PARTNERING FOR BLUETOOTH: THE SMART ROAD TO CONNECTIVITY

Wireless communication can be used to improve the effectiveness of smart devices in several ways, such as offering better data sharing, helping users find lost devices or sending reminders to take treatments. Director of Business Development at Nordic Semiconductor, Thomas Soederholm explains how advances in wireless technology, such as new Bluetooth Low Energy chips and design tools, are now being used in wireless medical product development and how incorporating them can be made much easier by partnering with a specialist vendor.

Wireless communication, using the globally licence-free 2.4 GHz Industrial, Scientific and Medical (ISM) radio frequency (RF) spectrum, offers many advantages for monitoring and analysing data captured from medical devices. A medical product equipped with a bidirectional RF link can join the Internet of Things (IoT) via a bridge or hub. IoT connectivity transforms the product into a smart device ensuring, for example, that the user can locate a misplaced device or be reminded when to administer medication. In addition, a smart medical device can share data on drug dosage and timing remotely with physicians.

Bluetooth Low Energy (LE) is a low-power form of Bluetooth wireless – the popular consumer-oriented 2.4 GHz RF technology. It is a leading option for adding wireless connectivity to medical products as it has low power consumption, proven RF interference immunity, strong security, good data throughput and satisfactory range. Moreover, its key advantage over competing technologies is smartphone interoperability; medical products employing Bluetooth LE can wirelessly communicate with virtually all modern mobile devices (and PCs) with little user input beyond initial pairing of the devices. This connectivity allows data from the medical device to be wirelessly transmitted to a smartphone for analysis, then being forwarded to the IoT via an app hosted on the handset.

> "Nordic Semiconductor has introduced a proof-of-concept printed circuit board that simplifies drug delivery device development."

INCORPORATING BLUETOOTH TECHNOLOGY IN DRUG DELIVERY PRODUCTS

Drug delivery products employing Bluetooth LE wireless technology are in development, some having already achieved US FDA approval. For example, Aterica Health Inc. (Waterloo, Canada) has developed Veta Smart Case, a Bluetooth LE-connected carrier for EpiPen auto-injectors, as well as authorised generic auto-injectors made by Mylan (Morgantown, USA). Also, Dexcom (San Diego, USA) has received FDA approval for its G5 Platinum mobile continuous glucose monitoring (CGM) system which includes a Bluetooth LE component to transmit glucose levels from a monitor mounted on the patient's skin to a hand-held receiver.[1]

However, RF engineering is a challenging discipline requiring skilled practitioners who are in short supply, potentially restricting

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Figure 1: Nordic's nRF52810 is a flexible, mature and reliable Bluetooth 5-certified solution optimised for low power and high performance wireless connectivity.

Figure 2: The FDA-approved Dexcom G5 Mobile CGM transmits blood glucose readings to a smartphone using Bluetooth Low Energy wireless technology.

the use of Bluetooth LE wireless technology.

But now, Nordic Semiconductor ("Nordic"), a semiconductor company based in Trondheim, Norway, has introduced a proof-of-concept (PoC) printed circuit board (PCB) that simplifies wireless drug delivery device development. The PoC PCB uses the company's nRF52810 Bluetooth LE solution for hardware and

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S112 SoftDevice (Bluetooth LE RF protocol "stack") for its software. The product is an extremely flexible, mature and reliable Bluetooth 5-certified solution optimised for low power and high performance in a tiny footprint (Figure 1).

Bluetooth LE is based in part on Nordic's proven proprietary ultra-low power wireless technology, and the company's engineers played a key role in writing the specification upon which the standard is based. In 2016, the company's integrated circuit (IC) Systems-on-Chip (SoCs) were used in 45% of registered Bluetooth LE-equipped products.

ENHANCING MEDICAL PRODUCTS WITH WIRELESS CONNECTIVITY

Several studies suggest the efficacy of drug treatment programmes is undermined because patients fail to administer the correct dose of medication, mistime delivery or fail to take the medication at all.[2] A smart medical product could assist the patient in rectifying these problems whilst additionally recording useful data about medication delivery. In addition, wirelessly connecting the product to the IoT establishes a bidirectional link along which not only can data be transmitted but also information returned in the form of guidance for the patient, or software enhancements and security patches for the product.

