Perspective

Biofpr
Biofuels Bioproducts & Biorefining

Emerging green routes to nanocellulose

Rosaria Ciriminna, Istituto per lo Studio dei Materiali Nanostrutturati, CNR, Palermo, Italy
Mina Ghahremani, **Babak Karimi**, Faculty of Chemistry, Institute for Advanced Studies in Basic Sciences, Zanjan, Iran
Mario Pagliaro, Istituto per lo Studio dei Materiali Nanostrutturati, CNR, Palermo, Italy

Received May 09 2022; Revised August 02 2022; Accepted August 03 2022;
View online September 13, 2022 at Wiley Online Library (wileyonlinelibrary.com);
DOI: 10.1002/bbb.2423; *Biofuels, Bioprod. Bioref*. 17:10–17 (2023)

Abstract: Nanocellulose is an exceptional biomaterial whose industrial applications in widely different sectors and technologies so far have been limited by the high cost of its multi-step extraction routes. Extraction methods of cellulose nanocrystals or nanofibers, indeed, generally involve the energy-intensive mechanical treatment of wood pulp, treatment with concentrated H_2SO_4 to obtain cellulose nanocrystals or chemical oxidation followed by mechanical fibrillation of the partly oxidized fibers. In the last decade (2011–2021) a number of green routes to cellulose nanofibers and nanocrystals have been developed. This study provides a critical outlook of said emerging new green routes to this versatile and safe bionanomaterial that, once sustainably produced, preferably from low cost cellulosic biowaste, will become ubiquitous in a number of different industrial products. © 2022 The Authors. *Biofuels, Bioproducts and Biorefining* published by Society of Chemical Industry and John Wiley & Sons, Ltd.

Key words: nanocellulose; microfibrillated cellulose; cellulose nanocrystal; bacterial nanocellulose; green extraction; cellulose nanofiber

Introduction

First isolated in 1977 in the form of a translucent hydrogel at a USA-based paper and pulp company by repeated treatment of a 3% slurry of chopped wood pulp fibers with a high-pressure milk homogenizer, the new biomaterial later called nanocellulose was termed 'microfibrillated cellulose' (MFC).[1] 'At the high temperature the high forces (pressure/cavitation/shear/impact) of the homogenizer acting in tandem or sequentially' wrote Turbak in 2015 'had broken down the cell walls of the microfibers and liberated the desired nanofibrils.'[2]

Nanocellulose, namely cellulose fibrils with widths in the nanometer range,[3] was born. Explicitly mentioning its 'uses and commercial potential' in early research reports,[1] chemists understood that the material had numerous potential applications.

In the subsequent four decades, scientists from across the world discovered the exceptional mechanical, optical, chemical, biological and thermal properties of the new bionanomaterial.[3,4] Coupled to full recyclability, biodegradability and lack of toxicity, said properties make nanocellulose and nanocellulose-based composites suitable for application in a vast array of industrial fields. Composites, indeed, are easily obtained through the straightforward combination of highly hydrophilic nanocellulose with inorganic and organic substances.[5]

Numerous excellent books[6–8] describe the structure and the preparation routes of different nanocelluloses, with recent monographs devoted to specific applications

Correspondence to: Mario Pagliaro, Istituto per lo Studio dei Materiali Nanostrutturati, CNR, via U. La Malfa 153, 90146 Palermo, Italy. E-mail: mario.pagliaro@cnr.it

SCI where science meets business

of nanocellulose for instance in electronics[9] or in water treatment.[10]

From nanocellulose-based aerogels,[11] through energy storage systems,[12] applications in biomedicine,[13] environmental remediation,[14] and catalysis,[15] numerous review articles on nanocellulose uses have been published. Hence, rather than adding a new review in a rapidly evolving research field, this study provides a critical outlook on the emerging green production routes of this 'ageless bionanomaterial'.[4]

To put the discussion in context, we first briefly discuss the current production routes, some of which have been commercialized, from an economic viewpoint. We then present the main emerging green chemistry production methods. The study concludes by suggesting new avenues to tackle environmental issues using nanocelluloses sourced from cellulosic biowaste[16] based on these new environmentally friendly production routes.

Current production routes

Nanocellulose is generally sourced from wood pulp as cellulose nanofiber (CNF) or cellulose nanocrystal (CNC). In addition, highly pure (and expensive) bacterial nanocellulose is industrially synthesized on small scale from glucose using *Gluconoacetobacter xylinus* bacteria. 'The way to produce bacterial nanocellulose today', however, 'is expensive and the methods are inefficient'.[17]

A recent review describes the main nanocellulose production routes.[18] In general, harsh chemical conditions and large amounts of energy and harmful chemical compounds are required, with the undesired production of large effluent amounts. This has intrinsically limited the large-scale production of nanocellulose.

