

## Specific structural features of microfluidic devices and their application

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### Abstract

It is commonly known that the major advances in science in recent decades are associated with reducing the size of various laboratory and diagnostic equipment and improving their technological characteristics. The tendency is centred around the use of microfluidic devices that are currently an important tool for the modern scientific community. In other words, microfluidic and micro-capillary systems are a new and actively developing area of contemporary science. Microfluidics can be characterised as an applied science that is integrated in multiple fields: from integrated circuits and applied crystallography (protein crystallization) to biological and medical research. The technology has come a long way from the first miniature gas chromatograph in the 1970s to the present day organ and tissue chip models. Due to the synthetic study of microfluidic systems, these devices can act as cooling systems on high-performance chips with the coolant pumped through microchannels; as systems of microchannels of various shapes and sizes for experimental research; as microreactors for enhanced reagent mixing; as biochips for express testing with an opportunity of simultaneous detection of several substances using a single device and only 1 µl of the test material, etc. The profound interest in this area is largely due to the number of advantages that microfluidics has over other technologies, such as, for example, considerable reduction in the reagent consumption and the possibility to accurately monitor heat and mass transfer. However, it should also be noted that despite the obvious advantages of the technology, microfluidic systems still have a number of disadvantages. The purpose of this review is to summarize and consolidate the current data on materials, devices, application peculiarities of microfluidic systems in various research fields and the resulting prospects for their further development and application.

### Contents

- Introduction**
- 1. Definition of microfluidic reactor**
- 2. Materials for microfluidic devices**
- 3. Microfluidic device production technologies**
- 4. Design of microfluidic devices**
- 5. Application of microfluidic devices**

### References

- [1] M. Zanavezkin, A. Mironova, A. Popov. Microfluidics and its perpectives in medicine. *Molecular Medicine*. **2012**. No.5. P.1-8. (russian)
- [2] C.C. Lee et al. Multistep synthesis of a radiolabeled imaging probe using integrated microfluidics *Science*. **2005**. Vol.310. No.5755. P.1793-1796.
- [3] R.L. Hartman, J.P. McMullen, K.F. Jensen. Deciding whether to go with the flow: evaluating the merits of flow reactors for synthesis. *Angew. Chem. Int. Ed.* **2011**. Vol.50. No.33. P.7502-7519.
- [4] N. Zaborenko, M.W. Bedore, T.F. Jamison, K.F. Jensen. Kinetic and scale-up investigations of epoxide aminolysis in microreactors at high temperatures and pressures. *Org. Process Res. Dev.* **2010**. Vol.15. No.1. P.131-139.

