Chapter 1
Introduction

Modern analytical techniques should be highly specific and sensitive enough to identify and quantify an analyte of interest with minimum requirements for sample pretreatment. Raman spectroscopy is a highly specific technique that enables identification of molecules through their specific molecular fingerprint information as observed in their Raman spectra. However, the Raman scattering (RS) effect is intrinsically quite weak and the Raman spectra cannot be obtained from low analyte concentrations. Surface-enhanced Raman scattering (SERS) spectroscopy can overcome this problem by using certain metallic[1] nanoparticles (NPs) or nanostructures which significantly amplify the RS signals coming from analytes attached to (or at least be in close proximity to) such nanostructural surface. "S" means that SERS is a "surface" spectroscopy technique (the analytes must be on or close to the surface), "E" means signal "enhancement" (ensured by plasmon resonances in the metal) and "R" means "Raman" (providing fingerprint information about studied analyte). Last "S" can mean "scattering" or "spectroscopy".[2] Thus, the SERS technique efficiently combines the specificity of Raman signature with high sensitivity.

Surface-enhanced Raman scattering (SERS) was discovered in the seventies by the Fleischmann group who observed a surprisingly strong Raman signal of a single monolayer of pyridine on an electrochemically roughened silver electrode (Fleischmann et al. 1974). The experiment was soon confirmed and quantified by the Van Duyne group (Jeanmaire and Van Duyne 1977) and Creighton group (Albrecht and Creighton 1977), reporting that enhancement of RS of pyridine is in order of 10^5–10^6. For more details about SERS discovery see reviews of McQuillan from the Fleischmann group (McQuillan 2009), Creighton (Creighton 2010) and Van Duyne (Haynes et al. 2005). Nowadays, SERS is understood as a very large enhancement of RS effect (basically 10^4–10^6, but even 10^{11} in some special cases) coming from

[1]The term "metallic" is used in meaning of "made from metal" (e.g. metallic substrate, metallic structure, metallic NP). On the other hand, the term "metal" is used in the case of the "metal properties" will be emphasized (e.g. metal surface).

[2]In certain literature, the abbreviation RS means "Raman spectroscopy" to emphasize the technique. Here, RS for "Raman scattering" is used to emphasize the Raman scattering effect. By analogy "S" means "scattering" in RRS, SERS, SERRS, TERS, etc.

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molecules adsorbed on metal nanostructural surfaces. The decade following the SERS discovery was a period of intense activity in theoretical aspects of SERS with special emphasis on finding the origin of this enhancement (Moskovits 1985). Because of a poor understanding of the enhancement mechanism as well as many experimental problems, SERS remained a technique only used by a limited number of research groups. The simple use of Ag hydrosols as SERS-enhancing media (Creighton et al. 1979) opened up many possible applications of SERS for biomolecular studies (Koglin and Séquaris 1986; Cotton 1988). The observation of single-molecule (SM) detection by SERS (SM-SERS) reported in 1997 (Kneipp et al. 1997; Nie and Emory 1997) also significantly stimulated the interest in SERS applications.

The improvement of Raman instrumentation and the development of nanotechnologies (notably in terms of SERS enhancing substrate design and functionalization) in the end of the 1990s dramatically extended the field of SERS applications. Nowadays, scientists from a large range of disciplines including chemistry, physics, material and life sciences are beginning to use the SERS technique and fully exploit its tremendous potential. This can be seen in the growing number of publications about SERS and its applications as illustrated in Fig. 1.1. It includes several excellent review papers namely the first SERS review by Moskovits from 1985 (Moskovits 1985) and a recent one by Schlücker (2014). I would like to highlight many themed Journal issues namely in Journal of Raman Spectroscopy (2005, Editor Z.Q. Tian), in Faraday Discussions (2006, Editor Susan Weatherby), in Chemical Society Review (2008, Editors D. Graham and R. Goodacre), in Physical Chemistry Chemical Physics (2009, Editor P.G. Etchegoin), in Analytical Bioanalytical Chemistry (2009, Editors J. Popp and T. Mayerhöfer), in Chemical Communications (2011, Editors D. Graham, Z.Q. Tian and R. Van Duyne) and in MRS Bulletin (2013, Editors N.J. Halas and M. Moskovits). Several monographs covering SERS theory and applications are also available: "Surface-Enhanced Vibrational Spectroscopy" (R. Aroca, Wiley, 2006), "Surface-Enhanced Raman Scattering: Physics and