Nanocellulose fibrils are extracted from wood pulp obtained *via* pulping and bleaching either *via* acid hydrolysis with sulfuric acid (further adding wastewater to the process), enzymatically (requiring long extraction times and with relatively low efficiency) or mechanically *via* high-pressure homogenization.[19] Steam explosion or ultrasonication, with high-energy consumption, are also suitable.[20]

Hydrolysis with aqueous H_2SO_4 affords nanocellulose in nanocrystal form. Comprising cellulose I only, CNC has a low length/diameter 'aspect' ratio (10–100), and a tensile strength similar to that of aramid-fibers (10 GPa). Its industrial production has an estimated production cost ranging from \$3632 t^{-1} to \$4420 t^{-1}, with feedstock cost and capital investment being the major cost drivers.[21] Remarkably, in the same year of these estimates (2017) for large scale production, CNC was reported to be actually sold at \$1000/kg.[22]

Chiefly manufactured using TEMPO-mediated oxidation of wood cellulose followed by mechanical dispersion of the oxidized fibers, CNF has a higher length/diameter ratio (100–150). Its structure includes both amorphous cellulose and crystalline cellulose I. The 2,2,6,6-tetramethylpiperidine-1-oxyl radical (TEMPO) used for the selective oxidation of primary alcohol groups in polysaccharides (aqueous NaOCl as primary oxidant in the presence of a catalytic amount of bromide at pH 9–10)[23] partly oxidizes the primary alcohol groups of water-insoluble cellulose to carboxylate groups.[24]

It is enough to mechanically grind or sonicate the TEMPO-oxidized cellulose to liberate the oxidized cellulose fibers into a homogeneous, highly viscous suspension of 3–5 nm cellulose nanofibrils.[24] The electrostatic repulsion between the cellulose fibrils bearing the COO^- groups ensures good dispersion and high stability of the nanofibrils in solution. Repulsion among the carboxylated fibers, furthermore, causes a decrease in the electricity consumed to power the mechanical fibrillation process.

Since 2017, the process has been used by a large paper company in Japan to manufacture CNF in the form of dispersed nanofibers with uniform fiber widths of 3–4 nm.[25] The company starts from bleached wood pulp at two different paper mills, and supplies the 'Cellenpia' product series to different industrial customers producing CNF-reinforced tires, paper barrier cups for beverages, and personal care, hygiene and cosmetic products.[25] In 2019, the same company successfully developed a CNF-reinforced composite subsequently used to produce a car whose weight was about 10% lower than that of a conventional car made from steel.[26]

Currently CNF is sold at a cost of \$90–100/kg.[27] This high cost is due to the high cost of TEMPO and to the cost of processing the spent hypochlorite dilute solution containing the genotoxic TEMPO catalyst (as well as corrosive NaBr).[28] Separating nitroxyl radicals in solution is a multi-step, expensive process,[29] whereas the TEMPO concentration in any material suitable for biomedical use must be lower than the threshold of toxicological concern (i.e. 4 ppm).[30]

Emerging green routes

Reviewing research published between 2015 and 2020 concerning new CNF/CNC preparation routes, Li and co-workers identified 69 studies.[18] All new processes included two or three pretreatment steps, followed by chemical and mechanical treatment. Amid the mechanical treatment processes, ultrasonication was found to be dominant.

Another recent comprehensive review on new extraction methods from cellulosic biowaste reported that sugarcane bagasse with its high lignocellulose content, loose structure and algae residues are the biowaste most suited to the extraction of nanocellulose.[31]

Poor in lignin and available in huge yearly amounts, citrus processing waste (CPW) obtained from the citrus juice industry is another ideal cellulose feedstock. The annual production of citrus fruits exceeds 120 million tons. More than half of the fruit is non-edible and discarded as waste. The global volume of citrus fruits yearly squeezed at citrus juice plants alone exceeds 31 million tonnes, 50–60% of which is waste.[32]

Unfortunately, the routes to citrus nanocellulose starting from CPW based on enzymatic,[33] microwave-assisted hydrothermal treatment[34] and acid hydrolysis,[35] all present significant technical limitations. For example, the nanocellulose fibrils obtained *via* multi-step microwave-assisted extraction of dried depectinated orange peel are deeply colored brown.[34] This is due to both caramelized sugars and the Maillard reaction between sugars and residual proteins at the high temperatures (120–180°C) required for extraction.[34]

One entirely green route to nanocellulose in CNC form was reported by Huang and co-workers in 2018.[36] The team used ball milling of cellulose in water only, followed by centrifugation. The process quickly affords cellulose disintegration down to elementary fibrils 3–10 nm wide and 120–400 nm long.

To understand the relevance of this discovery, it is instructive to compare it with enzymatic hydrolysis with cellulase enzymes. Applied to eucalyptus cellulose pulp using a new commercial enzymatic complex at a cellulose loading of 10% (w/v) and an enzyme loading of 10 mg g^{-1},[37] or even relying on a cellulolytic enzymatic complex produced on-site by *Aspergillus niger* followed by sonication,[38] the optimal enzymatic process affords a 24.6% yield of CNC (after 96 h of enzymatic hydrolysis of cellulose pulp, followed by 5 min of sonication).

As mentioned above, the TEMPO-mediated carboxylation of cellulose and the production of nanocellulose have already been commercialized.[25] Numerous practically relevant discoveries using heterogenized TEMPO catalysts showed evidence, on a laboratory scale, of how shifting the CNF production process from using TEMPO in solution to new-generation heterogeneous TEMPO catalysts has substantial benefits in terms of enhanced quality of the resulting CNF and reduced environmental impact.[39]

Interestingly, Turbak recognized that cavitation was among the 'high forces of the homogenizer'[2] responsible for cellulose fibrillation using the high-pressure homogenizer. More than 40 years after Turbak and co-workers' discovery,[1] in 2010 Pandit and Pinjari were the first to report the outcomes of acoustic cavitation (AC) and hydrodynamic cavitation (HC) applied to a 1% w/v (0.5 kg in 50 L water) aqueous suspension of 63 μm cellulose microparticles.[40]

The team called 'declumping' the fibrillation of the bulk cellulose diven by by both AC and HC (Fig. 1). Indeed, ultrasonically processed cellulose was completely fibrillated into individually separated fibrils less than 100 nm thick owing to the more intense cavitational collapse and absence of fluid flow of AC, whereas HC resulted in full cellulose fiber–fiber detachment, with some fibers at the nano level and most of the fibers of micrometer thickness.