Wireless connectivity not only helps patients improve their quality of life, but the technology also brings huge economic benefits. For example, through assisting patients with adherence to a medication regime, money is saved through a reduction in the complications that could occur without proper treatment of the primary illness.

Another significant benefit is that data are available from the Cloud to help medical equipment manufacturers understand how, when and where devices and medication are being used – leading to better products.

The FDA-approved Dexcom G5 Mobile CGM, for example, takes a blood glucose measurement every five minutes and transmits the information to the user's smartphone (and up to five additional phones via the cellular network). The device provides hyper- and hypo-glucose alerts, rate of change values and alerts, and calibration. The Bluetooth profile also allows for configurable high and low alerts to be set at levels specified by the user. The information enables the patient to control blood glucose levels by either administering insulin or ingesting carbohydrates to boost glucose levels (Figure 2).

Bluetooth LE Builds on Interoperability

Provided output power is restricted to below specified levels (and local regulatory instructions are complied with), the ISM portion of the RF spectrum centred on 2.45 GHz (the "2.4 GHz band") can be used without the requirement for a licence. Additionally, unlike several other licence-free bands, the 2.4 GHz band is recognised globally, enabling manufacturers to produce a single version of a product for worldwide distribution. Such advantages have encouraged the development of a range of wireless technologies using the 2.4 GHz band, for example, open standard-based Wi-Fi, Bluetooth, Bluetooth LE and Zigbee, plus a slew of proprietary technologies.

Wi-Fi and Bluetooth wireless technology claim the largest market share, their popularity having resulted in both

technologies being incorporated into PCs, smartphones and portable computers across global consumer electronics makers[3], which is not so for competing technologies. Interoperability with such devices is a key advantage because it enables drug delivery product makers to connect their products wirelessly to a wide range of established computing and communication infrastructure.

Wi-Fi was designed for high throughput wireless transmission, such as accessing the Internet or transferring large files. Such high throughput typically demands rechargeable Li-ion batteries that are too large and expensive for most drug delivery products. Bluetooth LE features lower throughput (but nonetheless ample for medical applications) and, crucially, the technology can be powered for long periods (up to several years, depending on the application) from primary batteries as small as 3V/220 mAh CR2032 coin cells.

A second key advantage of Bluetooth LE is the wireless standard's rapid evolution to meet the demands of new use cases. In 2017, for example, a revised version of the Bluetooth LE standard, Bluetooth 5, was introduced. Bluetooth 5 promises up to four times increased range or doubled throughput, together with improved interference immunity, enhanced security and lower power consumption. With the release of Bluetooth 5, a given amount of data can be transmitted twice as fast, halving the time the radio spends in a relatively high power state and thus extending battery life.

CASE STUDY: THE VETA SMART CASE

EpiPen auto-injectors are used to mitigate the effects of anaphylaxis. Because the reaction can occur at any time, users must continuously carry the auto-injector. Also, because the adrenaline injection only provides short-term relief, patients need to visit hospital soon after a reaction to check if further treatment is needed.

Aterica Health Inc, formed in 2012, is addressing both these challenges with the Veta Bluetooth LE-connected EpiPen smart case. The auto-injector is inserted into the smart case, which employs Nordic wireless technology, and is wirelessly paired with the patient's iOS or Android smartphone. The Veta App on the smartphone notifies the user (and their invited support network) should he or she become separated from the smart case by, for example, leaving the auto-injector at home (Figure 3). In addition, the smart case notifies the support network if the auto-injector is removed (indicating that it is being used) so that they can offer quick assistance. Other notifications trigger if the auto-injector is subject to high or low temperatures or if it is approaching expiry.

Figure 3: Aterica's Veta EpiPen smart case employs low-power wireless connectivity to notify the user in the event they become separated from the device.

SIMPLIFYING WIRELESS DESIGN

Single-Chip Solutions

Early Bluetooth LE solutions demanded a "connectivity chip" – in essence, just the Bluetooth LE radio – teamed with a separate microcontroller to supervise operation. While there are some situations where a separate microcontroller is an advantage, so-called "two-chip" solutions complicate design and development, increase power consumption and require more space in the end-product.