- [5] M.R. Özdemir, A. Koşar, O. Demir, C. Özenel, O. Bahçivan. Thermalhydraulic, exergy and exergy-economic analysis of micro heat sinks at high flow rates. *Proc. 10th ASME Bienn. Conf. Engineering Systems Design and Analysis*. **2010**. P.703-710.
- [6] J. Pelleter, F. Renaud. Facile, fast and safe process development of nitration and bromination reactions using continuous flow reactors. *Org. Process Res. Dev.* **2009**. Vol.13. No.4. P.698-705.
- [7] T. Asai, A. Takata, Y. Ushiogi, Y. Iinuma, A. Nagaki, J. Yoshida. Switching reaction pathways of benzo [b] thiophen-3-yllithium and benzo [b] furan-3-yllithium based on high-resolution residence-time and temperature control in a flow microreactor. *Chem. Lett.* **2011**. Vol.40. No.4. P.393-395.
- [8] T. Illg, V. Hessel, P. Löb, J.C. Schouten. Continuous synthesis of tert-butyl peroxy pivalate using a single-channel microreactor equipped with orifices as emulsification units. *Chem Sus Chem*. **2011**. Vol.4. No.3. P.392-398.
- [9] S.J. Haswell, P. Watts. Green chemistry: synthesis in micro reactors. *Green Chem.* **2003**. Vol.5. No.2. P.240-249.
- [10] N. Kockmann, M. Gottsponer, B. Zimmermann, D.M. Roberge. Enabling continuous-flow chemistry in microstructured devices for pharmaceutical and fine-chemical production. *Chem. Eur. J.* **2008**. Vol.14. No.25. P.7470-7477.
- [11] K.S. Elvira, X.C. Solvas, R.C.R. Wootton, A.J. deMello. The past, present and potential for microfluidic reactor technology in chemical synthesis. *Nat. Chem.* **2013**. Vol.5. No.11. P.905-915.
- [12] L. Frenz et al. Droplet-based microreactors for the synthesis of magnetic iron oxide nanoparticles. *Angew. Chem. Int. Ed.* **2008**. Vol.47. No.36. P.6817-6820.
- [13] Y. Ren, K.S. Koh, Y. Zhang. Synthesis of Functional Materials by Non-Newtonian Microfluidic Multiphase System. *Advances in Microfluidics-New Applications in Biology, Energy, and Materials Sciences. – InTech*. **2016**.
- [14] J.P. McMullen, K.F. Jensen. Integrated microreactors for reaction automation: new approaches to reaction development. *Annu. Rev. Anal. Chem.* **2010**. Vol.3. P.19-42.
- [15] D.T. Chiu et al. Small but perfectly formed? Successes, challenges, and opportunities for microfluidics in the chemical and biological sciences. *Chem.* **2017**. Vol.2. No.2. P.201-223.
- [16] D. Erickson, D. Li. Integrated microfluidic devices. *Anal. Chim. Acta*. **2004**. Vol.507. P.11-26.
- [17] N.K. Inamdar, J.T. Borenstein. Microfluidic cell culture models for tissue engineering. *Curr. Opin. Biotech.* **2011**. Vol.22. P.681-689.
- [18] N.B. Rubtsov, V.M. Popik, S.E. Peltek, N.A. Kolchanov. Microfluidic devices in biology and biosensor design. *G.I. Budker establishment of RAS Institute of a nuclear physics. Novosibirsk*. **2004**. No.4. P.84-87. (russian)
- [19] Y. Lei et al. Gold nanoclusters-assisted delivery of NGF siRNA for effective treatment of pancreatic cancer. *Nat. Commun.* **2017**. Vol.8. P.1-15.
- [20] P. Watts, S.J. Haswell. The application of micro reactors for organic synthesis. *Chem. Soc. Rev.* **2005**. Vol.34. No.3. P.235-246.
- [21] E.R. Murphy, J.R. Martinelli, N. Zaborenko, S.L. Buchwald, K.F. Jensen. Accelerating reactions with microreactors at elevated temperatures and pressures: profiling aminocarbonylation reactions. *Angew. Chem. Int. Ed.* **2007**. Vol.46. No.10. P.1734-1737.
- [22] S. Roesner, S.L. Buchwald. Continuous-flow synthesis of biaryls by negishi cross-coupling of fluoro-and trifluoromethyl-substituted (hetero) arenes. *Angew. Chem. Int. Ed.* **2016**. Vol.55. No.35. P.10463-10467.
- [23] L. Kim, Y. Toh, J. Voldman, H. Yu. A practical guide to microfluidic perfusion culture of adherent mammalian Cells. *Lab Chip*. **2007**. Vol.7. P.681- 694.
- [24] W.K. Edmond Young and David J. Beebe. Fundamentals of microfluidic cell culture in controlled microenvironments. *Chem. Soc. Rev.* **2010**. Vol.39. No.3. P.1036-1048.
- [25] G.M. Whitesides, E. Ostuni, S. Takayama, X. Jiang, D.E. Ingber. Soft lithography in biology and biochemistry. *Annu. Rev. Biomed. Eng.* **2001**. Vol.3. No.1. P.335-373.
- [26] J. Garra. Dry etching of polydimethylsiloxane for microfluidic systems. *J. Vacuum Sci. Tech. A: Vacuum, Surfaces, and Films*. **2002**. Vol.20. No.3. P.975-982.
- [27] K.I. Min et al. Monolithic and flexible polyimide film microreactors for organic microchemical applications fabricated by laser ablation. *Angew. Chem. Int. Ed.* **2010**. Vol.49. No.39. P.7063-7067.
- [28] J.H. Sung, M.L. Shuler. Microtechnology for mimicking in vivo tissue environment. *Annal. Biomed. Eng.* **2012**. Vol.40. No.6. P.1289-1300.
- [29] A. Khademhosseini, R. Langer, J. Borenstein, J.P. Vacanti. Microscale technologies for tissue engineering and biology. *PNAS*. **2006**. Vol.103. No.8. P.2480-2487.
- [30] D.K. Maurya, W.Y. Ng, K.A. Mahabadi, Y.N. Liang, I. Rodriguez. Fabrication of lab-on chip platforms by hot embossing and photo patterning. *J. Biotech.* **2007**. Vol.2. P.1381-1388.

