

References

1. Peeling, R. W.; Smith, P. G.; Bossuyt, P. M. M., A guide for diagnostic evaluations. *Nat. Rev. Microbiol.* **2010**, *8* (12 Suppl), S2-6.
2. Yager, P.; Domingo, G. J.; Gerdes, J., Point-of-care diagnostics for global health. *Annu. Rev. Biomed. Eng.* **2008**, *10*, 107-144.
3. Mabey, D.; Peeling, R. W.; Ustianowski, A.; Perkins, M. D., Diagnostics for the developing world. *Nat. Rev. Microbiol.* **2004**, *2* (3), 231-240.
4. Gubala, V.; Harris, L. F.; Ricco, A. J.; Tan, M. X.; Williams, D. E., Point of Care Diagnostics: Status and Future. *Anal. Chem.* **2012**, *84* (2), 487-515.
5. Karim, O.; Rao, A.; Emberton, M.; Cochrane, D.; Partridge, M.; Edwards, P.; Walker, I.; Davidson, I., Point-of-care PSA testing: An evaluation of PSAwatch. *Prostate Cancer Prostatic Dis.* **2007**, *10* (3), 270-273.
6. www.cephid.com, www.idahotech.com, www.twistdx.co.uk
7. (a) Toner, M.; Irimia, D., Blood-on-a-chip. *Annu. Rev. Biomed. Eng.* **2005**, *7*, 77-103; (b) Chin, C. D.; Linder, V.; Sia, S. K., Lab-on-a-chip devices for global health: Past studies and future opportunities. *Lab Chip* **2007**, *7* (1), 41-57.
8. Ismagilov, R. F., Witters, D., Sun, B., Begolo, S., Rodríguez-Manzano, J., Robles, W., Digital Biology and Chemistry. *Lab Chip* **2014**, accepted.
9. Edd, J. F.; Di Carlo, D.; Humphry, K. J.; Koster, S.; Irimia, D.; Weitz, D. A.; Toner, M., Controlled encapsulation of single-cells into monodisperse picolitre drops. *Lab Chip* **2008**, *8* (8), 1262-1264.
10. Hong, J. W.; Studer, V.; Hang, G.; Anderson, W. F.; Quake, S. R., A nanoliter-scale nucleic acid processor with parallel architecture. *Nat. Biotechnol.* **2004**, *22* (4), 435-439.
11. Rissin, D. M.; Kan, C. W.; Campbell, T. G.; Howes, S. C.; Fournier, D. R.; Song, L.; Piech, T.; Patel, P. P.; Chang, L.; Rivnak, A. J.; Ferrell, E. P.; Randall, J. D.; Provuncher, G. K.; Walt, D. R.; Duffy, D. C., Single-molecule enzyme-linked immunosorbent assay detects serum proteins at subfemtomolar concentrations. *Nat. Biotechnol.* **2010**, *28* (6), 595-599.
12. Wheeler, A. R.; Throdsset, W. R.; Whelan, R. J.; Leach, A. M.; Zare, R. N.; Liao, Y. H.; Farrell, K.; Manger, I. D.; Daridon, A., Microfluidic device for single-cell analysis. *Anal. Chem.* **2003**, *75* (14), 3581-3586.
13. Du, W.; Li, L.; Nichols, K. P.; Ismagilov, R. F., SlipChip. *Lab Chip* **2009**, *9* (16), 2286-2292.