Both forms of cavitation reduced cellulose crystallinity from 87% to 38%. Such a dominant presence of amorphous domains enhances the flexibility and plasticity of the material, and lowers both stiffness and elasticity.[18] The particle size decreased from 63 μm to 1.36 and 0.3 μm for the hydrodynamically and ultrasonically processed cellulose samples, respectively. Owing to decrystallization, the thermal stability of the newly obtained nanocelluloses was significantly higher.

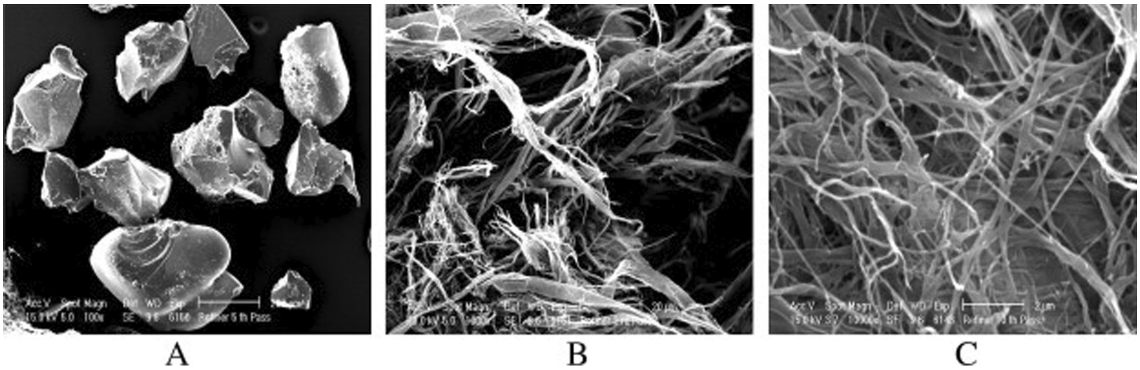


Figure 1. SEM images of (a) initial sample at 100×, (b) hydrodynamically processes sample at 5000×, and (c) ultrasonically processes sample at 10000×. [reproduced from Ref.40, creative commons attribution (CC BY) license].

We briefly remind that the cavitation bubbles generated in water *via* AC or HC upon collapse locally release short-lived (μs duration) shockwaves of extreme pressures (1000–2000 atm) and temperatures (5000 K) that are ideally suited for the extraction of natural products.[41]

Two years later, Paquin and co-workers in Quebec reported that by carrying out the TEMPO-mediated oxidation of a diluted suspension (1 wt%) of bleached hardwood kraft pulp in a 45 L flow-through sonoreactor, a 87.5% decrease in energy consumption (in comparison with the process in batch reactor) and a 95% higher production rate of oxidized fibers (compared with the reaction without any ultrasound in batch mode) could be achieved.[42] These results, the team concluded, suggest the possibility of scaling up the process on an industrial scale directly in continuous mode.[42]

The original discovery of Pandit and Pinjari using no added chemicals to fibrillate crystalline cellulose, however, remained without further investigation until the teams of Meneguzzo and Pagliaro demonstrated the process on a semi-industrial scale by processing *via* HC more than 30 kg of citrus (lemon and grapefruit) processing waste in 120 L of water.[43]

The team dubbed 'CytroCell' the new micronized cellulose. Both new CytroCell materials consist of cellulose of low crystallinity index (0.33 for lemon and 0.36 for grapefruit). Lemon 'CytroCell' consists of 0.5–3 μm long microfibrils whose section varies between about 110 and 420 nm. Grapefruit CytroCell comprises ramified microfibrils whose diameter varies from 500 nm to 1 μm (Fig. 2).[44]

The one-pot process requires no subsequent mechanical treatment of the fibrillated nanofibers. In brief, the highly efficient HC creates cavitation bubbles which fibrillate and promote decrystallization of the citrus peel microcrystalline cellulose fibers. The effect is intensified by the presence of the residual citric acid that is relatively abundant in the wet CPW used as a cellulose source, such as in the case of AC applied to microcystalline cellulose in the presence of 0.2 mol L^{-1} citric acid.[45]

Outlook and perspectives

Comparing four routes to wood pulp-derived nanocellulose (TEMPO-oxidation followed by sonication or homogenization and chloroacetic etherification followed by sonication or homogenization), Renneckar and co-workers recently found that TEMPO oxidation followed by homogenization is the lowest-impact nanocellulose process.[46] For comparison, the energy and environmental impact factors for nanocellulose industrial production using the latter optimal route are, respectively, 4 and 20 times larger than the kraft pulp production.