- [31] J. Wang et al. A microfluidic tubing method and its application for controlled synthesis of polymeric nanoparticles. *Lab Chip.* **2014**. Vol.14. No.10. P.1673-1677.
- [32] Z. Zhang, X. Wang, Y. Luo, S. He, L. Wang. Thermal assisted ultrasonic bonding method for poly (methyl methacrylate)(PMMA) microfluidic devices. *Talanta.* **2010**. Vol.81. No.4. P.1331-1338.
- [33] H. Kim, K. Min, K. Inoue, D.J. Im, D. Kim, J. Yosh. Submillisecond organic synthesis: Outpacing Fries rearrangement through microfluidic rapid mixing. *Science.* **2016**. Vol.352. No.6286. P.691-694
- [34] J.S. Lee, S.H. Lee, J.H. Kim, C.B. Park. Artificial photosynthesis on a chip: microfluidic cofactor regeneration and photoenzymatic synthesis under visible light. *Lab Chip.* **2011**. Vol.11. No.14. P.2309-2311.
- [35] N.T. Nguyen, Z. Wu. Micromixers – a review. *J. Micromech. Microeng.* **2004**. Vol.15. No.2. P.R1-R16.
- [36] Z. Yang, S. Matsumoto, H. Goto, M. Matsumoto, R. Maeda. Ultrasonic micromixer for microfluidic systems. *Sens. Act. A Phys.* **2001**. Vol.93. No.3. P.266-272.
- [37] H.H. Bau, J. Zhong, M. Yi. A minute magneto hydro dynamic (MHD) mixer. *Sens. Act. B Chem.* **2001**. Vol.79. No.2. P.207-215.
- [38] Beebe D.J., Mensing G.A., Walker G.M. Physics and applications of microfluidics in biology. *Annu. Rev. Biomed. Eng.* **2002**. Vol.4. No.1. P.261-286.
- [39] A.D. Stroock, S.K. Dertinger, A. Ajdari, I. Mezic, H.A. Stone, G.M. Whitesides. Chaotic mixer for microchannels. *Science.* **2002**. Vol.295. No.5555. P.647-651.
- [40] I. Glasgow, N. Aubry. Enhancement of microfluidic mixing using time pulsing. *Lab Chip.* **2003**. Vol.3. No.2. P.114-120.
- [41] A.D. Stroock, S.K. Dertinger, G.M. Whitesides, A. Ajdari. Patterning flows using grooved surfaces *Anal. Chem.* **2002**. Vol.74. No.20. P.5306-5312.
- [42] D. Gobby, P. Angelis, A. Gavriilidis. Mixing characteristics of T-type microfluidic mixers. *J. Micromech. Microeng.* **2001**. Vol.11. No.2. P.126.
- [43] T.J. Johnson, D. Ross, L.E. Locascio. Rapid microfluidic mixing. *Anal. Chem.* **2002**. Vol.74. No.1. P.45-51.
- [44] S.H. Wong et al. Investigation of mixing in a cross-shaped micromixer with static mixing elements for reaction kinetics studies. *Sens. Act. B: Chemical.* **2003**. Vol.95. No.1. P.414-424.
- [45] T.T. Veenstra, T.S.J. Lammerink, M.C. Elwenspoek, A. Berg. Characterization method for a new diffusion mixer applicable in micro flow injection analysis systems. *J. Micromech. Microeng.* **1999**. Vol.9. No.2. P.199-202.
