A Mathematical Investigation of the Turkevich Organizer Theory in the Citrate Method for the Synthesis of Gold Nanoparticles

Emmanuel Agunloye, Asterios Gavriilidis, Luca Mazzei

Abstract—Gold nanoparticles are commonly synthesized by reducing chloroauric acid with sodium citrate. This method, referred to as the citrate method, can produce spherical gold nanoparticles (NPs) in the size range 10-150 nm. Gold NPs of this size are useful in many applications. However, the NPs are usually polydisperse and irreproducible. A better understanding of the synthesis mechanisms is thus required. This work thoroughly investigated the only model that describes the synthesis. This model combines mass and population balance equations, describing the NPs synthesis through a sequence of chemical reactions. Chloroauric acid reacts with sodium citrate to form aurous chloride and dicarboxy acetone. The latter organizes aurous chloride in a nucleation step and concurrently degrades into acetone. The unconsumed precursor then grows the formed nuclei. However, depending on the pH, both the precursor and the reducing agent react differently thus affecting the synthesis. In this work, we investigated the model for different conditions of pH, temperature and initial reactant concentrations. To solve the model, we used Parsival, a commercial numerical code, whilst to test it, we considered various conditions studied experimentally by different researchers, for which results are available in the literature. The model poorly predicted the experimental data. We believe that this is because the model does not account for the acid-base properties of both chloroauric acid and sodium citrate.

Keywords—Gold nanoparticles, Citrate method, Turkevich organizer theory, population balance modelling.

I. Introduction

TODAY, nanotechnology is one of the most important research areas that scientists investigate for new materials. These materials, which are called nanoparticles, have sizes in the range 1 – 100 nm and can be of different shapes: spherical, cylindrical, oblong, just to mention a few. Nanoparticles (NPs) exhibit properties that are unique, different from the properties of the substance in the bulk, thus opening new frontiers for material engineering. NPs can be synthesized by breaking the bulk material in pieces down to the nanometer size or by bringing a sufficient number of molecules together [1]. Examples of the latter are liquid phase reactions for the NPs synthesis while milling of a material is an example of the former. Unlike milling, the liquid phase reactions require less energy. In addition, they are safe and simple to operate, and have been used to produce metal NPs such as gold and silver,

Emmanuel Agunloye and Asterios Gavriilidis are with the Chemical Engineering Department, University College London, WCIE 7JE, London, UK.

Luca Mazzei is with the Chemical Engineering Department, University College London, WCIE 7JE, London, UK (corresponding author, e-mail: l.mazzei@ucl.ac.uk).

which are the two of the most researched NPs. Our focus in this work is on gold nanoparticles (GNPs).

GNPs find various applications such as cancer treatments and catalysis. These applications, however, depend on size and shape. Dreissfuss et al. [2] reported two size-dependent applications of GNPs: cancer therapy and diagnosis, which require 20 and 50 nm GNPs, respectively. From the different liquid phase reactions, specific sizes of GNPs can be produced. While various methods can be used to produce GNPs that have narrow range of sizes, the Turkevich synthesis has been used to produce NPs with spherical shape with size in the range 10-150 nm. However, the particles are often polydisperse and irreproducible. We believe that a model able to accurately describe the Turkevich synthesis would be very helpful to form particles with improved monodispersity in a more reproducible way.

The synthesis derives its name from the pioneer researchers, Turkevich et al. [3], who investigated experimentally how GNPs evolve with time. They concluded that the NPs evolve by a nucleation-growth mechanism. Further they advanced the idea that dicarboxyl acetone (DCA), which forms when citrate is oxidised while reducing tetrachloroauric acid to gold, organizes gold atoms in the nucleation step. Hence, this theory is called the Turkevich organizer theory. The investigation of Turkevich et al. [3] were followed by Frens [4] and Freund and Spiro [5], who explored it to produce different sizes of GNPs, by changing the ratio of citrate to gold. In disagreement with the observation by Turkevich et al. [3], Chow and Zukoski [6] reported NPs aggregation along with nucleation and growth. Subsequently, Kumar et al. [7] developed a model to explain the synthesis that considers all the previous observations. From a number of possible reactions, they considered only five: citrate reacts with auric chloride to form DCA and aurous chloride; DCA organizes aurous chloride to form the GNP nuclei; DCA decomposes into acetone; unconsumed aurous chloride grows the particles, and acetone can reduce auric chloride if citrate is unavailable. From this model, which comprises the material balance equations for the fluid components and the population balance equation for GNPs, the nucleation step and the DCA decomposition determine the final NP diameter. When the model was tested against the experimental data of Frens [4], it gave reasonably good predictions. In this work, we want to thoroughly test the model using other experimental data available in the literature.