Whether using concentrated H_2SO_4 to hydrolyze the amorphous regions of cellulose and isolate CNC[21] or relying on the TEMPO-catalyzed process with bleach as the primary oxidant and bromide as the co-catalyst followed by mechanical treatment to afford CNF,[24,25] current nanocellulose production methods are capital intensive and have high operating costs. In the case of CNC, feedstock cost and capital investment are the major cost drivers, with sulfuric acid and lime consumption alone accounting for 25% of production costs for the lowest plant configuration (without acid recovery).[21]

In the case of CNF, high manufacturing costs are due to the large amount of electrical energy required for homogenization, followed by the high cost of the TEMPO catalyst.[47] Furthermore, a large amount of solvent is needed to separate the CNF from genotoxic TEMPO, while the expensive TEMPO catalyst is lost in the reaction effluents. The method to recover the TEMPO catalyst in a mixture of a water-miscible organic solvent and water[29] could not be

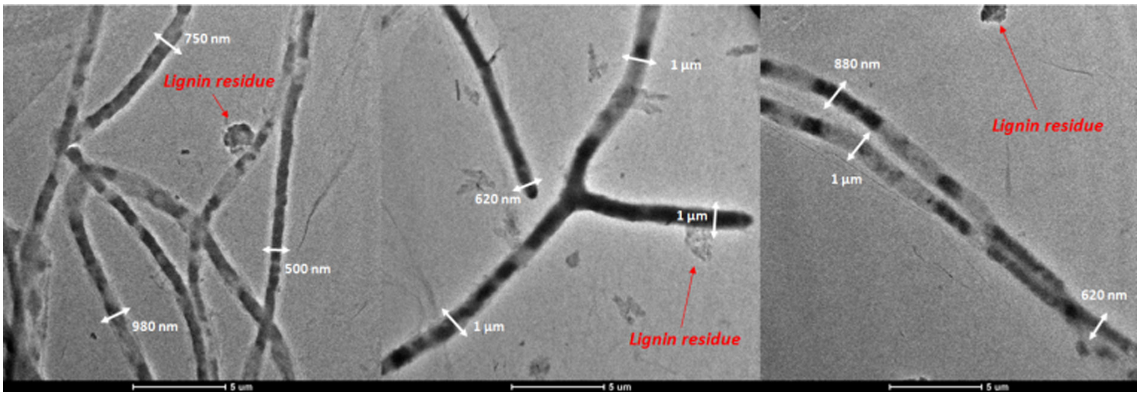


Figure 2. TEM images of grapefruit CytroCell focusing on selected single fibrils. [Reproduced from Ref.43, under a creative commons attribution (CC BY) license.]

industrialized in the cellulose oxidation process carried out in water only owing to the high cost.[48]

It is perhaps not surprising to find that the first large nanocellulose production plants are operated by paper and pulp companies.[25] Paper companies indeed are facing a dramatic fall in paper demand following the advent of the internet and other digital technologies.[49] Beyond the aforementioned paper and pulp company producing CNF at two production sites in Japan,[25] another paper and pulp company based in Norway has since late 2016 produced MFC at a production site with a 1000 t a^{-1} capacity. The ingredient is shipped to different industrial customers as a 2 or 10% aqueous formulation.[50]

Comparing CNC chiefly extracted from different producers *via* hydrolysis with concentrated H_2SO_4 and purified according to different procedures, Cranston and Reid lately found that all products share the same basic chemical structure and physicochemical properties of laboratory-made CNC.[51]

Still, both main nanocellulose production methods need to be made less energy and capital intensive. Beyond enzymatic extraction,[38] three methods are ready for optimization, scale up and commercialization: the heterogeneously catalyzed oxidation over new-generation solid TEMPO catalysts[39] (including magnetically recoverable Karimi's nanocatalyst),[52] ball-milling in the presence of water of cellulose[36] and (for applications of nanocellulose of low crystallinity) AC and HC.[40,42,43] All are promising considering that many of the aforementioned catalysts are now commercial (Karimi's nanocatalyst in the form of 50 nm beads easily recovered with a magnet),[53] whereas the safe and robust HC process for the extraction of natural products such as waste orange peel is easily scaled up.[54]

Enzymatic extraction, too, is an eminently clean nanocellulose production process.[37,38] Dr Farinas in Brazil is one of the leading scholars in the field. Asked whether companies are using enzymatic extraction, she noted that:

> *The use of enzymes to obtain nanocellulose is very challenging, but I believe it is a very promising alternative route. I believe that there are few companies using enzymes to obtain nanocellulose, but mostly to facilitate the production of nanofibrillated cellulose, as far as I know. One of them is VTT, using the HefCel concept in which enzymes facilitate the mechanical process.*[55]

'HefCel' stands for 'high-consistency enzymatic fibrillation technology', a process developed at VTT Technical Research Centre of Finland, in which cellulose fibrils are produced at high consistency (20–40%) by stirring concentrated cellulose pulp (20–40%) in the presence of a tailored cellulase enzyme mixture.[56] The process results in a 90% yield of fibrillated cellulose, while the low water content lowers the cost of drying.

