## Computer science meets medical science

In the past 20–30 years at least two technical advances have made quantification in pathology at a large scale possible. At the time the computing power of affordable computers increased, interest to deploy tasks emerged that were previously very laborious to perform. Combined with digital camera systems, many new possibilities became available. Examples of such measurements that were previously very tedious if not impossible to perform are to measure the optical density of a nucleus, the area of a cell and the ratio of the red versus the green signal. Together, these techniques became known as "Quantitative Pathology" and were pioneered by Baak et al. and others [1–3,7].

Often, papers that report these novel techniques, especially papers on texture features [8], are accompanied by an impressive amount of mathematical formulas in the materials and methods section. This also goes for the paper of Nielsen et al. in the present issue of Cellular Oncology [14]. To the reader, it may be a daunting task to delve into the details and to get complete understanding of the measurements being performed. However, to the technically inclined (as the author of this editorial, having a degree in computer science) these formulas are essential to be able to reproduce the measurements and to optimize one's own technique for a certain task. In general, a single formula is able to communicate a much larger part of source code that actually implements the described technique. As is true for a natural language (e.g., English) the language of mathematics is a common language which is understood by a large audience. From this point of view the current practice with many formulas is the most concise way to present this information.

However, in an interdisciplinary field, where computer science is applied in medical science, these technical sections might shy away readers that are less used to the language of mathematics. As a worst-case consequence, the entire paper can be put aside while the novel technique might have a large impact on patient diagnosis or prognosis. Mostly in-text formulas are still in use [6,12,13], but sometimes they are moved to the appendix section [11]. The use of an appendix for this purpose is a good compromise between the ability to be able to reproduce an experiment and to keep the paper readable for a larger audience. The criterion for this decision should be whether the total number of formulas is large enough ( $\sim$ 5 or more) to justify an appendix. Another solution is to present the techniques in a table in the appendix and provide an exhaustive list of references [9]. The advantage is that the paper is very orderly, but a disadvantage might be that it is more complicated to repeat the measurement in a different institute.

When science develops, a basic set of primitives is obtained and usually it is sufficient to refer to these common concepts without providing the details. This concept is known as abstraction, and is used in everyday life. Eventually, this will reduce the need to present the level of detail often seen in current publication. However, new technologies in medicine will always require custom-made solutions and hence it is expected that difficult papers will always be part of medical literature.

As an example, focus is currently moving from 2D applications [5] towards 3D applications [4,15,16]. An important driving force is the development of better imaging techniques in confocal laser scanning microscopy like the development of  $4\pi$  microscopy [10]. This technology will present detail that was previously imperceptible. Understanding the corrections required to achieve this resolution is still a daunting task, but researchers that are aiming at a better image quality should be informed about all important aspects. Another subject of study is improvement of image quality by deconvolution [17]. Deconvolution by itself is a very complicated technique, and it is an important subject of several conferences. Therefore, it is anticipated that literature on deconvolution, with an abundance of formulas, will soon appear in medical journals.

In conclusion, technical papers form an important part of medical literature and this will also be the case in the future. When the technical details are accurately addressed, these papers should be readable to both the reader that has less experience with mathematics and computer science and the reader that wishes to learn about all the details.

> Lennert S. Ploeger, PhD Department of Pathology, University Medical Center Utrecht, The Netherlands