Today's Bluetooth LE solutions are typically supplied in the form of the aforementioned System-on-Chip (SoC) – a device that incorporates the radio, microprocessor, memory and power management onto a single chip measuring 6x6 mm or less. The SoC approach was pioneered by Nordic with the launch of its nRF51822 in 2012, the company having since enhanced the concept with its nRF52 Series products. SoCs overcome the drawbacks of two-chip designs and additionally offer a common software development environment for both the Bluetooth LE RF protocol and the product's application software.

For example, Nordic's nRF52810 Bluetooth LE SoC – the baseline device in the nRF52 Series, offering an excellent cost/performance ratio and Bluetooth 5 capability – features:

- A 100 dBm link budget 2.4 GHz multiprotocol radio
- 64 MHz, 32 bit ARM Cortex M4 MCU
- 196 kB Flash
- 24 kB RAM.

Notably, the memory allocation is ample enough to run the application code typical of high volume, low cost applications required for medical applications. Like all Nordic's nRF51 and nRF52 Series SoCs,

the nRF52810 supports Over-the-Air Device Firmware Updates (OTA-DFUs), allowing the software of devices in the field to be upgraded using just the radio link. The nRF52810 SoC is supplied with the latest version of Nordic's S112 SoftDevice – a Bluetooth 5 certified stack.

The nRF52 Series also brings other features crucial to medical product development, notably "out-of-band" (OOB) pairing via Near Field Communication (NFC). This enables Bluetooth LE pairing to be established by simply touching an NFC-equipped smartphone to the medical device with no other interaction required from the user. Second, once the medical device is paired with the smartphone, data is secured by protecting the Bluetooth LE link with 128 bit AES encryption – a widely accepted and proven security protocol.

Bluetooth LE Modules

While Nordic's nRF52810 SoC incorporates all the hardware and software for a Bluetooth LE solution, further development effort is required to construct a working solution. Wireless (RF) products demand the addition of passive components that form matching circuits, antenna and crystal(s) to function correctly. Such additional circuitry can be difficult to design, particularly for those with limited RF expertise. Further, no Bluetooth LE-based product can be commercially offered without certification and testing from the Bluetooth Special Interest Group (the custodians of the Bluetooth standard) as well as meeting regional RF regulations, for example those of the Federal Communications Commission (FCC) in the US. Such testing can be both time consuming and expensive.

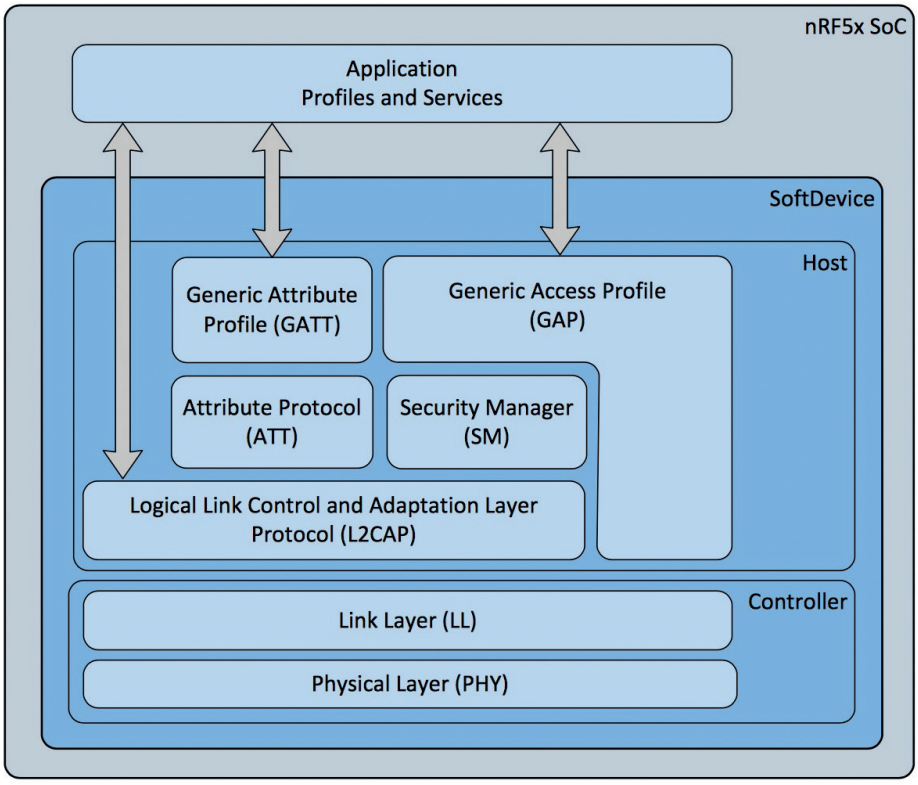

Figure 4: Nordic's software architecture separates the application code from the SoftDevice (the Bluetooth LE stack).