- [46] I.N. Raebiger et al. Experimental and numerical investigations of T-shaped micromixers. *Proc. 11th European Conf. Mixing.* **2003**.
- [47] A. Soleymani, E. Kolehmainen, I. Turunen. Numerical and experimental investigations of liquid mixing in T-type micromixers. *Chem. Eng. J.* **2008**. Vol.135. P.S219-S228.
- [48] J. Cha et al. A highly efficient 3D micromixer using soft PDMS bonding. *J. Micromech. Microeng.* **2006**. Vol.16. No.9. P.1778-1782.
- [49] C.H. Lin, C.H. Tsai, L.M. Fu. A rapid three-dimensional vortex micromixer utilizing self-rotation effects under low Reynolds number conditions. *J. Micromech. Microeng.* **2005**. Vol.15. No.5. P.935-943.
- [50] C. Erbacher et al. Towards integrated continuous-flow chemical reactors. *Microchim. Acta.* **1999**. Vol.131. No.1. P.19-24.
- [51] F.G. Bessoth, A.J. deMello, A. Manz. Microstructure for efficient continuous flow mixing. *Anal. Commun.* **1999**. Vol.36. No.6. P.213-215.
- [52] S.W. Lee, D.S. Kim, S.S. Lee, T.H. Kwon. A split and recombination micromixer fabricated in a PDMS three-dimensional structure. *J. Micromech. Microeng.* **2006**. Vol.16. No.5. P.1067-1072.
- [53] S. Hardt, H. Pennemann, F. Schönfeld. Theoretical and experimental characterization of a low-Reynolds number split-and-recombine mixer. *Microfluid. Nanofluid.* **2006**. Vol.2. No.3. P.237-248.
- [54] A.D. Radadia et al. A 3D micromixer fabricated with dry film resist. *Micro Electro Mechan. Syst., 2007. MEMS. IEEE 20th International Conference on. – IEEE.* **2007**. P.361-364.
- [55] J. Branebjerg et al. Fast mixing by lamination. *Micro Electro Mechanical Systems, 1996, MEMS'96, Proceedings. An Investigation of Micro Structures, Sensors, Actuators, Machines and Systems. IEEE, The Ninth Annual International Workshop on. – IEEE.* **1996**. P.441-446.
- [56] F. Schönfeld, V. Hessel, C. Hofmann. An optimised split-and-recombine micro-mixer with uniform ‘chaotic’mixing. *Lab Chip.* **2004**. Vol.4. No.1. P.65-69.
- [57] A. Bertsch, S. Heimgartner, P. Cousseau, P. Renaud. Static micromixers based on large-scale industrial mixer geometry. *Lab Chip.* **2001**. Vol.1. No.1. P.56-60.
- [58] A.A. Deshmukh, D. Liepmann, A.P. Pisano. Continuous micromixer with pulsatile micropumps. *Technical Digest of the IEEE Solid State Sensor and Actuator Workshop (Hilton Head Island, SC).* **2000**. Vol.736.