Although not providing a timeline, market projections dating back to 2014 estimated a potential volume of nanocellulose exceeding 6.4 million t a^{-1} only in the USA (5.9 million t a^{-1} only in the high-volume category and 0.48 t a^{-1} in the low-volume category).[57] Four years later, however, the nanocellulose market had not reached 40 000 t (39,600 t), with the large majority being produced at pulp mills in form of MFC used in their own paper and paperboard products.[58]

In 2020, the nanocellulose market value amounted to about \$300 million globally, with dried bacterial nanocellulose selling at \$50 g^{-1},[59] and the world's largest nanocellulose production plant having a capacity of 2.5 t per day.[58]

It is instructive to learn that, besides the use of MFC in paper and paperboard products, the main uses of nanocellulose currently concern low-volume and high-value applications of CNF. For example, in Japan, the world's leading CNF manufacturing country, products using CNF include biodegradable cutlery of enhanced strength; foam materials for the midsole of sport shoes; a CNF-coated diaphragm for speakers and television sets; coating agents to prevent concrete adhesion; and undercoat paint preventing discoloration of the base material and cracks in the paint film.[60]

For nanocellulose-enabled technologies[5–10] to find practical utilization and large industrial uptake, there is a need for green production technologies through which scaled-up production lowers production costs and makes nanocellulose available to industrial customers at affordable price. This, *inter alia*, requires a switch from expensive wood pulp (priced at \$907 t^{-1} as of April 2021)[61] to low-cost and abundant biowaste as cellulose source.

Poor in lignin, and available at over 31 million t a^{-1}, citrus biowaste (whose other main component, pectin, has been in high and increasing demand for more than a decade)[62] is an ideal nanocellulose source in an integrated citrus biorefinery.[63]

As put it by Jessop and Reyes, in scientific publications that use the 'green chemistry' terminology, 'there is an inversely proportional relationship between the number of papers published in an area and its associated environmental impact'.[64] This is true also for nanocellulose production where the raw material originates from agrifood and forestal (paper and pulp, citrus, sugarcane, etc.) companies which are slowly, but inevitably, transforming into bioeconomy firms.[25,50]

Although originating from apparently distant areas such as heterogeneous catalysis, enzymatic catalysis and AC or HC, the new green chemistry technologies to manufacture nanocellulose are ready to be scaled up and, if found to be technically and economically viable, taken up by industry. To accelerate this progress, the new bioeconomy industry needs young researchers and young managers with an updated critical knowledge of the field, including new green chemistry technologies.[65]

This study offers such critical outlook *en route* to mass uptake of this versatile, robust and safe bionanomaterial that will be sustainably sourced using the said technologies from low-cost cellulosic biowaste.

Acknowledgements

This study is dedicated to the memory of Professor Franco Piozzi (1928–2022), for nearly 40 years eminent Professor of organic chemistry at the University of Palermo. We thank Dr Cristiane Sanchez Farinas, Empresa Brasileira de Pesquisa Agropecuária (Embrapa), Brazil, for helpful correspondence. Open Access Funding provided by Consiglio Nazionale delle Ricerche within the CRUI-CARE Agreement.

Conflict of interest

The authors declare no conflict of interest.