Reference designs from the Bluetooth LE SoC makers like Nordic significantly ease the design process. Adhering to a reference design ensures reasonable performance from a first prototype, which is then much easier to optimise for the specific application and shepherd through the certification process.

The design process can be further eased by adopting a module from the Bluetooth LE vendor or an approved third party. These modules are based on the same Bluetooth LE SoCs as discrete designs but also include pre-optimised external circuitry and antennas. A further key advantage is that the module will (in most cases) already be certified to Bluetooth Special Interest Group and regional RF regulations.[4]

Software Development

In addition to the hardware, some software development will be required for medical products. The factory supplied Bluetooth LE RF protocol looks after the communication link, but some application code is typically required to optimise the software for the target product. If the target application is, for example, an asthma inhaler, some coding will be required to monitor how often and when the device is used.

Among Bluetooth LE vendors, Nordic has a unique advantage during application code development. The company's software architecture separates the SoftDevice (the Bluetooth LE stack) from the application code, thereby removing the complexity of integrating the application software with the RF stack (Figure 4). Without this separation, it can be all too easy for the RF stack to be corrupted during software compilation – extending the development and debugging process. Nordic's SoftDevices are delivered as tested and verified binary files that always remain separated from the developer's application code. The company's development tools look after interfacing the application code to the SoftDevice during compilation.

Nordic also supplies a development kit (DK) and software development kit (SDK), which ease the design process. The DK includes the target nRF51 or nRF52 Series SoC and the SDK makes it simple to interface the SoC to the developer's preferred ARM integrated development environment (IDE). Notably, the SDK also includes simple application code examples which developers can use to accelerate the coding of their own application.

ABOUT THE AUTHOR

Thomas Soederholm is currently Director of Business Development at Nordic Semiconductor ASA in Oslo, Norway. He has a background in digital microelectronics design and has been in the microelectronics business for 18 years. Building on experience as a Regional Sales Manager in Europe, he now holds worldwide responsibility as Business Development Manager for sport, wearable and medical applications. Thomas has helped to establish 2.4 GHz connectivity (proprietary, ANT+ and Bluetooth LE) in the sport and fitness market. Today his focus is centred on applications in the medical and drug delivery space.