14. Li, L.; Du, W.; Ismagilov, R. F., Multiparameter Screening on SlipChip Used for Nanoliter Protein Crystallization Combining Free Interface Diffusion and Microbatch Methods. *J. Am. Chem. Soc.* **2010**, *132* (1), 112-119.
15. Liu, W.; Chen, D.; Du, W.; Nichols, K. P.; Ismagilov, R. F., Slip Chip for Immunoassays in Nanoliter Volumes. *Anal. Chem.* **2010**, *82* (8), 3276-3282.
16. Shen, F.; Du, W.; Kreutz, J. E.; Fok, A.; Ismagilov, R. F., Digital PCR on a SlipChip. *Lab Chip* **2010**, *10* (20), 2666-2672.
17. (a) Cheng, C.-M.; Martinez, A. W.; Gong, J.; Mace, C. R.; Phillips, S. T.; Carrilho, E.; Mirica, K. A.; Whitesides, G. M., Paper-Based ELISA. *Angew. Chem., Int. Ed.* **2010**, *49* (28), 4771-4774; (b) Fang, X.; Liu, Y.; Kong, J.; Jiang, X., Loop-Mediated Isothermal Amplification Integrated on Microfluidic Chips for Point-of-Care Quantitative Detection of Pathogens. *Anal. Chem.* **2010**, *82* (7), 3002-3006.
18. Huynh, T.; Sun, B.; Li, L.; Nichols, K. P.; Koyner, J. L.; Ismagilov, R. F., Chemical Analog-to-Digital Signal Conversion Based on Robust Threshold Chemistry and Its Evaluation in the Context of Microfluidics-Based Quantitative Assays. *J. Am. Chem. Soc.* **2013**, *135* (39), 14775-14783.
19. Dharnidharka, V. R.; Kwon, C.; Stevens, G., Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. *Am. J. Kidney. Dis.* **2002**, *40* (2), 221-6.
20. Shlipak, M. G.; Matsushita, K.; Ärnlöv, J.; Inker, L. A.; Katz, R.; Polkinghorne, K. R.; Rothenbacher, D.; Sarnak, M. J.; Astor, B. C.; Coresh, J.; Levey, A. S.; Gansevoort, R. T., Cystatin C versus Creatinine in Determining Risk Based on Kidney Function. *N. Engl. J. Med.* **2013**, *369* (10), 932-943.
21. Spahillari, A.; Parikh, C. R.; Sint, K.; Koyner, J. L.; Patel, U. D.; Edelstein, C. L.; Passik, C. S.; Thiessen-Philbrook, H.; Swaminathan, M.; Shlipak, M. G., Serum Cystatin C– Versus Creatinine-Based Definitions of Acute Kidney Injury Following Cardiac Surgery: A Prospective Cohort Study. *Am. J. Kidney. Dis.* **2012**, *60* (6), 922-929.
22. Ferguson, M. C., Current therapies for chronic hepatitis C. *Pharmacotherapy* **2011**, *31* (1), 92-111.
23. Kreutz, J. E.; Munson, T.; Huynh, T.; Shen, F.; Du, W.; Ismagilov, R. F., Theoretical Design and Analysis of Multivolume Digital Assays with Wide Dynamic Range Validated Experimentally with Microfluidic Digital PCR. *Anal. Chem.* **2011**, *83* (21), 8158-8168.
24. Vogelstein, B.; Kinzler, K. W., Digital PCR. *Proc. Natl. Acad. Sci. U. S. A.* **1999**, *96* (16), 9236-9241.

25. Beer, N. R.; Hindson, B. J.; Wheeler, E. K.; Hall, S. B.; Rose, K. A.; Kennedy, I. M.; Colston, B. W., On-chip, real-time, single-copy polymerase chain reaction in picoliter droplets. *Anal. Chem.* **2007**, *79* (22), 8471-5.
26. Analytical Chemistry (Washington, D., United States) Sundberg, Scott O.; Wittwer, C. T.; Gao, C.; Gale, B. K., Spinning Disk Platform for Microfluidic Digital Polymerase Chain Reaction. *Anal. Chem.* **2010**, *82* (4), 1546-1550.
27. <http://www.lifetechnologies.com/us/en/home/life-science/pcr/real-time-pcr/real-time-openarray.html>
28. Shen, F.; Sun, B.; Kreutz, J. E.; Davydova, E. K.; Du, W.; Reddy, P. L.; Joseph, L. J.; Ismagilov, R. F., Multiplexed Quantification of Nucleic Acids with Large Dynamic Range Using Multivolume Digital RT-PCR on a Rotational SlipChip Tested with HIV and Hepatitis C Viral Load. *J. Am. Chem. Soc.* **2011**, *133* (44), 17705-17712.
29. Pawlotsky, J. M., Use and interpretation of virological tests for hepatitis C. *Hepatology* **2002**, *36* (5), S65-S73.
30. Curtis, K. A.; Rudolph, D. L.; Nejad, I.; Singleton, J.; Beddoe, A.; Weigl, B.; LaBarre, P.; Owen, S. M., Isothermal Amplification Using a Chemical Heating Device for Point-of-Care Detection of HIV-1. *PLoS One* **2012**, *7* (2), e31432.
31. Compton, J., NUCLEIC-ACID SEQUENCE-BASED AMPLIFICATION. *Nature* **1991**, *350* (6313), 91-92.
32. Wharam, S. D.; Marsh, P.; Lloyd, J. S.; Ray, T. D.; Mock, G. A.; Assenberg, R.; McPhee, J. E.; Brown, P.; Weston, A.; Cardy, D. L. N., Specific detection of DNA and RNA targets using a novel isothermal nucleic acid amplification assay based on the formation of a three-way junction structure. *Nucleic Acids Res.* **2001**, *29* (11), e54.
33. Vincent, M.; Xu, Y.; Kong, H. M., Helicase-dependent isothermal DNA amplification. *EMBO Rep.* **2004**, *5* (8), 795-800.
34. Notomi, T.; Okayama, H.; Masubuchi, H.; Yonekawa, T.; Watanabe, K.; Amino, N.; Hase, T., Loop-mediated isothermal amplification of DNA. *Nucleic Acids Res.* **2000**, *28* (12), e63.
35. Piepenburg, O.; Williams, C. H.; Stemple, D. L.; Armes, N. A., DNA detection using recombination proteins. *PLoS Biol.* **2006**, *4* (7), 1115-1121.
36. Fire, A.; Xu, S. Q., Rolling replication of short DNA circles. *Proc. Natl. Acad. Sci. U. S. A.* **1995**, *92* (10), 4641-4645.
37. Walker, G. T.; Fraiser, M. S.; Schram, J. L.; Little, M. C.; Nadeau, J. G.; Malinowski, D. P., STRAND DISPLACEMENT AMPLIFICATION - AN ISOTHERMAL, INVITRO DNA AMPLIFICATION TECHNIQUE. *Nucleic Acids Res.* **1992**, *20* (7), 1691-1696.