References

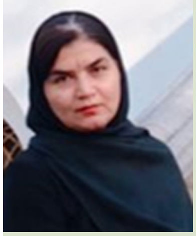
1. Turbak AF, Snyder FW and Sandberg KR, Microfibrillated cellulose, a new cellulose product: properties, uses, and commercial potential, in *Proceedings of the Ninth Cellulose Conference, Applied Polymer Symposia, 37*, ed. by Sarko A. Wiley, New York, pp. 815–827 (1983).
2. A.F. Turbak, Birth of nanocellulose, Tappi Over the Wire, 2015. www.naylornetwork.com/PPI-OTW/articles/?aid=150993&issueID=22333 (accessed August 2, 2022).
3. Klemm D, Kramer F, Moritz S, Lindström T, Ankerfors M, Gray D *et al*., Nanocelluloses: a new family of nature-based materials. *Angew Chem Int Ed* **50**:5438–5466 (2011). https://doi.org/10.1002/anie.201001273.
4. Dufresne A, Nanocellulose: a new ageless bionanomaterial. *Mater Today* **16**:220–227 (2012). https://doi.org/10.1016/j.mattod.2013.06.004.
5. Kargarzadeh H, Ahmad I, Thomas S and Dufresne A eds, *Handbook of Nanocellulose and Cellulose Nanocomposites, volumes 1 and 2*. Wiley-VCH, Weinheim (2017).
6. Dufresne A, *Nanocellulose*. De Gruyter, Berlin (2013).
7. Huang J, Dufresne A and Lin N eds, *Nanocellulose*. Wiley-VCH, Weinheim (2019).
8. Lee K-Y ed, *Nanocellulose and Sustainability*. CRC Press, Boca Raton, FL (2020).
9. Thomas S and Beeran Pottathara Y eds, *Nanocellulose Based Composites for Electronics*. Elsevier, Cambridge, MA (2020).
10. Kumar D ed, *Nanocellulose and its Composites for Water Treatment Applications*. Routledge, London (2021).
11. Ahankari S, Paliwal P, Subhedar A and Kargarzadeh H, Recent developments in nanocellulose-based aerogels in thermal applications: a review. *ACS Nano* **15**:3849–3874 (2021). https://doi.org/10.1021/acsnano.0c09678.
12. Kim J-H, Lee D, Lee Y-H, Chen W and Lee S-Y, Nanocellulose for energy storage systems: beyond the limits of synthetic materials. *Adv Mater* **31**:1804826 (2019). https://doi.org/10.1002/adma.201804826.
13. Lin N and Dufresne A, Nanocellulose in biomedicine: current status and future prospect. *Eur Polym J* **59**:302–325 (2014). https://doi.org/10.1016/j.eurpolymj.2014.07.025.
14. Shak KPY, Pang YL and Mah SK, Nanocellulose: recent advances and its prospects in environmental remediation. *Beilstein J Nanotechnol* **9**:2479–2498 (2018). https://doi.org/10.3762/bjnano.9.232.
15. Kaushik M and Moores A, Review: nanocelluloses as versatile supports for metal nanoparticles and their applications in catalysis. *Green Chem* **18**:622–637 (2016). https://doi.org/10.1039/c5gc02500a.
16. García A, Gandini A, Labidi J, Belgacem N and Bras J, Industrial and crop wastes: a new source for nanocellulose biorefinery. *Ind Crops Prod* **93**:26–38 (2016). https://doi.org/10.1016/j.indcrop.2016.06.004.
17. B. Alriksson, cit. in: S. Matthis, Bacterial nanocellulose can become a strength enhancer, pulpapernews.com*, 2 May 2018*. www.pulpapernews.com/20190803/9456/bacterial-nanocellulose-can-become-strength-enhancer (accessed August 2, 2022).
18. Yadav C, Saini A, Zhang W, You X, Chauhan I, Mohanty P *et al*., Plant-based nanocellulose: a review of routine and recent preparation methods with current progress in its applications as rheology modifier and 3D bioprinting. *Int J Biol Macromol* **166**:1586–1616 (2021). https://doi.org/10.1016/j.ijbiomac.2020.11.038.
19. Phanthong P, Reubroycharoen P, Hao X, Xu G, Abudula A and Guan G, Nanocellulose: extraction and application. *Carbon Resour Convers* **1**:32–43 (2018). https://doi.org/10.1016/j.crcon.2018.05.004.
20. Titton Dias OA, Konar S, Lopes Leão A, Yang W, Tjong J and Sain M, Current state of applications of nanocellulose in flexible energy and electronic devices. *Front Chem* **8**:420 (2020). https://doi.org/10.3389/fchem.2020.00420.
21. Abbati de Assis C, Houtman C, Phillips R, Bilek EM, Rojas OJ, Pal L *et al*., Conversion economics of forest biomaterials: risk and financial analysis of CNC manufacturing. *Biofuels Bioprod Biorefin* **11**:682–700 (2017). https://doi.org/10.1002/bbb.1782.
22. B. Sithole, Roadmap towards innovation-driven forestry manufacturing, Biorefinery Industry Development Facility, Durban, South Africa, 4 October 2017. See at the URL: https://slideplayer.com/slide/13304284/ (accessed August 2, 2022).
23. de Nooy AE, Besemer AC and van Bekkum H, Highly selective nitroxyl radical-mediated oxidation of primary alcohol groups in water-soluble glucans. *Carbohydr Res* **269**:89–98 (1995). https://doi.org/10.1016/0008-6215(94)00343-e.
24. Saito T, Nishiyama Y, Putaux J-L, Vignon M and Isogai A, Homogeneous suspensions of individualized microfibrils from TEMPO-catalyzed oxidation of native cellulose. *Biomacromolecules* **7**:1687–1691 (2006). https://doi.org/10.1021/bm060154s.
25. Nippon Paper Group, Cellulose nanofiber manufacturing technology and application development, 2022. https://www.nipponpapergroup.com/english/research/organize/cnf.html (accessed August 2, 2022).
26. Research Institute for Sustainable Humanosphere, Nano cellulose vehicle project, 2019. http://www.rish.kyoto-u.ac.jp/ncv/ (accessed August 2, 2022).
27. Pagliaro M, Cellulose nanofiber: an advanced biomaterial soon to become ubiquitous. *Chim Oggi* **36**(4):61–62 (2018).
28. Szekely G, Amores de Sousa MC, Gil M, Castelo Ferreira F and Heggie W, Genotoxic impurities in pharmaceutical manufacturing: sources, regulations, and mitigation. *Chem Rev* **115**:8182–8229 (2015). https://doi.org/10.1021/cr300095f.

