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# Performance of novel high throughput multi electrospray systems for forming of polymeric micro/nanoparticles

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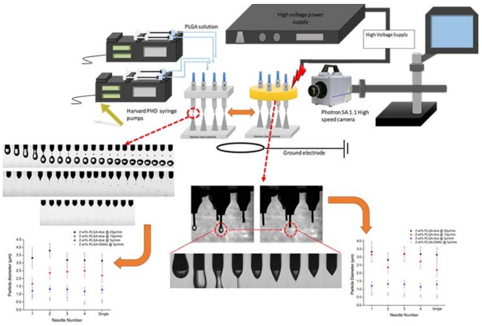
## ABSTRACT

In order to maintain a stable cone-jet mode in electrospray low flow rates are used while most applications require a high throughput. We compare two different designs of the multiple electrospray system in order to increase the output for large scale production applications. In this study, the solution was fed through four separate needles that were attached to either a circular or a rectangular metallic plate that were connected to a high voltage DC power supply. The behaviour of the electrospray jets as well as the deposition of particles were investigated. It was shown that the throughput of particles was increased while particles with narrow size distribution were produced from all four uniform electrospray jets.

## GRAPHICAL ABSTRACT



Multi Electrospray Systems for the Production of Polymeric Carries

## 1. Introduction

Particles generated via electrospraying have many applications in several technological and scientific processes [1,2]. Following the pioneering work by Zeleny [3], needles or tips are being used as an important part of the electrospray experimental setups for production of particles. In order to produce particles of micrometre and submicrometre dimension via electrospray, very low flow rates and high values of the electrical conductivity of the liquid sample are often required [4]. This causes severe limitations to the use of a single electrospray emitter in industrial applications [5]. A solution to this problem is to increase the number of emitters.

Multiplexed electrospray setups have been primarily investigated by several researches in order to increase the throughput for the purpose of

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large scale production [6]. Various configurations for electrospray deposition have been proposed [7,8], while the nozzle-substrate system was mostly used in both experimental and numerical studies [9]. Multiple-electrospraying using microchannels was also investigated owing to the development of microfabrication techniques [10]. The limitations of these designs are however multiple. The advantages of using separate needles that are fed through parallel tubing compared to nozzles or channels are mostly that they are easier and cheaper to manufacture [11]. This technology enables cheap mass production in many industrial scale applications. Multiplexing involves the presence of a reservoir from which each emitter is fed. One of the issues related to multi nozzle electrospraying is the equal distribution of liquid in all nozzles [12].

In multi needle systems, increasing the quantity of needles lead to having a high number of stable cone-jet mode electrosprays per unit area. This causes the space charge to increase significantly due to the cloud of charged droplets [8]. As a result, shielding of the electric field occurs near the surface of some conical menisci which can lose their conical shape. Depending on the geometry of the multi spray system, this phenomena usually affects the needles located in the central region of the atomizer [13]. One of the most difficult issues associated with the multi-needle system is that the adjacent jets repel each other and as a result the electric field on the tip of each needle at different positions is not uniform [14]. This causes instability and in some cases dripping or non-working needles during the electrospraying process occur. In order to have uniform particle size, it is important to ensure that all the emitters or needles operate in a steady cone-jet mode [15]. One of the primary goals of particle synthesis, is the ability to produce monodisperse particles at flow rates sufficient for various applications. Regardless of the application, from drug delivery [16], to the synthesis of nanoparticles for other non-biomedical applications [17], superconductors [18], quantum dots [19] and thin films, it is crucial that the processing method can be tailored to suit the criteria. For instance, in controlled drug release application, the size and composition of particles has a dramatic impact on the release profile of the drug [16]. The processes involved in drug release from biodegradable polymeric matrices are complex and not only the size of the particles but also other factors such as drug solubility and its diffusion coefficient in the polymer matrix can contribute to the process. The difference in the surface/volume ratio of the polymeric microspheres with different size due to differences in the rates of solvent extraction between smaller and larger emulsion droplets during preparation have an impact on the drug loading of these particles [20].