38. Van Ness, J.; Van Ness, L. K.; Galas, D. J., Isothermal reactions for the amplification of oligonucleotides. *Proc. Natl. Acad. Sci. U. S. A.* **2003**, *100* (8), 4504-4509.
39. Ménová, P.; Raindlová, V.; Hocek, M., Scope and Limitations of the Nicking Enzyme Amplification Reaction for the Synthesis of Base-Modified Oligonucleotides and Primers for PCR. *Bioconjugate Chem.* **2013**, *24* (6), 1081-1093..
40. Seelig, G.; Soloveichik, D.; Zhang, D. Y.; Winfree, E., Enzyme-free nucleic acid logic circuits. *Science* **2006**, *314* (5805), 1585-1588.
41. (a) Selck, D. A.; Karymov, M. A.; Sun, B.; Ismagilov, R. F., Increased Robustness of Single-Molecule Counting with Microfluidics, Digital Isothermal Amplification, and a Mobile Phone versus Real-Time Kinetic Measurements. *Anal. Chem.* **2013**, *85* (22), 11129-11136; (b) Goto, M.; Honda, E.; Ogura, A.; Nomoto, A.; Hanaki, K.-I., Colorimetric detection of loop-mediated isothermal amplification reaction by using hydroxy naphthol blue. *Biotechniques* **2009**, *46* (3), 167-172.
42. Sun, B.; Shen, F.; McCalla, S. E.; Kreutz, J. E.; Karymov, M. A.; Ismagilov, R. F., Mechanistic Evaluation of the Pros and Cons of Digital RT-LAMP for HIV-1 Viral Load Quantification on a Microfluidic Device and Improved Efficiency via a Two-Step Digital Protocol. *Anal. Chem.* **2013**, *85* (3), 1540-1546.
43. Gansen, A.; Herrick, A. M.; Dimov, I. K.; Lee, L. P.; Chiu, D. T., Digital LAMP in a sample self-digitization (SD) chip. *Lab Chip* **2012**, *12* (12), 2247-2254.
44. Curtis, K. A.; Rudolph, D. L.; Owen, S. M., Rapid detection of HIV-1 by reverse-transcription, loop-mediated isothermal amplification (RT-LAMP). *J. Virol. Methods* **2008**, *151* (2), 264-270.
45. Ghany, M. G.; Strader, D. B.; Thomas, D. L.; Seeff, L. B., Diagnosis, Management, and Treatment of Hepatitis C: An Update. *Hepatology* **2009**, *49* (4), 1335-1374.
46. Hnatyszyn, H. J., Chronic hepatitis C and genotyping: the clinical significance of determining HCV genotypes. *Antivir. Ther.* **2005**, *10* (1), 1-11.
47. Hsu, C.-S., Sofosbuvir for Previously Untreated Chronic Hepatitis C Infection. *N. Engl. J. Med.* **2013**, *369* (7), 678-678.
48. Kargar, M.; Askari, A.; Doosti, A.; Ghorbani-Dalini, S., Loop-Mediated Isothermal Amplification Assay for Rapid Detection of Hepatitis C virus. *Indian J. Virol.* **2012**, *23* (1), 18-23.
49. Sun, B., Rodriguez-Manzano, J., Selck, D. A., Khorosheva, E., Karymov, M. A., and Ismagilov, R. F., Measuring Fate and Rate of Single-Molecule Competition of Amplification and Restriction Digestion, and Its Use for Rapid Genotyping Tested with Hepatitis C Viral RNA. *Angew. Chem., Int. Ed.* **2014**, accepted.