After the work by Kumar et al. [7], authors such as Ji et al. [8], Polte et al. [9], and Kettemann et al. [10] studied in detail

the role of pH in the Turkevich synthesis. They varied the pH and observed that the reactions and, more importantly, the particles evolve differently. Ji et al. [8] identified 6.5 as a threshold pH value. For larger values, NPs evolve according to the nucleation-growth mechanism, whilst for lower pH values NPs evolve according to the nucleation-aggregation-growth mechanism described, for instance, by Polte et al. [9]. These findings prompted us to investigate the model of Kumar et al. [7] for different conditions (including different pH values) and verify whether its predictions are accurate or not.

The model is complex because it comprises a set of ordinary differential equations that describe the material balances of the fluid components and a population balance that describes the evolution of GNPs size distribution. To investigate the model, we considered different different temperatures of synthesis and different values of the pH of the reactive mixture. To solve the model, we used the numerical code Parsival, which solves population balance equations for lumped systems [11].

Because of the simplicity of this synthesis and of its general applicability, various experimental data are available in the literature. Takiyama [12] conducted the synthesis at 80 °C using different ratios of citrate to gold, while Wuithschick et al. [13] and Li et al. [14] reported the effects of temperature and pH, respectively, on the mean particle size. We used the experimental findings of these authors to test the model. In this report, we briefly present the model of Kumar et al. [7] (in the mathematical form which we implemented in Parsival) and then discuss the results. In particular, Section II illustrates the model, Section III discusses the tests, in which we investigated the effects of temperature and pH, and Section IV reports our conclusions on the validity of the model.

II. THE MODEL

We present an equivalent formulation of the model of Kumar et al. [7], and we first solve it to replicate some of the results therein reported (to check the validity of our implementation). We had to formulate the model differently because, while the original model is in terms of particle volume, the numerical code requires, as internal coordinate, the particle diameter.

The model comprises the material balance equations for the fluid components (reactants and products) and the population balance for the NPs. Auric chloride reacts with citrate to form both aurous chloride and DCA (1). In the presence of DCA, aurous chloride reacts to form the GNP nuclei (2). This nucleation process stops prematurely because DCA is unstable and decomposes into acetone (3). The remaining aurous chloride, grows the nuclei to the final particle size (4). In case some auric chloride remains, acetone reduces it into aurous chloride while the former is converted into an undefined "product" (5) [7]. In the model, T, C, M, S, D, and P represent auric chloride, citrate, aurous chloride, DCA, acetone and "product", respectively; Y and C denote the molar mass and concentration of a generic fluid component, respectively; k, V, ρ and v_0 are a generic reaction rate constant, the volume of the

reacting mixture, the density of gold and the volume of the NP nucleus, respectively; finally, s and m_v are the diameter and volume shape factor of the particles (which are assumed to be spherical, so that $m_v = \pi/6$). The equivalent model is reported below.

Auric chloride

$$\frac{d[C_T Y_T V]}{dt} = Y_T V\left[-k_c C_T C_C - k_d C_T C_D + k_n \rho v_0 C_M{}^3 C_S{}^2 + k_h m_v C_M \int_{s_0}^{\infty} s^2 f(s,t)ds\right] \quad (1)$$

Citrate

$$\frac{d[C_C Y_C V]}{dt} = -Y_C V[k_c C_T C_C] \quad (2)$$

Aurous chloride

$$\frac{d[C_M Y_M V]}{dt} = Y_M V\left[k_c C_T C_C + k_d C_T C_D - 3k_n \rho v_0 C_M{}^3 C_S{}^2 - 3k_h m_v C_M \int_{s_0}^{\infty} s^2 f(s,t)ds\right] \quad (3)$$

Dicarboxy acetone

$$\frac{d[C_S Y_S V]}{dt} = Y_S V[k_c C_T C_C - k_s C_S] \quad (4)$$

Acetone

$$\frac{d[C_D Y_D V]}{dt} = Y_D V\left[k_s C_S - \frac{1}{2.5}k_d C_T C_D\right] \quad (5)$$