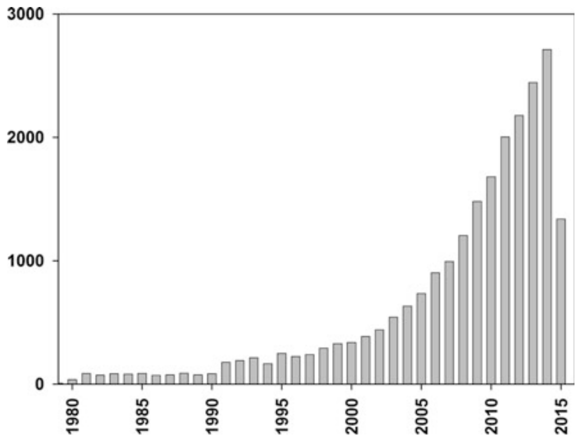

Fig. 1.1 Growing popularity of the SERS technique. This plot shows citation data in Web of Science for the term "surface enhanced Raman or SERS" (for 2015, it is incomplete, showing its value on June 30)

Applications", (Editors K. Kneipp, M. Moskovits, H. Kneipp, Springer, 2006), "Principles of Surface-Enhanced Raman Spectroscopy and Related Plasmonic Effects" (E. C. Le Ru, P. G. Etchegoin, Elsevier, 2009), "Surface-Enhanced Raman Spectroscopy: Analytical, Biophysical and Life Science Applications" (Editor S. Schlücker, Wiley, 2011) and "Frontiers of Surface-Enhanced Raman Scattering: Single Nanoparticles and Single Cells" (Editors Y. Ozaki, K. Kneipp, R. Aroca, Wiley 2014). A prestigious Faraday Discussion event about SERS spectroscopy was held at Imperial College London at September 2006. After over 40 years of SERS, hundreds of scientists are actively working in SERS field and the number of publications about SERS has exceeded 26,000 (Fig. 1.1).

SERS has many advantages over ordinary spectroscopic analytical techniques such as extremely high sensitivity, molecular selectivity, intense signals and great precision. However, the development of SERS technique so that it can become a standard analytical tool is still a big challenge and at least two main problems must be solved. First, a major issue for a routine quantitative SERS application (SERS sensing) is the requirement of a uniform SERS-enhancing substrates providing reliable and reproducible spectral signature of the studied analyte. A big effort is being made to rational designing of new SERS-enhancing substrates with aim to improve their sensitivity and spectral reproducibility (Banholzer et al. 2008). Second, SERS is a highly molecular specific technique and SERS detection is usually limited to molecules with surface-seeking groups since only molecules on or near the metal surface experience high surface enhancements. The problem to detect molecules with no surface-seeking groups or providing only weak SERS effect can be solved by chemical modification such as the labelling with highly SERS-active label (Smith 2008). With this approach the SERS spectra of labels instead of molecules are obtained leading to indirect but extremely sensitive detection. An alternative to the labelling of a target molecule is a SERS tag formed by attaching a molecule (called Raman reporter) to the metallic NPs providing a strong SERS signal (Wang et al. 2013). The surface of SERS tag can be further functionalized with a biorecognition element such as an antibody to make the tags with a specific binding feature (such as cancer biomarkers). The possibility of introducing metallic NPs or rationally designed NP tags into living cells or living organisms enables many in vitro and in vivo medical applications including diagnostics, therapy, theranostics and surgery guidance with sufficient sensitivity (Zavaleta et al. 2011; Vo-Dinh et al. 2013).