- [59] C.Y. Lim, Y.C. Lam, C. Yang. Mixing enhancement in microfluidic channel with a constriction under periodic electro-osmotic flow. *Biomicrofluidics*. **2010**. Vol.4. No.1. P.014101.
- [60] A.A. Deshmukh, D. Liepmann, A.P. Pisano. Characterization of a micro-mixing, pumping, and valving system. *Transducers' 01 Eurosensors XV. – Springer Berlin Heidelberg*. **2001**. P.922-925.
- [61] I. Glasgow, N. Aubry. Enhancement of microfluidic mixing using time pulsing. *Lab Chip*. **2003**. Vol.3. No.2. P.114-120.
- [62] M.H. Oddy, J.G. Santiago, J.C. Mikkelsen. Electrokinetic instability micromixing. *Anal. Chem.* **2001**. Vol.73. No.24. P.5822-5832.
- [63] D. Yan, C. Yang, J. Miao, Y. Lam, X. Huang. Enhancement of electrokinetically driven microfluidic T-mixer using frequency modulated electric field and channel geometry effects. *Electrophoresis*. **2009**. Vol.30. No.18. P.3144-3152.
- [64] J. Deval, P. Tabeling, C.M. Ho. A dielectrophoretic chaotic mixer. *Micro Electro Mechanical Systems, 2002. The Fifteenth IEEE International Conference on. – IEEE*. **2002**. P.36-39.
- [65] G. Goet, T. Baier, S. Hardt. Micro contactor based on isotachophoretic sample transport. *Lab Chip*. **2009**. Vol.9. No.24. P.3586-3593.
- [66] P. Paik, V.K. Pamula, M.G. Pollack, R.B. Fair. Electrowetting-based droplet mixers for microfluidic systems. *Lab Chip*. **2003**. Vol.3. No.1. P.28-33.
- [67] J. Fowler, H. Moon, C.J. Kim. Enhancement of mixing by droplet-based microfluidics. *Micro Electro Mechanical Systems, 2002. The Fifteenth IEEE International Conference on. – IEE*. **2002**. P.97-100.
- [68] L. Capretto, W. Cheng, M. Hill, X. Zhang. Micromixing within microfluidic devices. *Top. Curr. Chem.* **2011**. Vol.304. P.27-68.
- [69] L.S. Jang, S. Chao, M.R. Holl, D.R. Meldrum. Resonant mode-hopping micromixing. *Sens. Act. A: Phys.* **2007**. Vol.138. No.1. P.179-186.
- [70] P. Lob, V. Hessel, H. Klefenz, H. Lowe, K. Mazanek. Bromination of thiophene in micro reactors. *Lett. Org. Chem.* **2005**. Vol.2. No.8. P.767-779.
- [71] J. D'Attoma et al. Fast functionalization of (7-aza) indoles using continuous flow processes. *ChemistrySelect*. **2016**. Vol.1. No.3. P.338-342.
- [72] T. Gustafsson, R. Gilmour, P.H. Seeberger. Fluorination reactions in microreactors. *Chem. Commun.* **2008**. No.26. P.3022-3024.
- [73] A.J. Blacker, K.E. Jolley. Continuous formation of N-chloro-N, N-dialkylamine solutions in well-mixed meso-scale flow reactors. *Beilstein J. Org. Chem.* **2015**. Vol.11. P.2408-2417.
- [74] Q. Deng, R. Shen, R. Ding, L. Zhang. Bromination of aromatic compounds using bromine in a microreactor. *Chem. Eng. Technol.* **2016**. Vol.39. No.8. P.1445-1450.
- [75] H. Ehrich et al. Application of microstructured reactor technology for the photochemical chlorination of alkylaromatics. *CHIMIA Int. J. Chem.* **2002**. Vol.56. No.11. P.647-653.
- [76] D. Cambié, C. Bottecchia, N.J.W. Straathof, V. Hessel, T. Noël. Applications of continuous-flow photochemistry in organic synthesis, material science, and water treatment. *Chem. Rev.* **2016**. Vol.116. No.17. P.10276-10341.
- [77] D. Šterk, M. Jukič, Z. Časar. Application of flow photochemical bromination in the synthesis of a 5-bromomethylpyrimidine precursor of rosuvastatin: improvement of productivity and product purity. *Org. Proc. Res. Dev.* **2013**. Vol.17. No.1. P.145-151.
- [78] B.A. Frontana-Uribe, R.D. Little, J.G. Ibanez, A. Palmad, R. Vasquez-Medranoc. Organic electrosynthesis: a promising green methodology in organic chemistry. *Green Chem.* **2010**. Vol.12. No.12. P.2099-2119.
- [79] E. Garcia-Egido, S.Y.F. Wong, B.H. Warrington. A Hantzsch synthesis of 2-aminothiazoles performed in a heated microreactor system. *Lab Chip*. **2002**. Vol.2. No.1. P.31-33.
- [80] P. Watts, C. Wiles, S.J. Haswell, E. Pombo-Villar, P. Styring. The synthesis of peptides using micro reactors. *Chem. Commun.* **2001**. P.990-991.
- [81] P. Watts, C. Wiles, S.J. Haswell, E. Pombo-Villar. Solution phase synthesis of  $\beta$ -peptides using micro reactors. *Tetrahedron*. **2002**. Vol.58. No.27. P.5427-5439.
- [82] P. Watts, S.J. Haswell, E. Pombo-Villar. Electrochemical effects related to synthesis in micro reactors operating under electrokinetic flow. *Chem. Eng. J.* **2004**. Vol.101. No.1-3. P.237-240.
- [83] V. Skelton, G.M. Greenway, S.J. Haswell, P. Styring, D.O. Morgan, B. Warrington, S.Y.F. Wong. The preparation of a series of nitrostilbene ester compounds using micro reactor technology. *Analyst*. **2001**. Vol.126. No.1. P.7-10.
- [84] M. Sands, S.J. Haswell, S.M. Kelly, V. Skelton, D.O. Morgan, P. Styring, B.H. Warrington. The investigation of an equilibrium dependent reaction for the formation of enamines in a microchemical system. *Lab Chip*. **2001**. No.1. P.64-65.