## References

- J.P. Baak, P.H. Kurver and M.E. Boon, Computer-aided application of quantitative microscopy in diagnostic pathology, *Pathol. Annu.* 17 Pt 2 (1982), 287.
- [2] J.P. Baak, P.H. Kurver, S. de Graaf and M.E. Boon, Morphometry for prognosis prediction in breast cancer, *Lancet* 2 (1981), 315.
- [3] J.P. Baak, S. Makkink-Nombrado, P. Tekola, E. Bergers, J.A. Belien and A.H. van Ginkel, Quantitative microscopical and confocal laser scanning microscopy for intermediate endpoint biomarkers in breast cancer: potential and reproducibility, *J. Cell Biochem. Suppl.* **17G** (1993), 98.
- [4] J.A. Belien, A.H. van Ginkel, P. Tekola, L.S. Ploeger, N.M. Poulin, J.P. Baak and P.J. van Diest, Confocal DNA cytometry: a contour-based segmentation algorithm for automated three-dimensional image segmentation, *Cytometry* 49 (2002), 12.
- [5] M. Brinkhuis, J.P. Baak, G.A. Meijer, P.J. van Diest, O. Mogensen, P. Bichel and J.P. Neijt, Value of quantitative pathological variables as prognostic factors in advanced ovarian carcinoma, *J. Clin. Pathol.* **49** (1996), 142.
- [6] D. Chiu, M. Guillaud, D. Cox, M. Follen and C. Macaulay, Quality assurance system using statistical process control: an implementation for image cytometry, *Cell. Oncol.* 26 (2004), 101.
- [7] P.C. Diegenbach and J.P. Baak, Quantitative nuclear image analysis: differentiation between normal, hyperplastic and

malignant appearing uterine glands in a paraffin section. II. Computer assisted recognition by discriminant analysis, *Eur. J. Obstet. Gynecol. Reprod. Biol.* **7** (1977), 389.

- [8] A. Doudkine, C. Macaulay, N. Poulin and B. Palcic, Nuclear texture measurements in image cytometry, *Pathologica* 87 (1995), 286.
- [9] M. Guillaud, D. Cox, A. Malpica, G. Staerkel, J. Matisic, D. Van Niekirk, K. Adler-Storthz, N. Poulin, M. Follen and C. Macaulay, Quantitative histopathological analysis of cervical intra-epithelial neoplasia sections: methodological issues, *Cell. Oncol.* 26 (2004), 31.
- [10] S.W. Hell, M. Schrader and H.T. van der Voort, Far-field fluorescence microscopy with three-dimensional resolution in the 100-nm range, J. Microsc. 187 (1997), 1.
- [11] A. Huisman, L.S. Ploeger, H.F. Dullens, N. Poulin, W.E. Grizzle and P.J. van Diest, Development of 3D chromatin texture analysis using confocal laser scanning microscopy, *Cell. Oncol.* 27 (2005), 335.
- [12] H.G. Hwang, H.J. Choi, B.I. Lee, H.K. Yoon, S.H. Nam and H.K. Choi, Multi-resolution wavelet-transformed image analysis of histological sections of breast carcinomas, *Cell. Oncol.* 27 (2005), 237.
- [13] T. Mattfeldt, D. Trijic, H.W. Gottfried and H.A. Kestler, Classification of incidental carcinoma of the prostate using learning vector quantization and support vector machines, *Cell. Oncol.* 26 (2004), 45.
- [14] B. Nielsen and H.E. Danielsen, Prognostic value of adaptive textural features – the effect of standardizing nuclear first-order gray level statistics and mixing information from nuclei having different area, *Cell. Oncol.* 28 (2006), 85.
- [15] L.S. Ploeger, J.A. Belien, N.M. Poulin, W. Grizzle and P.J. van Diest, Confocal 3D DNA cytometry: assessment of required coefficient of variation by computer simulation, *Cell. Oncol.* 26 (2004), 93.
- [16] L.S. Ploeger, A. Huisman, J. van der Gugten, D.M. van der Giezen, J.A. Belien, A.Y. Abbaker, H.F. Dullens, W. Grizzle, N.M. Poulin, G.A. Meijer and P.J. van Diest, Implementation of accurate and fast DNA cytometry by confocal microscopy in 3D, *Cell. Oncol.* 27 (2005), 225.
- [17] H. Yoo, I. Song and D.G. Gweon, Measurement and restoration of the point spread function of fluorescence confocal microscopy, J. Microsc. 221 (2006), 172.



The Scientific **World Journal** 



Gastroenterology Research and Practice





Journal of Diabetes Research



**Disease Markers** 



Immunology Research





Submit your manuscripts at http://www.hindawi.com





BioMed **Research International** 



Journal of Ophthalmology

Computational and Mathematical Methods in Medicine



Stem Cells International



Behavioural Neurology

CAM







Research and Treatment





Oxidative Medicine and Cellular Longevity