The main aim of this book is to provide a compact and full-length review of bioanalytical, biomolecular and medical applications of SERS spectroscopy reported during the last two decades. Following this introduction you will find two chapters describing basic principles of RS and SERS spectroscopy including some practical aspects related to bioapplications. The next four chapters summarized key concepts and bioanalytical (Chap. 4), biomolecular (Chap. 5), cellular (Chap. 6) and medical (Chap. 7) applications of SERS. The last chapter gives conclusions and outlook. Of course, it was impossible to include all applications from the extensive SERS literature in this book. Besides the monographs and themed Journal issues mentioned above many recent reviews covering SERS bioapplications are highly recommended for a complete overview: Cotton (1988), Cotton et al. (1991), Dou and Ozaki (1999), Kneipp et al. (2002), Hering et al. (2008), Chourpa et al. (2008), Huh et al. (2009), Abalde-Cela et al. (2010), Alvarez-Puebla and Liz-Marzán (2010), Vo-Dinh et al. (2010), Li (2010), Procházka and Štepánek (2012), Banz et al. (2011), Aoki et al. (2013), McNay et al. (2011), Culha et al. (2012), Han et al. (2012), Larmour and Graham (2011), Faulds (2012), Ochsenkühn and Campbell (2012), Drescher and Kneipp (2012), Harper et al. (2013), Vendrell et al. (2013), Culha (2013), Xie and Schlücker (2013), Wang et al. (2013), Vo-Dinh et al. (2013), Xie and Schlücker (2014), Schlücker (2014), Nima et al. (2014), McAughtrie et al. (2014), Howes et al. (2014a, b), Cialla et al. (2014), Zheng and He (2014), Li et al. (2015), Vo-Dinh et al. (2015).

References

S. Abalde-Cela, P. Aldeanueva-Potel, C. Mateo-Mateo, L. Rodriguez-Lorenzo, R.A. Alvarez-Puebla, L.M. Liz-Marzan, Surface-enhanced Raman scattering biomedical applications of plasmonic colloidal particles. J. R. Soc. Interface **7**, S435 (2010)

M.G. Albrecht, J.A. Creighton, Anomalously intense Raman spectra of pyridine at a silver surface. J. Am. Chem. Soc. **99**, 5215 (1977)

R.A. Alvarez-Puebla, L.M. Liz-Marzán, SERS-based diagnosis and biodetection. Small **6**, 604 (2010)

P.H.B. Aoki, L.N. Furini, P. Alessio, A.E. Aliaga, C.J.L. Constantino, Surface-enhanced Raman scattering (SERS) applied to cancer diagnosis and detection of pesticides, explosives, and drugs. Rev. Anal. Chem. **32**, 55 (2013)

M.J. Banholzer, J.E. Millstone, L. Qin, C.A. Mirkin, Rationally designed nanostructures for surface-enhanced Raman spectroscopy. Chem. Soc. Rev. **37**, 885 (2008)

K.C. Bantz, A.F. Meyer, N.J. Wittenberg, H. Im, O. Kurtulus, S.H. Lee, N.C. Lindquist, S.H. Oh, C.L. Haynes, Recent progress in SERS biosensing. Phys. Chem. Chem. Phys. **13**, 11551 (2011)

I. Chourpa, F.H. Lei, P. Dubois, M. Manfait, G.D. Sockalingum, Intracellular applications of analytical SERS spectroscopy and multispectral imaging. Chem. Soc. Rev. **37**, 993 (2008)

D. Cialla, S. Pollok, C. Steinbrücker, K. Weber, J. Popp, SERS-based detection of biomolecules. Nanophotonics **3**, 383 (2014)

T.M. Cotton, The applications of SERS to biological systems, in *Spectroscopy of Surfaces*, ed. by R.J.H. Clark, R.E. Hester (Wiley, Chichester, 1988), pp. 90–153

T.M. Cotton, J.-H. Kim, G.D. Chumanov, Application of surface-enhanced Raman spectroscopy to biological systems. J. Raman Spectrosc. **22**, 729 (1991)

J.A. Creighton, Contributions to the early development of surface-enhanced Raman spectroscopy. Notes Rec. R. Soc. **64**, 175 (2010)

J.A. Creighton, C.G. Blatchford, M.G. Albrecht, Plasma resonance enhancement of Raman scattering by pyridine adsorbed on silver and gold sol particles of size comparable to the excitation wavelength. J. Chem. Soc., Faraday Trans. 2 **75**, 790 (1979)