- [85] C. Wiles, P. Watts, S.J. Haswell, E. Pombo-Villar. 1,4-Addition of enolates to  $\alpha,\beta$ -unsaturated ketones within a micro reactor. *Lab Chip.* **2002**. No.2. P.62-64.
- [86] J. Yoshida, S. Suga. Basic concepts of “Cation Pool” and “Cation Flow” methods and their applications in conventional and combinatorial organic synthesis. *Chem. Eur. J.* **2002**. Vol.8. No.12. P.2650-2658.
- [87] V. Skelton, G.M. Greenway, S.J. Haswell. Microreactor synthesis: synthesis of cyanobiphenyls using a modified Suzuki coupling of an aryl halide and aryl boricacid, in *Microreaction Technology. 3<sup>rd</sup> International Conference on Microreaction Technology, Proceedings of IMRET 3*, Ed. W. Ehrfeld, Springer, Berlin, Germany. **2000**. P.235.
- [88] T. Schwalbe, V. Autze, G. Wille. Chemical synthesis in microreactors. *CHIMIA Int. J. Chem.* **2002**. Vol.56. No.11. P.636-646.
- [89] R.C.R. Wootton, R. Fortt, A.J. Mello. A microfabricated nanoreactor for safe, continuous generation and use of singlet oxygen. *Org. Process Res. Dev.* **2002**. Vol.6. P.187-189.
- [90] CPC – Cellular Process Chemistry SystemsGmbH, EP 0116024-A2, **2001**.
- [91] E. Kumacheva, P. Garstecki. Microfluidic Reactors for Polymer Particles-John Wiley & Sons, Ltd, West Sussex, UK. **2011**.
- [92] T. Nisisako, S. Okushima, T. Torii. Controlled formulation of monodisperse double emulsions in a multiple-phase microfluidic system. *Soft Matter.* **2005**. No.1. P.23-27.
- [93] D. Velasco, E. Tumarkin, E. Kumacheva. Microfluidic encapsulation of cells in polymer microgels. *Small.* **2012**. Vol.8. No.11. P.1633-1642.
- [94] J. Greener, W. Li, J. Ren, D. Voicu, V. Pakharenko, T. Tang, E. Kumacheva. Rapid, cost-efficient fabrication of microfluidic reactors in thermoplastic polymers by combining photolithography and hot embossing. *Lab Chip.* **2010**. Vol.10. No.4. P.522-524.
- [95] Z. Nie, S. Xu, M. Seo, P.C. Lewis, E. Kumacheva. Polymer particles with various shapes and morphologies produced in continuous microfluidic reactors. *J. Am. Chem. Soc.* **2005**. Vol.127. No.22. P.8058-8063.
- [96] A.S. Utada, L.-Y. Chu, A. Fernandez-Nieves, D.R. Link, C. Holtze, D.A. Weitz. Dripping, jetting, drops, and wetting: the magic of microfluidics. *MRS Bull.* **2007**. Vol.32. No.9. P.702-708.
- [97] E. Tumarkin, L. Tzadu, E. Csaszar, M. Seo, H. Zhang, A. Lee, R. Peerani, K. Purpura, P.W. Zandstra, E. Kumacheva. High-throughput combinatorial cell co-culture using microfluidics. *Integr. Biol.* **2011**. Vol.3. No.6. P.653-662.
- [98] D. Dendukuri, D.C. Pregibon, J. Collins, T.A. Hatton, P.S. Doyle. Continuous-flow lithography for high-throughput microparticle synthesis. *Nat. Mater.* **2006**. Vol.5. P.365-369.
- [99] D.C. Pregibon, M. Toner, P.S. Doyle. Multifunctional encoded particles for high-throughput biomolecule analysis. *Science.* **2007**. Vol.315. No.5817. P.1393-1396.