Product

$$\frac{d[C_P Y_P V]}{dt} = Y_P V\left[\frac{1}{2.5}k_d C_T C_D\right] \quad (6)$$

The particles evolve by nucleation, growth and aggregation according to the following population balance equation:

$$\partial_t f(s) = -\partial_s[G_s(s)f(s)] + J_{nuc}(s) + B(s) - D(s) \quad (7)$$

where $f(s)$ is the number density function (NDF), defined so that $f(s)ds$ is the expected number of particles with size in the range ds around s at time t. $J_{nuc}(s)$ and $G_s(s)$ denote the nucleation and growth rates, respectively, and are given by:

$$J_{nuc}(s) = 2k_n C_M{}^3 C_S{}^2 \delta(s - s_0) \quad (8)$$

$$G_s(s) = \frac{2}{3}\frac{k_h}{m_v{}^{1/3}}\frac{C_M}{\rho} \quad (9)$$

$B(s)$ and $D(s)$ are the birth and death aggregation rates, respectively, given by:

$$B(s) = \frac{1}{2}\int_{s_0}^{s}\frac{\alpha(\xi,s')}{W}\frac{s^2}{\xi^2}f(s',t)f(\xi,t)ds'$$

with

$$\xi \equiv (s^3 - s'^3)^{1/3} \quad (10)$$

$$D(s) = f(s,t) \int_{s_0}^{\infty} \frac{\alpha(s,s')}{W} f(s',t)\, ds' \qquad (11)$$

$$\alpha(s,s') = \frac{2k_B T}{3\mu}\left(\frac{1}{s} + \frac{1}{s'}\right)(s+s') \qquad (12)$$

$$\ln W = \frac{560}{\varphi}\log_{10}\left[(3C_{C_0} + C_{T_0}) \times 10\right] + 27.5 \qquad (13)$$

where W is a stability factor, C_{T_0} and C_{C_0} are the initial molar concentrations of chloroauric acid and sodium citrate, respectively, and φ is the surface charge, given by:

$$\varphi = -90[f + 1.5(1-f)]; \quad f = \frac{1}{1 + 0.1C_C/(C_T + C_M)} \qquad (14)$$

We solved the model [i.e., (1)–(14)] in Parsival with the following parameters, as reported by Kumar et al. [7]:

$$k_c = 1.25\ \frac{m^3}{mol.s}$$

$$k_n = N_{av}\, 1.67 \times 10^{-3} \left(\frac{m^3}{mol}\right)^5 \frac{1}{m^3.s} \quad ; \quad k_s = 1\ \frac{1}{s}$$

$$k_h = 2.5 \times 10^{-4}\ \frac{m^3}{m^2.s}; \quad k_d = 4 \times 10^{-1}\ \frac{m^3}{mol.s}$$

$$\rho = 1 \times 10^5\ \frac{mol}{m^3}; \quad v_0 = 4.18 \times 10^{-27} m^3$$

In this comparison, we report only one case of how the model predictions compare to those of Kumar et al. [7]. For this case, C_{T_0} is constant at 0.3 mol/m^3 while C_{C_0} changes from 0.12 to 2.1 mol/m^3 at 100 °C. These initial conditions translate into citrate to gold ratios from about 0.4 to 7. Fig. 1 shows how the solutions in Parsival are compared to those by Kumar et al. [7].

Citrate reacts with auric ions to produce aurous ions and DCA. The stoichiometry of this reaction is 1.5 [7]. DCA organizes the aurous ions in the nucleation step, but concurrently degrades into acetone. When C_{C_0}/C_{T_0} is less than 1.5, the concentration of citrate limits the amount of DCA produced. As this ratio decreases, the rate of nucleation decreases. Because the concentration of the precursor is kept constant, these nuclei grow to bigger sizes. However, when C_{C_0}/C_{T_0} is higher than 1.5, the concentration of chloroauric acid, which is kept constant, limits the amount of DCA produced. As the ratio increases, the rate of nucleation remains constant yielding GNPs of almost the same mean size.