29. J. Jetten, A. Besemer, Process for the recovery of nitroxy compounds from organic solutions and oxidation process, US20050154206A1 (2005).
30. Strohmeyer HE and Sluggett GW, Determination and control of TEMPO, a potentially genotoxic free radical reagent used in the synthesis of filibuvir. *J Pharm Biomed* **62**:216–219 (2012). https://doi.org/10.1016/j.jpba.2011.12.036.
31. Yu S, Sun J, Shi Y, Wang Q, Wu J and Liu J, Nanocellulose from various biomass wastes: its preparation and potential usages towards the high value-added products. *Environ Sci Ecotechnol* **5**:100077 (2021). https://doi.org/10.1016/j.ese.2020.100077.
32. Raimondo M, Caracciolo F, Cembalo L, Chinnici G, Pecorino B and D'Amico M, Making virtue out of necessity: managing the citrus waste supply chain for bioeconomy applications. *Sustainability* **10**:4821 (2018). https://doi.org/10.3390/su10124821.
33. Mariño M, Da Silva LL, Durán N and Tasic L, Enhanced materials from nature: nanocellulose from citrus waste. *Molecules* **20**:5908–5923 (2015). https://doi.org/10.3390/molecules20045908.
34. De Melo EM, Clark JH and Matharu AS, The Hy-MASS concept: hydrothermal microwave assisted selective scissoring of cellulose for in situ production of (meso)porous nanocellulose fibrils and crystals. *Green Chem* **19**:3408–3417 (2017). https://doi.org/10.1039/c7gc01378g.
35. Naz S, Ahmad N, Akhtar J, Ahmad NM, Ali A and Zia M, Management of citrus waste by switching in the production of nanocellulose. *IET Nanobiotechnol* **10**:395–399 (2016). https://doi.org/10.1049/iet-nbt.2015.0116.
36. Kang X, Kuga S, Wang C, Zhao Y, Wu M and Huang Y, Green preparation of cellulose nanocrystal and its application. *ACS Sustainable Chem. Eng.* **6**:2954–2960 (2018). https://doi.org/10.1021/acssuschemeng.7b02363.
37. Bondancia TJ, Corrêa LJ, Cruz AJ, Mattoso LHC, Marconcini JM, Badino AC *et al.*, Production of cellulose nanofibers by enzymatic hydrolysis in a stirred tank reactor, in *XXI Simpósio Nacional de Bioprocessos e XII Simpósio de Hidrólise Enzimática de Biomassas, 3–6 September 2017*. Aracaju, Brasil.
38. Squinca P, Bilatto S, Badino AC and Farinas CS, Nanocellulose production in future biorefineries: an integrated approach using tailor-made enzymes. *ACS Sustainable Chem. Eng.* **8**:2277–2286 (2020). https://doi.org/10.1021/acssuschemeng.9b06790.
39. Ciriminna R, Scurria A and Pagliaro M, Enhanced polysaccharide nanofibers via oxidation over Silia*Cat* TEMPO. *Chem Commun* **57**:7863–7868 (2021). https://doi.org/10.1039/d1cc02684d.
40. Pinjari DV and Pandit AB, Cavitation milling of natural cellulose to nanofibrils. *Ultrason Sonochem* **17**:845–852 (2010). https://doi.org/10.1016/j.ultsonch.2010.03.005.
41. Panda D and Manickam S, Cavitation technology - the future of greener extraction method: a review on the extraction of natural products and process intensification mechanism and perspectives. *Appl Sci* **9**:766 (2019). https://doi.org/10.3390/app9040766.
42. Paquin M, Loranger É, Hannaux V, Chabot B and Daneault C, The use of Weissler method for scale-up a Kraft pulp oxidation by TEMPO-mediated system from a batch mode to a continuous flow-through sonoreactor. *Ultrason Sonochem* **20**:103–108 (2013). https://doi.org/10.1016/j.ultsonch.2012.08.007.
43. Scurria A, Albanese L, Pagliaro M, Zabini F, Giordano F, Meneguzzo F *et al.*, CytroCell: valued cellulose from citrus processing waste. *Molecules* **26**:596 (2021). https://doi.org/10.3390/molecules26030596.
44. Al Jitan S, Scurria A, Albanese L, Pagliaro M, Meneguzzo F, Zabini F *et al.*, Micronized cellulose from citrus processing waste using water and electricity only. *Int J Biol Macromol* **204**:587–592 (2022). https://doi.org/10.1016/j.ijbiomac.2022.02.042.
45. Robles E, Izaguirre N, Dogaru B-I, Popescu C-M, Barandiaran I and Labidi J, Sonochemical production of nanoscaled crystalline cellulose using organic acids. *Green Chem* **22**:4627–4639 (2020). https://doi.org/10.1039/d0gc01283a.
46. Li Q, McGinnis S, Sydnor C, Wong A and Renneckar S, Nanocellulose life cycle assessment. *ACS Sustainable Chem Eng* **1**:919–928 (2013). https://doi.org/10.1021/sc4000225.
47. Serra A, González I, Oliver-Ortega H, Tarrès Q, Delgado-Aguilar M and Mutjé P, Reducing the amount of catalyst in TEMPO-oxidized cellulose nanofibers: effect on properties and cost. *Polymers* **9**:557 (2017). https://doi.org/10.3390/polym9110557.
48. Delgado-Aguilar M, González I, Tarrés Q, Alcalá M, Pèlach MA and Mutjé P, Approaching a low-cost production of cellulose nanofibers for papermaking applications. *Biores* **10**:5345–5355 (2015). https://doi.org/10.15376/biores.10.3.5345-5355.
49. Latta G, Plantiga AJ and Sloggy MR, The effects of internet use on global demand for paper products. *J For* **114**:433–440 (2016). https://doi.org/10.5849/jof.15-096.
50. R. Blell, Exilva cellulose fibrils to reduce environmental footprint and improve performance, *2nd Annual Cleaning Product Sustainability Conference in Milan*, February 5, 2019.
51. Reid MS, Villalobos M and Cranston ED, Benchmarking cellulose nanocrystals: from the laboratory to industrial production. *Langmuir* **33**:1583–1598 (2017). https://doi.org/10.1021/acs.langmuir.6b03765.
52. Patankar SC and Renneckar S, Greener synthesis of nanofibrillated cellulose using magnetically separable TEMPO nanocatalyst. *Green Chem* **19**:4792–4797 (2017). https://doi.org/10.1039/c7gc02383a.
53. For a recent application of the Silia*Cat* TEMPO and Karimi's catalyst TurboBeads TEMPO to high yield electrocatalytc oxidation of 5-hydroxymethylfurfural to 2,5-diformylfuran, see: Kisszekelyi P, Hardian R, Vovusha H, Chen B, Zeng X, Schwingenschlögl U *et al.*, Selective electrocatalytic oxidation of biomass-derived 5-hydroxymethylfurfural to 2,5-diformylfuran: from mechanistic investigations to catalyst recovery. *ChemSusChem* **13**:3127–3136 (2020). https://doi.org/10.1002/cssc.202000453.
54. Meneguzzo F, Brunetti C, Fidalgo A, Ciriminna R, Delisi R, Albanese L *et al.*, Real-scale integral valorization of waste orange peel via hydrodynamic cavitation. *Processes* **7**:581 (2019). https://doi.org/10.3390/pr7090581.
55. Dr. Cristiane Sanchez Farinas, personal correspondence with M.P., June 2021.
56. Pere J, Tammelin T, Niemi P, Lille M, Virtanen T, Penttilä PA *et al.*, Production of high solid nanocellulose by enzyme-aided fibrillation coupled with mild mechanical treatment. *ACS Sustainable Chem. Eng.* **8**(51):18853–18863 (2020). https://doi.org/10.1021/acssuschemeng.0c05202.
57. Shatkin JA, Wegne TH, Bilek EM and Cowie J, Market projections of cellulose nanomaterial-enabled products-part 1: applications. *Tappi J* **13**:9–16 (2014).
58. K. Nelson, D. Turpin Advancing commercialization of Nanocellulose: critical challenges workshop report, *Advancing Commercialization of Nanocellulose: Critical Challenges Workshop* Washington, DC, May 7–8, 2019, https://doi.org/10.13140/rg.2.2.33789.59363
59. S. Dastager, Highly yield production of bacterial nano-cellulose useful for making medical and personal