M. Culha, Surface-enhanced Raman scattering: An emerging label-free detection and identification technique for proteins. Appl. Spectrosc. **67**, 355 (2013)

M. Culha, B. Cullum, N. Lavrik, C.K. Klutse, Surface-enhanced Raman scattering as an emerging characterization and detection technique. J. Nanotechnol. **2012**, 971380 (2012)

X.M. Dou, Y. Ozaki, Surface-enhanced Raman scattering of biological molecules on metal colloids: basic studies and applications. Rev. Anal. Chem. **18**, 285 (1999)

D. Drescher, J. Kneipp, Nanomaterials in complex biological systems: insights from Raman spectroscopy. Chem. Soc. Rev. **41**, 5780 (2012)

K. Faulds, Multiplexed SERS for DNA detection, in *Raman Spectroscopy for Nanomaterials Characterization*, ed. by C.S.S.R. Kumar (Springer, Berlin Heidelberg, 2012), pp. 353–378

M. Fleischmann, P.J. Hendra, A.J. McQuillan, Raman spectra of pyridine adsorbed at a silver electrode. Chem. Phys. Lett. **26**, 163 (1974)

X.X. Han, B. Zhao, Y. Ozaki, Label-free detection in biological applications of surface-enhanced Raman scattering. Trend. Anal. Chem. **38**, 67 (2012)

M.M. Harper, K.S. McKeating, K. Faulds, Recent developments and future directions in SERS for bioanalysis. Phys. Chem. Chem. Phys. **15**, 5312 (2013)

C.L. Haynes, C.R. Yonzon, X. Zhang, R.P. Van Duyne, Surface-enhanced Raman sensors: early history and the development of sensors for quantitative biowarfare agents and glucose detection. J. Raman Spectrosc. **36**, 471 (2005)

K. Hering, D. Cialla, K. Ackermann, T. Dörfer, R. Möller, H. Schneidewind, R. Mattheis, W. Fritzsche, P. Rösch, J. Popp, SERS: a versatile tool in chemical and biochemical diagnostics. Anal. Bioanal. Chem. **390**, 113 (2008)

P.D. Howes, R. Chandrawati, M.M. Stevens, Colloidal nanoparticle as advanced biological sensors. Science **346**, 1247390 (2014a)

P.D. Howes, S. Rana, M.M. Stevens, Plasmonic nanomaterials for biodiagnostics. Chem. Soc. Rev. **43**, 3835 (2014b)

Y.S. Huh, A.J. Chung, D. Erickson, Surface enhanced Raman spectroscopy and its applications to molecular and cellular analysis. Microfluid. Nanofluid. **6**, 285 (2009)

D.J. Jeanmaire, R.P. Van Duyne, Heterocyclic, aromatic, and aliphatic amines adsorbed on the anodized silver electrode. J. Electroanal. Chem. **84**, 1 (1977)

K. Kneipp, Y. Wang, H. Kneipp, L.T. Perelman, I. Itzkan, R.R. Dasari, M.S. Feld, Single molecule detection using surface-enhanced Raman scattering (SERS). Phys. Rev. Lett. **78**, 1667 (1997)

K. Kneipp, H. Kneipp, I. Itzkan, R.R. Dasari, M.S. Feld, Surface-enhanced Raman scattering and biophysics. J. Phys.: Condens. Matter **14**, R597 (2002)

E. Koglin, J.-M. Séquaris, Surface enhanced Raman scattering of biomolecules. Top. Curr. Chem. **134**, 1 (1986)

I.A. Larmour, D. Graham, Surface enhanced optical spectroscopies for bioanalysis. Analyst **136**, 3831 (2011)

M. Li, The applications of surface-enhanced Raman spectroscopy to identify and quantify chemical adulterants or contaminants in food, in *Applications of vibrational spectroscopy in food science* ed. by E. Li-Chan, P.R. Griffiths, J.M. Chalmers (John Wiley, Chichester, 2010), pp. 649–662