One of the key issues of commercializing the multi electrospraying technology is to design a setup that reduces the interference between the neighboring needles and disruption of the stable cone jet at each needle. In addition, a suitable design should control the spraying jets travelling towards the collector simultaneously, ensuring homogeneous deposition of particles. Recently, there has been an intense amount of interest in the design and investigation of multi needle systems for production of particles and fibres. Xie et al. [21] studied the effect of electric field on the multi needle electrospinning technique. They proposed spinnerets with two kinds of needle array, linear three-needle and triangular three-needle. They produced finer and more uniform nanofibers using an auxiliary plate. Zhang et al. [22] proposed multi pore electrospraying for high throughput production of biodegradable microparticles using a flute-like multi-pore emitter device. Almeria and co workers [1] produced PLGA particles using a multiplex electrospray system. They used multiplexed arrays consisting of multiple electrospray nozzles operating in parallel to encapsulate amphiphilic agents such as doxorubicin, Rhodamine B and Rhodamine B octadecyl ester perchlorate.

The present study focuses on the design of a multi needle system that can provide electrospray in the cone-jet mode. The aim is to propose a device that can produce monodisperse droplets/particles over a wide size range, from a few hundred nanometers to tens of micrometers. The ultimate purpose of the new multi-spray design is to overcome the main drawback of nanoparticle fabrication: low throughput. Experiments were performed to demonstrate the robust multi-needle electrospraying designs, as well as a comparison study on the particle size, production rate and spray/deposition pattern from each geometry with respect to the single electrospraying setup.

**Table 1**
Physical characteristics of the solutions used to prepare particles.

| | Viscosity (mPa s) | Surface tension (mN/m) | Electrical conductivity (mS/m) |
|---|---|---|---|
| 2 wt% PLGA-Acetone | 1.02 | 25 | 0.36 |
| 2 wt% PLGA-DMAc | 1.62 | 27 | 0.37 |
| Acetone | 0.36 | 23 | 0.02 |
| DMAc | 0.98 | 25 | 0.14 |

## 2. Materials and methods

### 2.1. Materials

PLGA (copolymer 50:50, Resomer RG503H, molecular weight of 33,000 Da, inherent viscosity 0.41 dl g$^{-1}$) was purchased from Boehringer Ingelheim (Ingelheim, Germany). Dimethylacetamide (DMAc) was obtained from Sigma Aldrich (Poole, UK). PLGA solutions (2 wt%) were prepared by dissolving the polymer in DMAc or Acetone and mechanically stirring for 400 s.

### 2.2. Characterization of solutions

The viscosity, surface tension, density and electrical conductivity of all the prepared solutions were measured. Density was measured using a standard density bottle DIN ISO 3507- Gay-Lussac. Viscosity measurements were conducted using a U-tube viscometer (size E, VWR, UK). Prior to measurements the viscometer was calibrated and checked with ethanol to remove any residue. A Kruss tensiometer (Model DSA100, Kruss GmbH, Hamburg, Germany) was used to measure the surface tension using the Wilhelmy's plate method. Electrical conductivity of each solution prepared was estimated using a conductivity probe (Jenway 3540 pH/conductivity meter). All the measurements, presented in Table 1, were conducted at the ambient temperature (21 °C) and relative humidity of 40–50% after calibrating the equipment with distilled water.

### 2.3. Experimental setup

Fig. 1 shows the experimental setups for the four-nozzle electrospray deposition process with the nozzle-substrate configuration used in this work. Two different configurations were considered. The first geometry consisted of nozzles that were arranged in a linear array and were mounted on a rectangular plate. The second nozzle array geometry composed of four electrospraying nozzles with capillary spacing set at 5 mm between centers of adjacent capillaries that were mounted on a circular plate. The needle distribution is shown in Fig. 1a and b for the circular and rectangular plate configurations, respectively. The four needle positions are labeled as 1, 2, 3 and 4. The nozzles were stainless steel capillaries (Bignell Surgical, USA) with outer and inner diameters of 0.8 and 0.5 mm, respectively. The liquid was fed through 4 separate chemically resistant Tygon tubing that were attached to two double pumps. The solutions were infused via two double syringe pumps (PHD 4400, Harvard Apparatus Limited, Edenbridge, UK) at constant flow rates of 2 to 20 μl/min. A positive voltage of up to 20 kV was applied to the nozzles with a positive-polarity high-voltage DC power supply. A high precision voltage generator (Glassman Europe