care products, match maker/ renewable chemicals & materials, TechEx.in, 16 April 2021. http://www.techex.in/matchmaker/02/wp-content/uploads/2021/04/03-BNC-Final-1.pdf (accessed August 2, 2022).
60. Products using nanocellulose in Japan, Nanocellulose.com, 2021. https://nanocellulose.biz/en/products/ (accessed August 9, 2022).
61. B. McClay cit, in: Meyersohn N (ed), Rising wood prices are making your toilet paper more expensive, CNN Business, May 7, 2021. https://edition.cnn.com/2021/05/07/business/wood-pulp-prices-toilet-paper/index.html (accessed August 9, 2022).
62. Ciriminna R, Chavarría-Hernández N, Rodríguez Hernández A and Pagliaro M, Pectin: a new perspective from the biorefinery standpoint. *Biofuels Bioprod Biorefin* **9**:368–377 (2015). https://doi.org/10.1002/bbb.1551.
63. Tsouko E, Maina S, Ladakis D, Kookos IK and Koutinas A, Integrated biorefinery development for the extraction of value-added components and bacterial cellulose production from orange peel waste streams. *Ren Energy* **160**:944–954 (2020). https://doi.org/10.1016/j.renene.2020.05.108.
64. Jessop PG and Reyes LM, GreenCentre Canada: an experimental model for green chemistry commercialization. *Phys Sci Rev* **3**:20170189 (2018). https://doi.org/10.1515/psr-2017-0189.
65. Ciriminna R, Albanese L, Meneguzzo F and Pagliaro M, Educating the managers of the bioeconomy. *J Clean Prod* **366**:132851 (2022). https://doi.org/10.1016/j.jclepro.2022.132851.

Rosaria Ciriminna

Rosaria Ciriminna is a senior research chemist based at the CNR Institute of Nanostructured Materials, Palermo, Italy. Focusing on the bioeconomy and on green chemistry, her collaborative research developed in partnership with teams from over 20 countries are published in nearly 300 research articles. Widely recognized for her effective mentoring of undergraduate and doctoral students, she has also co-authored numerous highly cited green chemistry and energy educational studies.



Mina Ghahremani

Mina Ghahremani in 2019 completed her doctoral studies at Institute for Advanced Studies in Basic Sciences (IASBS), Zanjan, Iran. Currently she works as a post-doc in Professor Karimi's research group. Her research interests focus on the development of new heterogeneous catalytic systems based on ionic liquids and periodic mesoporous organosilica to synthesize fine chemicals *via* one-pot, zero-waste organic transformations. Co-author of numerous educational studies, she also has a prominent interest in green chemistry education.

Babak Karimi

Babak Karimi is a professor in organic chemistry at the IASBS, Zanjan, Iran. His research includes the design of new types of supported catalysts based on nanoporous inorganic solids and polymers, as well as the development of novel synthetic methodologies, especially in the areas of carbon–carbon bond-forming reactions, asymmetric catalysis and the oxidation of organic compounds. He has published more than 190 scientific papers in prominent international journals and in 2014 was appointed a member of the Iranian Academy of Science. In 2021, the Alexander von Humboldt Foundation awarded him the Georg Forster Research Awards.

Mario Pagliaro

Mario Pagliaro, Research Director at Italy's Research Council, is a chemistry and energy scholar based at the Institute of Nanostructured Materials, Palermo, Italy, where he leads a research group focusing on nanochemistry, sustainability and the bioeconomy. Designated Fellow of the Royal Society of Chemistry in 2014, he was elected an ordinary member of the Academia Europaea in 2021. He has also co-authored numerous books and educational research papers, including some focusing on the practical uptake of open science within the chemistry community.