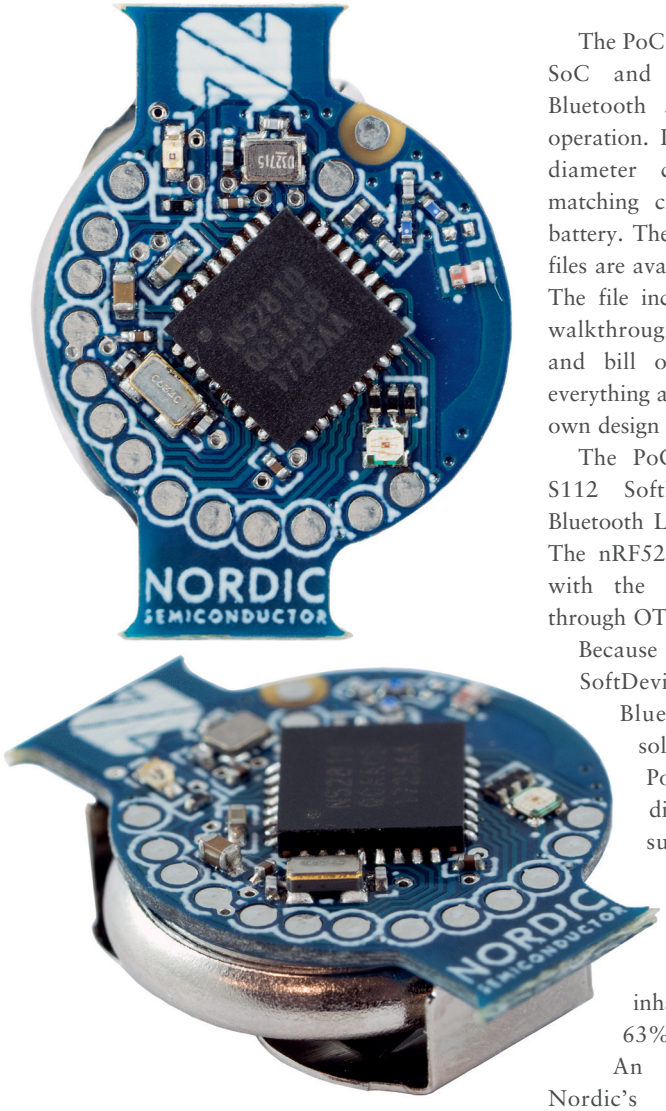

Figure 5: The proof-of-concept printed circuit board accelerates the development of Bluetooth LE-connected medical products.

Proof-of-Concept Development Tool

Nordic has brought together the key advantages of its nRF52 Series SoCs, Bluetooth LE SoftDevices, unique software architecture, reference designs and application code development environment in a PoC PCB designed to ease the process of adding wireless connectivity to medical products (Figure 5).

> "Adding Bluetooth LE wireless connectivity to a medical product promises to improve the effectiveness of drug delivery programmes dramatically..."

The PoC PCB is based on the nRF52810 SoC and S112 SoftDevice, enabling Bluetooth 5 certified peripheral device operation. It is assembled on a 13.5 mm diameter circuit board and includes matching circuits, antenna and coin-cell battery. The PoC and the necessary design files are available from Nordic on demand. The file includes a short description and walkthrough, circuit board schematics and bill of materials (BOM). This is everything a designer needs to develop their own design based on the PoC.

The PoC comes preloaded with the S112 SoftDevice and an Eddystone Bluetooth LE beacon application example. The nRF52810 SoC can be programmed with the developer's own application through OTA-DFU.

Because the nRF52810 with S112 SoftDevice forms a cost-effective Bluetooth 5/Bluetooth LE solution, the Nordic medical PoC PCB is suitable for targeting disposable drug delivery products such as asthma inhalers. According to a recent report from analyst Allied Market Research, the market for smart (wireless) asthma inhalers is set to grow at over 63% $CAGR_{2016\text{-}2022}$.[5]

An inhaler equipped with Nordic's Bluetooth LE technology can enable medication management by providing:

- An automatic medication diary, recording the amount and type of medication and when it was administered
- Notifications to remote family members and healthcare staff
- Usage statistics.

With the permission of the patient, the data could also be automatically sent to the manufacturer via the internet to allow for improvements to the performance of future products.

CONCLUSION

Adding Bluetooth LE wireless connectivity to a medical product promises to improve the effectiveness of drug delivery programmes dramatically by assisting patients with the management of medication while additionally recording useful data about drug usage for family members and healthcare professionals.

Designing wireless products can be daunting and many medical product companies may not have the necessary in-house RF skills to take advantage of the technology. The lack of such knowledge could prevent the company entering a market that not only promises to enhance patient care but is also likely to prove to be a rapidly expanding sector.

However, entry to the wireless medical product market can be considerably eased by partnering with a Bluetooth LE vendor such as Nordic. Such a partnership provides access to proven hardware, protocol firmware, reference designs, development tools and technical expertise which ease the path to prototypes, and then volume production, for companies lacking RF experience.

ABOUT THE COMPANY

Nordic Semiconductor is a fabless semiconductor company specialising in ultra-low and low power wireless communication in the license-free 2.4 GHz and sub 1 GHz Industrial, Scientific and Medical bands, and commercial LTE telecommunications bands targeting the Internet of Things and other wireless applications. Nordic is a Norwegian public company listed on the Oslo stock exchange (OSE: NOD).

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Nordic Semiconductor delivers the most flexible, mature and reliable connectivity solution on the market, while maintaining low power and high performance in a tiny footprint. All running the latest Bluetooth 5 implementation. Easy-to-use development tools and samples are available through a worldwide distribution network.
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