M. Li, S.K. Cushing, N. Wu, Plasmon-enhanced optical sensors: a review. Analyst **140**, 386 (2015)

S. McAughtrie, K. Faulds, D. Graham, Surface enhanced Raman spectroscopy (SERS): potential applications for disease detection and treatment. J. Photochem. Photobiol. C-Photochem. Rev. **21**, 40 (2014)

G. McNay, D. Eustace, W.E. Smith, K. Faulds, D. Graham, Surface-enhanced Raman scattering (SERS) and surface-enhanced resonance Raman scattering(SERRS): a review of applications. Appl. Spectrosc. **65**, 825 (2011)

A.J. McQuillan, The discovery of surface-enhanced Raman scattering. Notes Rec. R. Soc. **63**, 105 (2009)

M. Moskovits, Surface-enhanced spectroscopy. Rev. Modern Phys. **57**, 783 (1985)

S. Nie, S.R. Emory, Probing single molecules and single nanoparticles by surface-enhanced Raman scattering. Science **275**, 1102 (1997)

Z.A. Nima, A. Biswas, I.S. Bayer, F.D. Hardcastle, D. Perry, A. Ghosh, E. Dervishi, A.S. Biris, Applications of surface-enhanced Raman scattering in advanced bio-medical technologies and diagnostics. Drug Metab. Rev. **46**, 155 (2014)

M.A. Ochsenkühn, C.J. Campbell, Biomedical SERS studies using nanoshells, in *Raman Spectroscopy for Nanomaterials Characterization*, ed. by C.S.S.R. Kumar (Springer, Berlin Heidelberg, 2012), pp. 51–74

M. Procházka, J. Štěpánek, Surface-enhanced Raman scattering (SERS) and its application to biomolecular and cellular investigation, in *Applications of Raman Spectroscopy to Biology—from Basic Studies to Disease Diagnosis*, ed. by M. Ghomi (IOS Press, Amsterdam, 2012), pp. 1–30

S. Schlücker, Surface-enhanced Raman spectroscopy: concepts and chemical applications. Angew. Chem. Int. Ed. **53**, 4756 (2014)

W.E. Smith, Practical understanding and use of surface enhanced Raman scattering/surface enhanced resonance Raman scattering in chemical and biological analysis. Chem. Soc. Rev. **37**, 955 (2008)

M. Vendrell, K.K. Maiti, K. Dhaliwal, Y.T. Chang, Surface-enhanced Raman scattering in cancer detection and imaging. Trends. Biotechnol. **31**, 249 (2013)

T. Vo-Dinh, H.N. Wang, J. Scaffidi, Plasmonic nanoprobes for SERS biosensing and bioimaging. J. Biophoton. **3**, 89 (2010)

T. Vo-Dinh, A.M. Fales, G.D. Griffin, C.G. Khoury, Y. Liu, H. Ngo, S.J. Norton, J.K. Register, H. N. Wang, H. Yuan, Plasmonic nanoprobes: from chemical sensing to medical diagnostics and therapy. Nanoscale **5**, 10127 (2013)

T. Vo-Dinh, Y. Liu, A.M. Fales, H. Ngo, H.N. Wang, J.K. Register, H. Yuan, S.J. Norton, G.D. Griffin, SERS nanosensors and nanoreporters: golden opportunities in biomedical applications. WIREs Nanomed. Nanobiotechnol. **7**, 17 (2015)

Y. Wang, B. Yan, L. Chen, SERS tags: novel optical nanotags for bioanalysis. Chem. Rev. **113**, 1391 (2013)

W. Xie, S. Schlücker, Medical applications of surface-enhanced Raman scattering. Phys. Chem. Chem. Phys. **15**, 5329 (2013)

W. Xie, S. Schlücker, Rationally designed multifunctional plasmonic nanostructures for surface-enhanced Raman spectroscopy: a review. Rep. Prog. Phys. **77**, 116502 (2014)

C.L. Zavaleta, M.F. Kircher, S.S. Gambhir, Raman's "effect" on molecular imaging. J. Nucl. Med. **52**, 1839 (2011)

J. Zheng, L. He, Surface-enhanced Raman spectroscopy for the chemical analysis of food. Compr. Rev. Food. Sci. Food Saf. **13**, 317 (2014)

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