III. TEST OF THE MODEL

Sizes of GNPs from 10 – 150 nm can be produced by this method. To get a particular size, various authors tuned factors such temperature of synthesis, initial concentrations of reactants and pH of the mixture. Wuithschick et al. [13] and Li et al. [14] reported the effects of these factors on the final particle diameters. To test the model, we employed their data.
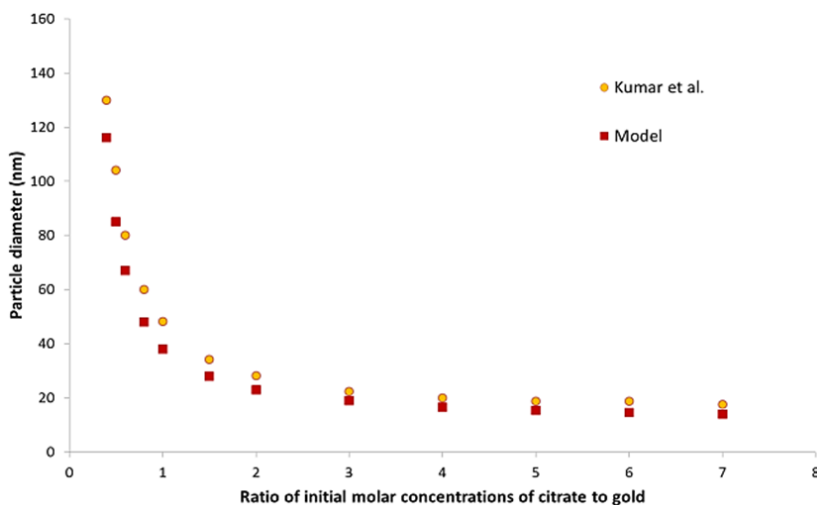

Fig. 1 The model predictions in Parsival compared to those of Kumar et al. [7]

A. Temperature of Synthesis

The temperature for the standard synthesis is 100 °C. Some authors have, however, carried out the synthesis at lower temperatures. For instance, during their pioneering work, Turkevich et al. [3] reported the synthesis at 70, 80, and 100 °C. Similarly, Wuithschick et al. [13] reported the final size at temperatures from 23 to 100 °C. The latter work provided a wide temperature investigation of the synthesis, and we thus used it to test the model. Kumar et al. [7] reported the reaction

rate constants for the reactions at 100 °C. To obtain the reaction rate constants at other temperatures, we used the activation energies of the reactions involved in the synthesis reported by various authors: 34, 10, 23.1, and 9.1 $kcal/mol$ for reactions 1 to 4 [3], [15], [16]. Since citrate is in excess in the work of Wuithschick et al. [13], reaction 5 is insignificant.

Table I shows the model predictions against the work of Wuithschick et al. [13]. The predictions do not agree with the experiment results. While the mean NP size in the experiments

decreases with temperature, reaches a minimum at around 60 °C and then increases, the model predictions decrease from 23 to 40 °C and then remain constant.

TABLE I
THE EFFECT OF TEMPERATURE ON THE MEAN DIAMETER USING THE DATA BY
WUITHSCHICK ET AL. [13]

Temperature (°C)	Wulthschick et al. (nm)	Model prediction
23	25.2	29.6
30	21.8	19.5
40	14.0	17.3
50	13.5	17.2
60	12.2	17.2
70	12.6	17.2
80	14.4	17.2
90	17.0	17.2
100	19.0	17.3

Section II reported the aggregation submodel adopted in the model. From our investigations, not reported in this article, we found out that with this submodel NPs aggregate indefinitely. Nevertheless, depending on how the characteristic time of aggregation (which depends on the synthesis conditions) compares with the synthesis time, aggregation may or may not occur significantly. The reactions in the synthesis require ca. 10^8 and 10^7 s to complete at 23 and 30 °C, respectively. At these temperatures, the characteristic times of aggregation (ca. 10^5 s) are shorter than the synthesis times. Thus, particles aggregate to bigger size. At higher temperatures, the mean size of the NPs remains constant because, within the synthesis time, the NPs do not aggregate. Moreover, from the simulation results, the ratio of the amount of precursor forming nuclei to the amount growing them does not change with temperature. The rates of the four reactions describing the synthesis increase in a similar way as the temperature increases; this is because the reactions have similar activation energies. The kinetic constant k_n of the nucleation rate increases, but so does the degradation rate of the catalyst (DCA) that causes nucleation; these two effects balance each other out so that the amount of precursor used for nucleation remains essentially the same. These four reactions do not sufficiently describe the synthesis according to recent experimental evidence [8], [13]; hence, the model fails to predict the mean size trend with temperature. The processes such as nucleation, aggregation and growth, in that order, manifest in the synthesis; they increase with temperature, but at different rates [13]. The aggregation rate, in particular, is negligible below 60 °C [17]. At low temperatures, such as 23 °C, the nuclei formed grow because they are few, consuming the entire precursor over a long time (slow growth). As the temperature increases, more nuclei form leaving less amount of precursor for growth. Thus, the mean size decreases from 23 to 60 °C. Aggregation starts affecting the synthesis significantly from 60 °C, thus increasing the particle mean size thereafter.