- [100] P. Hinsmann, J. Frank, P. Svasek, M. Harasek, B. Lendt. Design, simulation and application of a new micromixing device for time resolved infrared spectroscopy of chemical reactions in solution. *Lab Chip.* **2001**. No.1. P.16-21.
- [101] G. Walker, M. Ozers, D. Beebe. Insect cell culture in microfluidic channels. *Biomed. Microdev.* **2001**. Vol.227. No.2-4. P.237-240.
- [102] D. Bokenkamp, A. Besai, X. Yang, Y. Tai, E. Marzluff, S. Mayo. Microfabricated silicon mixers for submillisecond quench-flow analysis. *Anal. Chem.* **1998**. Vol.70. No.2. P.232-236.
- [103] S. Bohm, K. Greiner, S. Schlautmann, S. Vries, A. Berg. A rapid vortex micromixer for studying high speed chemical reactions. *See Ref. 2001*. Vol.11. P.25-27.
- [104] A. Webster, J. Greenman, S.J. Haswell. Development of microfluidic devices for biomedical and clinical application. *Chem. Technol. Biotechnol.* **2011**. Vol.86. P.10-17.
- [105] E. Primiceri, M.S. Chiriac, R.R. Maruccio. Cell chips as new tools for cell biology – results, perspectives and opportunities. *Lab Chip.* **2013**. Vol.19. No.13. P.3789-3802.
- [106] J.A. Benn, J. Hu, J. Bradley et all. Microfluidic DNA microarray analysis: A review. *Anal. Chim. Acta.* **2011**. Vol.687. P.12-27.
- [107] L.J. Millet, M.U. Gillette. Over a century of neuron culture: From the hanging drop to microfluidic devices. *Yale J. Biol. Med.* **2012**. Vol.85. P.501-521.
- [108] A.D. DerMeer, A.A. Poot, M.H.G. Duits, J. Feijen, I. Vermes. Microfluidic technology in vascular research. *J. Biomed. Biotech.* **2009**. Vol.2009. P.1-10.
- [109] H. Ayliffe, A. Frazier, R. Rabbitt. Electric impedance spectroscopy using microchannels with integrated metal electrodes. *J. Microelectromech. Syst.* **1999**. Vol.8. P.50-57.
- [110] L. Sohn, O. Saleh, G. Facer, A. Beavis, R. Allan, D. Notterman. Capacitance cytometry: measuring biological cells one by one. *Proc. Natl. Acad. Sci. USA.* **2000**. Vol.97. P.10687-10690.
- [111] G. Facer, D. Notterman, L. Sohn. Dielectric spectroscopy for bioanalysis: from 40 Hz to 26.5 GHz in a microfabricated wave guide. *Appl. Phys. Lett.* **2001**. Vol.78. P.996-998.

**Review** \_\_\_\_ L.V. Kovalenko, M.S. Oshchepkov, A.N. Mylnikova, A.O. Menkov, V.A. Udovenko, M.I. Semchukova,  
and I.N. Solovieva

- [112] A. Bernard, B. Michel, E. Delamarche. Micromosaic immunoassays. *Anal. Chem.* **2001**. Vol.73. No.1.  
P.8-12.
- [113] T. Yang, S. Jung, H. Mao, P. Cremer. Fabrication of phospholipid bilayercoated microchannels for on-  
chip immunoassays. *Anal. Chem.* **2001**. Vol.73. No.2. P.165-169.
- [114] E. Eteshola, D. Leckband. Development and characterization of an ELISA assay in PDMS microfluidic  
channels. *Sens. Actuators B.* **2001**. Vol.72. No.1-2. P.129-133.
- [115] Edmond W.K. Young. Advances in Microfluidic Cell Culture Systems for Studying Angiogenesis.  
*Journal of Laboratory Automation.* **2013**. Vol.18(6). P.427-437.