviral-driven expression of microRNA target sequences in mice and show dose-dependent inhibition of microRNA-mediated regulation of reporter constructs as well as of natural microRNA targets. With the inhibition of a miR-223, they can phenocopy the knockout of this microRNA.

[Abstract](#) | [Full Text](#) | [PDF \(358 KB\)](#) | [Supplementary information](#)

Sensitive, specific polymorphism discovery in bacteria using massively parallel sequencing pp67 - 69

Chad Nusbaum, Toshiro K Ohsumi, James Gomez, John Aquadro, Thomas C Victor, Robert M Warren, Deborah T Hung, Bruce W Birren, Eric S Lander & David B Jaffe

[doi:10.1038/nmeth.1286](https://doi.org/10.1038/nmeth.1286)

This variant ascertainment algorithm, or VAAL, uses short sequence reads of haploid bacterial genomes to first locally assemble the reads and then compare these assemblies to the reference genome. This allows VAAL to detect all types of variants ranging from single-nucleotide polymorphisms to large insertions or deletions.

[Abstract](#) | [Full Text](#) | [PDF \(124 KB\)](#) | [Supplementary information](#)

An *in vitro* microfluidic approach to generating protein-interaction networks pp71 - 74

Doron Gerber, Sebastian J Maerkl & Stephen R Quake

[doi:10.1038/nmeth.1289](https://doi.org/10.1038/nmeth.1289)

A combination of *in vitro* protein synthesis and microfluidics is used to measure protein-protein interactions between 43 proteins in *Streptococcus pneumoniae*. The method does not require expression within cells and is amenable to large-scale experiments.

[Abstract](#) | [Full Text](#) | [PDF \(492 KB\)](#) | [Supplementary information](#)

Integrated network analysis platform for protein-protein interactions pp75 - 77

Jianmin Wu, Tea Vallenius, Kristian Ovaska, Jukka Westermarck, Tomi P Mäkelä & Sampsa Hautaniemi

[doi:10.1038/nmeth.1282](https://doi.org/10.1038/nmeth.1282)

A web-based protein-protein interaction (PPI) analysis platform called PINA integrates PPI data from six public databases and provides tools to aid in the construction and analysis of PPI networks, including local recursion and annotation of existing records and manual addition of new records.

[Abstract](#) | [Full Text](#) | [PDF \(428 KB\)](#) | [Supplementary information](#)

Infrared laser-mediated gene induction in targeted single cells *in vivo* pp79 - 81

Yasuhiro Kamei, Motoshi Suzuki, Kenjiro Watanabe, Kazuhiro Fujimori, Takashi Kawasaki, Tomonori Deguchi, Yoshihiro Yoneda, Takeshi Todo, Shin Takagi, Takashi Funatsu & Shunsuke Yuba

[doi:10.1038/nmeth.1278](https://doi.org/10.1038/nmeth.1278)

An infrared laser is used to activate gene expression from a heat shock promoter in single cells in *Caenorhabditis elegans*, and is shown to be more effective and less detrimental to cells than a visible laser used for this purpose.

[Abstract](#) | [Full Text](#) | [PDF \(313 KB\)](#) | [Supplementary information](#)

ARTICLES

An empirical framework for binary interactome mapping pp83 - 90

Kavitha Venkatesan, Jean-François Rual, Alexei Vazquez, Ulrich Stelzl, Irma Lemmens, Tomoko Hirozane-Kishikawa, Tong Hao, Martina Zenkner, Xiaofeng Xin, Kwang-Il Goh, Muhammed A Yildirim, Nicolas Simonis, Kathrin Heinzmann, Fana Gebreab, Julie M Sahalie, Sebiha Cevik, Christophe Simon, Anne-Sophie de Smet, Elizabeth Dann, Alex Smolyar, Arunachalam Vinayagam, Haiyuan Yu, David Szeto, Heather Borick, Amélie Dricot, Niels Klitgord, Ryan R Murray, Chenwei Lin, Maciej Lalowski, Jan Timm, Kirstin Rau, Charles Boone, Pascal Braun, Michael E Cusick, Frederick P Roth, David E Hill, Jan Tavernier, Erich E Wanker, Albert-László Barabási & Marc Vidal

[doi:10.1038/nmeth.1280](https://doi.org/10.1038/nmeth.1280)

A framework based on numerous empirical data, including protein-protein interaction reference sets, provides parameters for assessing the quality and coverage of protein-protein interaction datasets and estimation of the size of the human interactome. Braun *et al.*, also in this issue, use the reference sets to help derive confidence scores for individual protein-protein interactions.

[Abstract](#) | [Full Text](#) | [PDF \(556 KB\)](#) | [Supplementary information](#)

An experimentally derived confidence score for binary protein-protein interactions pp91 - 97

Pascal Braun, Murat Tasan, Matija Dreze, Miriam Barrios-Rodiles, Irma Lemmens, Haiyuan Yu, Julie M Sahalie, Ryan R Murray, Luba Roncari, Anne-Sophie de Smet, Kavitha Venkatesan, Jean-François Rual, Jean Vandenhaute, Michael E Cusick, Tony Pawson, David E Hill, Jan Tavernier, Jeffrey L Wrana, Frederick P Roth & Marc Vidal

[doi:10.1038/nmeth.1281](https://doi.org/10.1038/nmeth.1281)

Use of the protein-protein interaction reference sets reported in this issue in Venkatesan *et al.* to benchmark four complementary protein-protein interaction assays, followed by the training of a logistic regression model, allows the assignment of standardized confidence scores to individual protein-protein interactions.

[Abstract](#) | [Full Text](#) | [PDF \(421 KB\)](#) | [Supplementary information](#)

High-resolution mapping of copy-number alterations with massively parallel sequencing pp99 - 103

Derek Y Chiang, Gad Getz, David B Jaffe, Michael J T O'Kelly, Xiaojun Zhao, Scott L Carter, Carsten Russ, Chad Nusbaum, Matthew Meyerson & Eric S Lander

[doi:10.1038/nmeth.1276](https://doi.org/10.1038/nmeth.1276)

Massively parallel sequencing is a precise way to analyze copy-number variations given the right computational tools. An algorithm now facilitates the detection and fine mapping of copy-number gains and losses from millions of short sequence reads.

[Abstract](#) | [Full Text](#) | [PDF \(1,440 KB\)](#) | [Supplementary information](#)

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TECHNOLOGY FEATURE**High-throughput screening: designer screens pp105 - 108**

Nathan Blow

[doi:10.1038/nmeth0109-105](https://doi.org/10.1038/nmeth0109-105)

Some researchers say an eighty-year-old statistical method can make setting up and analyzing high-throughput screens and large-scale experiments faster and more efficient. So why are more biologists not flocking to use this tool?

[Abstract](#) | [Full Text](#) | [PDF \(405 KB\)](#)

ERRATA**Erratum: On display on a bug: a systematic approach to characterize antibodies p109**

Thomas Knorpp & Markus F Templin

[doi:10.1038/nmeth0109-109a](https://doi.org/10.1038/nmeth0109-109a)

[Full Text](#) | [PDF \(40 KB\)](#)

Erratum: Much room for improvement in deposition rates of expression microarray datasets p109

Scott A Ochsner, David L Steffen, Christian J Stoeckert Jr & Neil J McKenna

[doi:10.1038/nmeth0109-109b](https://doi.org/10.1038/nmeth0109-109b)

[Full Text](#) | [PDF \(40 KB\)](#)

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