B. Final pH of the Mixture

Recent contributions on the synthesis focused on how to reduce the polydispersity and reproducibility by tuning the pH of the mixture. These contributions [8], [14] revealed that monodisperse and small GNPs are produced at high pH. To control the pH, researchers added sodium hydroxide to the reaction mixture. Li et al. [14] obtained decreasing particle size with increasing concentration of sodium hydroxide, while keeping the concentrations of tetrachloroauric acid and sodium citrate constant at 2.5 and 5 mol/m^3, respectively, at 100 °C. They only replaced the amount of water by the same amount of sodium hydroxide so as to keep the concentrations and ratio of the reactants constant while changing the pH of the mixture. Since sodium hydroxide is not part of the reactants considered by Kumar et al. [7], its amount only features as part of the inert in the reactant mixture, which is primarily water. Table II shows the model predictions with the experimental data.

As expected, the predictions do not agree with experiments because the effect of pH, which is a key factor that affects the reactivity of both precursor and reducing agent, is not properly accounted for. The model gives exactly the same prediction because, from the calculations of the initial conditions, the amount of inert does not change with OH^-. Sodium hydroxide only replaces an equal amount of water in the solution, thus keeping the concentrations and ratios of the reactants constant to yield exactly the same mean diameter.

Recent experimental data [10], [13] indicate that the precursor takes two paths: the reduction to form the nuclei and the passivation by OH^-. After nucleation, the nuclei aggregate to bigger sizes forming seeds. Afterwards, the passive form of the precursor reacts to produce gold atoms that grow the particles. As the concentration of OH^- increases, less amount of the precursor reduces, forming fewer nuclei that aggregate to smaller sizes. Although the passive form still grows the seeds, the final particle size results to be smaller.

TABLE II
THE EFFECTS OF PH ON THE MEAN DIAMETER USING THE DATA BY LI ET AL.
[14]

Concentration of NaOH (mol/m^3)	Li et al.	Model prediction (nm)
3.1	19.3	12.0
4.4	15.6	12.0
5.3	11.9	12.0
6.6	11.8	12.0

IV. CONCLUSIONS

In this work, we report investigations of the Turkevich organizer theory, whose mathematical model was developed by Kumar et al. [7]. We solved this model in Parsival and compared the results to those of Kumar et al. [7]. Further, we tested the model for the effects of temperature of synthesis, and pH of the mixture. We found that the model is accurately solved in Parsival. However, the model predictions do not agree with the experimental data considered. The model by Kumar et al. [7] cannot explain the effects of temperature and pH on the Turkevich synthesis.

Future work will focus on modelling the seed mediated mechanism proposed by Wuithschick et al. [13]. Although the mechanism is more complicated than the Turkevich organizer

theory, it should provide a more accurate description of the synthesis.

REFERENCES

[1] Liveri, V. T., Controlled Synthesis of Nanoparticles in Microheterogeneous Systems, Nanostructure Science and Technology, Springer Science, 2006.

[2] Tamar Dreifuss, Oshra Betzer, Malka Shilo, Aron Popovtzer, Menachem Motieia and Rachela Popovtzer A challenge for theranostics: is the optimal particle for therapy also optimal for diagnostics? Nanoscale, 2015, 7, 15175.

[3] Turkevich, J.; Stevenson, P.; Hillier, J. A Study of the Nucleation and Growth Process in the Synthesis of Colloidal Gold. *Discuss. Faraday Soc*. 1951, *11*, 55.

[4] Frens, G. Controlled Nucleation for the Regulation of the Particle Size in Monodisperse Gold Suspensions. *Nature* 1973, *241*, 20.

[5] Freund, P.; Spiro, M. Colloidal Catalysis: The Effect of Sol Sizeand concentration. *J. Phys. Chem.* 1985, *89*, 1074.

[6] Chow, M.; Zukoski, C. Gold Sol Formation Mechanisms: Role of Colloidal Stability. *J. Colloid Interface Sci.* 1994, *165*, 97.

[7] Kumar, S.; Kumar, R.; Gandhi, K. S. Modeling of Formation of Gold Nanoparticles by Citrate Method. *Ind. Eng. Chem. Res.* 2007, *46,* 3128-313.

[8] Ji, X. H.; Song, X. N.; Li, J.; Bai, Y. B.; Yang, W. S.; Peng, X. G. *J. Am. Chem. Soc.* 2007, *129*, 13939.

[9] Polte, J.; Erler, R.; Thü nemann, A. F.; Sokolov, S.; Ahner, T. T.; Rademann, K.; Emmerling, F.; Kraehnert, R. Nucleation and Growth of Gold Nanoparticles Studied via in situ Small Angle X-ray Scattering at Millisecond Time Resolution. ACS Nano 2010, 4, 1076−1082.

[10] Kettemann, F.; Birnbaum, A.; Witte, S.; Wuithschick, M.; Pinna, N.; Kraehnert, R.; Rademann, K.; Polte, J. Chem. Mater. 2016, 28 (11), 4072-4081.

[11] Wulkow, M., Gerstlauer, A., Nieken, U., 2001. Modeling and simulation of crystallization processes using parsival. Chem. Eng. Sci. 56, 2575–2588. http://dx.doi.org/10.1016/S0009-2509(00)00432-2.

[12] Takiyama, K. Formation and Aging of Precipitates. VIII. Formation of Monodisperse Particles (1) Gold Sol Particles by Sodium Citrate Method. Bull. Chem. Soc. Jpn. 1958, 31, 944–950.

[13] M. Wuithschick, S. Witte, F. Kettemann, K. Rademann, J. Polte *Phys. Chem. Chem. Phys.* 2015, *17*, 19895-19900.

[14] Chunfang Li, Dongxiang Li, Ganggiang Wan, Jie Xu and Wanguo Hou, "Facile synthesis of concentrated gold nanoparticles with low size-distribution in water: temperature and pH control", Nanoscale Research Letters, vol. 6, p.440, 2011.

[15] Ojea-Jiménez, I.; Campanera, J. M. Molecular Modeling of the Reduction mechanism in the Citrate-Mediated Synthesis of Gold Nanoparticles. J. Phys. Chem. C 2012, 116, 23682–23691.

[16] Wiig, E. O. *J. Phys. Chem.* 1928, *32*, 961.

[17] Wei Wang , Ning Li , and Stan Speaker External Factors Affecting Protein Aggregation, Hoboken, NJ, USA: John Wiley & Sons, Inc. 2010.

Emmanuel Agunloye received his BSc in Chemical Engineering from the University of Lagos in 2009. Became interested in studying the applications of computational fluid dynamics (CFD) to chemical engineering processes during his work experience at Richardson Oil and Gas Limited, Nigeria in 2011 and was stimulated to pursue postgraduate programmes. After completing his MSc in Chemical Process Engineering at UCL in 2014, he joined the department in 2015 as a research student.

Asterios Gavriilidis obtained a Diploma from the University of Thessaloniki, Greece in 1988, and an MSc in 1990 and PhD in 1993 from the University of Notre Dame, USA, all in Chemical Engineering. He joined the Department of Chemical Engineering at University College London in 1993, where he has been professor of Chemical Reaction Engineering since 2004. He is subject editor of chemical reaction engineering for Chemical Engineering Research and Design, Fellow of the IChemE, Chartered Engineer, and UK representative in the Working Party of Chemical Reaction Engineering of the European Federation of Chemical Engineers (EFChE). He is serving in the Scientific Committee of the IMRET (International Conference on Microreaction Technology) series of conferences as well as other international conferences in the fields of chemical reaction engineering and process intensification.He is a member of the Steering Group of the Dial-a-Molecule network and he is co-I and Steering Group member of the UK Catalysis Hub.

Luca Mazzei graduated in Chemical Engineering from the University of Naples "Federico II" in 2001. Then, he spent three years working for Technip KTI as a process and start-up engineer on sulphur recovery and refinery tail gas treatment. Subsequently, he joined the Department of Chemical Engineering at UCL first as a student, where he was awarded a Ph.D. in 2008, and then as a Lecturer, in 2009. He is a Chartered Member of the Institution of Chemical Engineers (IChemE) and Chartered Scientist.